MECHANISM OF WEIGHT LOSS IN THE MORBIDLY OBESE FOLLOWING ILEOGASTROSTOMY AND VALIDATION OF REPORTED ENERGY INTAKE IN NORMAL-WEIGHT AND MORBIDLY OBESE SUBJECTS

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To examine the mechanism of weight loss following ileogastrostomy, 16 morbidly obese subjects (36±2 years, 45.6±1.1 $kg.m^{2-1}$ body mass index (BMI), 48.2±1.0% body fat (BF) (mean±SEM)) were selected and tested prior to and after this procedure. Due to various reasons, complete data were not obtained from any one subject although a total of 16 bypass patients participated in the study. Therefore, the number of subjects in each part of the study varied from six to ten. Body composition was determined using the isotope dilution space (IDS) method and bioelectrical impedance analysis (BIA), which were compared with dual energy x-ray absorptiometry (DEXA) measurements in a subgroup of the participants. Gas exchange analysis was used to measure the changes in basal energy expenditure (BEE) and thermic effect of food (TEF). Total energy expenditure (TEE) was determined during 6-8 weeks after surgery using the doubly labeled water (DLW) method. Weighed food records were used to assess the changes in energy intake during the study period. A group of normal-weight women (48±1 years, 23.4±0.5 $kg.m^{2-1}$ BMI, 32.8±1.3 %BF (mean±SEM)) was selected to supplement the overall research.

Average body weight (111.1±3.2 kg, n=7) of the subjects completing the 3-month measurement decreased by 5.2, 4.2 and 7.8 kg during each of the three months. There was a significant decline ($p<0.0001$) in fat-free mass (FFM) and fat mass (FM) measured by both IDS and BIA methods. The percentage of FFM and FM determined by IDS method was not significantly changed during the study period. Presurgical total body mass

(125.6±4.5 kg) determined by DEXA was significantly different ($p=0.044$) from that (130.3±6.3 kg) obtained by scale, but postsurgical data did not demonstrate this difference. The results raised an important question about the validity of DEXA in the assessment of body composition in the morbidly obese subjects. With the decrease of body weight induced by ileogastrostomy, body mass assessment by DEXA was not different from that obtained from scale. There was a close agreement in fat mass (FM) and percentage of body fat (%BF) obtained by IDS method and DEXA postsurgically, however, BIA showed a significant difference from the TBW method or DEXA ($p<0.05$). Furthermore, the reduction of LBM and FM determined by IDS method and DEXA were found to be smaller than those obtained by BIA.

Ileogastrostomy did not significantly influence BEE levels but significantly affected TEF ($p=0.001$). A very high percentage (44%) of energy expended for physical activity was found at the second month after surgery. Because TEE was not measured presurgery, we were unable to assess the changes in TEE. However, our findings did show that TEE was closely correlated with the weight loss induced by ileogastrostomy ($r=0.719$, $p=0.019$, $n=10$). A almost significant relationship between weight loss and fecal energy ($r=0.808$, $p=0.052$, $n=6$) but not urinary energy loss ($r=0.011$, $p=0.983$, $n=6$) was observed in this study. Surprisingly, energy intake as assessed by weighed food records was not related to weight loss during the short-term energy balance study. Energy intake was insignificantly correlated with energy expenditure ($r=0.628$, $p=0.168$) and fecal energy ($r=0.732$, $p=0.084$).

Results of the validation of reported energy intake showed a large discrepancy between reported energy intake (EI) and expenditure (EE) in both obese (1429±271 kcal.d^{-1} EI vs 2933±239 kcal.d^{-1} EE, respectively) and normal-weight groups (1653±76 kcal.d^{-1} EI vs 2215±102 kcal.d^{-1} EE, respectively). Underestimation, defined as [(EE-EI)/EE×100], was 42.0% in the obese group and 20.5% in the normal-weight group after correcting for the changes in body energy stores. The degree of underestimation was not associated with body weight in the normal-weight group, however, a close relationship ($r=0.868$, $p=0.025$) between underestimation and body weight was observed in obese group.

From these findings it is concluded that ileogastrostomy can significantly reduce body weight, reflected in the decline of LBM and FM. However, the percentage of LBM and FM during 3-month postsurgical measurements was not significantly different from that presurgery. Isotope dilution method and DEXA appeared to be accurate in assessing the reduction in body composition after intestinal bypass surgery although measurement of total LBM and FM compartments by the methods presently used did not agree very well for these morbidly obese subjects. Factorial energy expenditure results showed that BEE was unchanged but TEF declined significantly. Total energy expenditure and fecal energy loss play very important roles in the weight loss following ileogastrostomy but energy intake was not associated with this weight loss.

TABLE OF CONTENTS IV

ABSTRACT I

TABLE OF CONTENTS IV

LIST OF TABLES VIII

LIST OF FIGURES X

LIST OF ABBREVIATIONS XI

ACKNOWLEDGMENTS XIII

SECTION

1. INTRODUCTION 1

2. LITERATURE REVIEW 4
- 2.1. Implications, Prevalence and Definition of Obesity 4
- 2.2. Causes of Obesity 5
- 2.3. Treatment of Obesity 6
- 2.4. Mechanisms of Weight Loss Following Intestinal Bypass Surgery 9
  - 2.4.1. Reduction in Food Intake 9
  - 2.4.2. Malabsorption 13
  - 2.4.3. Changes in Energy Expenditure 15
  - 2.4.4. Changes in Hormonal Response and Nutrient Partitioning 17
- 2.5. Methodological Studies 19
  - 2.5.1. Assessment of Body Composition 19
    - 2.5.1.1. Bioelectrical Impendance Analysis 20
    - 2.5.1.2. Isotope Dilution Space Method 22
    - 2.5.1.3. Dual Energy X-ray Absorptiometry 23
  - 2.5.2. Measurement of Energy Expenditure 25
  - 2.5.3. Food Intake Measurement 30

3. EXPERIMENTAL DESIGN AND METHODS 35

- 3.1. Examination of Mechanism of Weight Loss in Obese Subjects Following Ileogastrostomy 38
  - 3.1.1. Selection and Screening of Subjects 38
  - 3.1.2. Measurement of Energy Intake 40
  - 3.1.3. Measurement of Basal Energy Expenditure and Thermic Effect of Food 40

3.1.4. Body Composition Measurement 41
3.1.5. Measurement of Total Energy Expenditure 42
3.1.6. Measurement of Fecal and Urinary Energy Losses 43

3.2. Validation of Reported Energy Intake Using Doubly Labeled Water Technique in Normal-weight and Obese Subjects 44
3.2.1. Selection and Screening of Subjects 44
3.2.2. Measurement of Energy Intake Using Weighed Food Records 44
3.2.3. Measurement of Total Daily Energy Expenditure Using Doubly Labeled Water Technique 45

3.3. Analytical Procedures 47
3.3.1. Purification of Deuterium and Carbon Dioxide 47
3.3.2. Mass Spectrometric Determination 48

3.4. Data Calculation 49
3.4.1. Calculation of Total Body Water and Energy Expenditure 46
3.4.2. Estimation of Basal Energy Expenditure, Thermic Effect of Food and Substrate Utilization 50
3.4.3. Evaluation of Postsurgical Energy Balance 51
3.5. Statistical Analyses 52

4. RESULTS 54

4.1. Examination of Mechanism of Weight Loss in Obese Subjects Following Ileogastrostomy 54
4.1.1. Changes in Body Composition Following Ileogastrostomy 57
4.1.1.1. Weight Loss 57
4.1.1.2. Influence of Ileogastrostomy on Body Composition Measured by Isotope Dilution Method and Bioelectrical impedance Analysis 57
4.1.1.3. Differences in Body Composition Assessed By Isotope Dilution and Bioelectrical Impedance Analysis 59
4.1.2. Comparison of Isotope Dilution and Bioelectrical Impedance Analysis Methods with Dual Energy X-ray Absorptiometry Measurement 61
4.1.2.1. Dual Energy X-ray Absorptiometry Measurement 61
4.1.2.2. Comparison of Isotope Dilution and Bioelectrical Impedance Analysis Methods with Dual Energy X-ray Absorptiometry in Assessing Body Composition 61
4.1.2.3. Regional Changes in Body Composition Following Ileogastrostomy 65
4.1.2.4. Changes in Body Composition Measured by Isotope Dilution Method, Bioelectrical Impedance Analysis and Dual Energy X-ray Absorptiometry 65

4.1.3. Changes in Energy Expenditure Following Ileogastrostomy 67
4.1.3.1. Basal Energy Expenditure and Fasting Nutrient Utilization 67
4.1.3.2. Changes in Thermic Effect of Food 70
4.1.3.3. Changes in Fat and Carbohydrate Oxidation 73
4.1.3.4. Total Energy Expenditure in Bypassed Obese Subjects 75
4.1.3.5. Components of Total Energy Expenditure in Obese Subjects Following Ileogastrostomy 78
4.1.4. Changes in Energy Intake Following Ileogastrostomy 78
4.1.5. Factors Associated with Weight Loss Following Ileogastrostomy 81
4.2. Validation of Reported Energy Intake Using Doubly Labeled Water Technique 86
4.2.1. Physical Characteristics of Normal-weight and Obese Subjects 86
4.2.2. Total Energy Expenditure in Normal-weight Subjects 86
4.2.3. Accuracy of Reported Energy Intake in Normal-weight Subjects 89
4.2.4. Accuracy of Reported Energy Intake in Obese Subjects 93
4.2.5. Relationship between Underreporting of Energy Intake and Related Variables 96

5. DISCUSSION 99

5.1. Influence of Ileogastrostomy on Body Composition and Methodology in Assessing the Changes in Body Composition 99
5.2. Changes in Energy Expenditure 106
5.3. Changes in Energy Intake 114
5.4. Factors Associated with Weight Loss Following Ileogastrostomy 116
5.5. Validation of Reported Energy Intake Using DLW Method 120

6. SUMMARY AND CONCLUSIONS 129

REFERENCES 131

APPENDICES 145

1. Invitation Letter for Obesity Study 145

2. Sample Consent Form for Obesity Study 146

3. Food Record Instruction 148

4. Sample of Food Record 149

5. Sample of Test Meal 150

6. Sample of DEXA Measurement 151

7. Preparation of Doubly Labeled Water and Sample Instruction Sheet for Total Energy Expenditure Measurement 152

8. Postoperative Complications 153

9. Relationship between BEE and BW, LBM, FM and EI 154

LIST OF TABLES

Table 1. Methods for Dietary Intake Assessment 31

Table 2. Participation in Study Protocol in Obesity Study 55

Table 3. Physical Characteristics of Presurgical Obese Subjects 56

Table 4. Influence of Ileogastrostomy on Body Composition Determined by IDS and BIA Methods 58

Table 5. Changes in FFM and FM Measured by IDS and BIA Methods 60

Table 6. Individual Data of DEXA Measurement Before and After Ileogastrostomy 62

Table 7. Comparison of IDS and BIA methods with DEXA in Assessing Body Composition Before and After Ileogastrostomy 63

Table 8. Changes in Regional Body Composition Measured by DEXA 66

Table 9. Changes in FFM and FM Determined by IDS, BIA and DEXA Methods 68

Table 10. Basal Energy Expenditure and Thermic Effect of Food, Expressed as Absolute Amount and the Percentage of BEE and Ingested Energy 71

Table 11. Preprandial and Postprandial Fat and CHO Oxidation in the Obese Subjects Before and After Ileogastrostomy 76

Table 12. Individual Data of Total Body water, Elimination Rates and Total Energy Expenditure in Obese Subjects 77

Table 13. Changes of Energy Intake Following Ileogastrostomy 80

Table 14. Individual Data for Energy Balance in the Morbidly Obese Subjects Following Ileogastrostomy 82

Table 15. Correlation Coefficients Between Energy Loss and Energy Expenditure Fecal and Urinary Energy and Energy Intake 85

Table 16. Physical Characteristics of Normal-weight and Obese Subjects in the Validation Study 87

Table 17. Individual Data of Total Body water, Elimination Rates and Total Energy Expenditure in Normal-weight Subjects 88

Table 18. Accuracy of Reported Energy Intake in Normal-weight Subjects 90

Table 19. Accuracy of Reported Energy Intake in Obese Subjects 94

Table 20. Summary of Energy Intake, Expenditure and the Representativeness of Reported Energy Intake in Normal-weight and Obese Subjects. 97

Table 21. Multiple Correlation Coefficients Between Underreporting of Energy Intake and Some Physiological Variables in Obese and Normal-weight Subjects 98

Table 22. Reports of Decreased Food Consumption Following Intestinal Bypass Procedures in Humans. 117

Table 23. Studies Comparing TEE in Normal-weight and Obese Subjects Using DLW Method 124

LIST OF FIGURES

Figure 1. Procedures of Ileogastrostomy 8

Figure 2. Diagram of the Proposed Factors Associated with Weight Loss Following Intestinal Bypass Surgery 10

Figure 3. Principle of Doubly Labeled Water Method 28

Figure 4. Outline of Overall Experimental Design 36

Figure 5. Protocol of the Study 37

Figure 6. Measurements of Each Metabolic Test 39

Figure 7. Changes in Basal Energy Expenditure and Respiratory Quotients 69

Figure 8. The Time Course of Thermic Effect of Food in Morbidly Obese Women. 72

Figure 9. Changes in TEF Following Ileogastrostomy 74

Figure 10. The Percentage of Energy Expenditure for BEE, TEF and Physical Activity at the Second Month Following Ileogastrostomy 79

Figure 11. Relationship Between Weight Loss and Energy Expenditure Following Ileogastrostomy 83

Figure 12. Correlation Between Energy Intake and Expenditure in Normal-weight Subjects. 91

Figure 13. Difference Between Reported Energy Intakes and Total Energy Expenditure in Normal-weight and Obese Subjects, expressed as % TEE 95

ACOVA	Analysis of covariance
ANOVA	Analysis of variance
APE	Atom percent excess
BEE	Basal energy expenditure
BF	Body fat
%BFBIA	Percent of body fat determined by BIA
%BFDEXA	Percent of body fat determined by DEXA method
%BFIDS	Percent of body fat determined by IDS method
BIA	Bioeletrical impedance analysis
BMC	Bone mineral content
BMI	Body mass index
BW	Body weight
CCK	Cholecystokinin
CHO	Carbohydrates
D_2O	Deuterium oxide
DEXA	Dual energy x-ray absorptiometry
DLW	Doubly labeled water
DPA	Dual photon absorptiometry
EE	Energy expenditure
EI	Energy intake
FM	Fat mass

FQ	Food quotient
FE	Fecal energy
FFM	Fat-free mass
GIP	Gastric inhibitory polypeptide
Ht	Height
IBW	Ideal body weight
IDS	Isotope dilution space
JIB	Jejunoileal bypass
LBM	Lean body mass
ME	Metabolizable energy
rCO_2	Rate of carbon dioxide production
RQ	Respiratory quotient
SEE	Sleeping energy expenditure
SEM	Standard error of mean
SMOW	Standard mean ocean water
TBW	Total body water
TBMC	Total bone mineral content
TEE	Total energy expenditure
TEF	Thermic effect of food
TFM	Total fat mass
TLM	Total lean mass

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1. INTRODUCTION

Obesity has been clearly associated with adverse health consequences (Canadian Guidelines for Healthy Weights 1988; Reeder et al 1992). Most studies indicate that the relation between weight and total mortality is a J-shaped curve, with those at the highest weights experiencing highest mortality rates (Canadian Guidelines for Healthy Weights 1988; Canadian Health and Welfare 1991; Reeder et al 1992). The increased mortality associated with obesity is also significantly age-related with high mortality when obesity develops in the early ages. The secondary disorders of obesity include heart disease, diabetes, hypertension and certain forms of cancers which are collectively associated with approximately sevenfold increase in mortality in the obese compared with normal-weight individuals (Burton et al 1985; Reeder et al 1992).

Weight reduction and maintenance are the chief goals in the treatment of obesity. However, at present there are few effective approaches to achieve weight loss. Surgical treatment of obesity is one of such means of producing and maintaining weight loss, with intestinal bypass surgery being one of the available techniques for those patients who meet the criteria for obesity surgery. Although numerous studies have been conducted in humans (Cleator et al 1991; Condon et al 1978; Pilkington et al 1976), the exact mechanism of weight loss after intestinal bypass is still unclear. The initial objective of the surgery was to produce weight loss through malabsorption (Kremen et al 1954), but it is now well-established in human patients that intestinal bypass causes a substantial reduction in food intake that is the major cause of weight loss (Bray et al 1976a, 1978,1980;

Pilkington et al 1976). Changes in energy expenditure have also been proposed as a factor in the weight loss (Condon et al 1978; Pilkington 1979) but these measurements have not been carried out in previous studies. Also, there is evidence that intestinal bypass surgery can significantly change levels of gastrointestinal and systemic hormones (Besterman et al 1978). These hormonal changes may be signals that result in alterations in satiety or in metabolic disposition of macronutrients (Koopmans 1990).

There have been no energy balance studies conducted to determine the exact mechanisms in the weight loss following intestinal bypass surgery. Therefore, we sought to better examine the role of energy intake, expenditure and malabsorption in relation to weight loss following ileogastrostomy. The goal of this research was addressed by examination of weight loss, changes in energy expenditure, and factors associated with this weight loss during 90-day follow-up and 14-day balance studies after ileogastrostomy. A supplementary study was added to validate the reported energy intake in normal-weight and obese subjects using the DLW method. Specifically, changes in body composition were measured by IDS, BIA and DEXA, and the methods were compared to validate their applicability for determining the changes in body composition during weight loss; changes in energy intake and expenditure including BEE and TEF were determined before and following ileogastrostomy; a 14-day energy balance study was conducted to evaluate the role of energy intake, total energy expenditure and malabsorption in the weight loss following ileogastrostomy.

Null Hypotheses:

NH_1: Ileogastrostomy does not affect body composition in the morbidly obese.

NH_2: Isotope dilution space method, bioelectrical impedance analysis and dual energy x-ray absorptiometry cannot accurately assess the changes in body composition after ileogastrostomy.

NH_3: Basal energy expenditure and thermic effect of food are not significantly changed following ileogastrostomy.

NH_4: The changes in basal energy expenditure and thermic effect of food are not correlated with the changes in body composition following ileogastrostomy.

NH_5: Ileogastrostomy does not reduce energy intake in the morbidly obese.

NH_6: Energy intake, malabsorption and total energy expenditure are not the primary determinants of weight loss following ileogastrostomy.

NH_7: Reported food records cannot accurately assess energy intake in the morbidly obese after ileogastrostomy.

NH_8: Reported food records do not adequately measure energy intake in normal-weight individuals.

2. LITERATURE REVIEW

2.1. Implications, Prevalence and Definition of Obesity

Obesity, which is a major health problem in North America, is directly or indirectly associated with a wide variety of diseases that collectively account for 15-20% of the mortality rate (Burton et al 1985). Obesity complicates adult-onset diabetes mellitus, hypertension and cardiovascular diseases (Burton et al 1985; Reeder et al 1992). Morbidly obese individuals also develop an array of diseases directly related to excess weight (Burton et al 1985). For these reasons, weight reduction and maintenance are the chief priority in the morbidly obese.The prevalence of obesity from a survey on well-being in Canada is approximately 27% in adults (Canada, Health and Welfare 1991). The prevalence of men with a BMI above 26 and 28 was greater than that of women with a BMI above these values. However, the prevalence of women with a BMI above 30 and 35 was greater than the prevalence of men (Canada, Health and Welfare 1988). Also, the prevalence of obesity increased with age and abdominal obesity was higher in men than that in women (Reeder et al 1992).

Several criteria have been used in defining overweight and/or obesity. The commonly used definitions are percentage overweight and BMI range (Hunt and Groff 1990). In the first category, mild, moderate and severe obesity are classified as 28-40, 40-100 and >100% over the desirable body weight. Using BMI range as the basis for obesity classification,

three grades are defined as 25-29.9, 30-40 and >40, respectively. Morbid obesity is defined as BMI>40 or body weight more than 100 lb over ideal body weight (IBW) (Hunt and Groff 1990). A body fat content >25% in men or >35% in women is also used to define obesity (Weststrate 1993).

2.2. Causes of Obesity

A number of hypotheses have been proposed to explain the development and persistence of obesity. Among these are genetic factors; metabolic defects; dietary indiscretions and physical inactivity (Bray 1991; Burton et al 1985; Mayer 1953). Many investigators believe that obesity is caused by multiple factors in which unequivocal mechanisms for obesity have yet to be determined. Stability of body weight and body composition requires that over time, energy intake equals energy expenditure and also that the intakes of protein, carbohydrate and fat equal the oxidation of each (Flatt 1987,1988). Although it is understood that imbalance between energy intake and expenditure is the primary cause of obesity, mechanisms through which this imbalance occurs remain to be fully defined. The regulation of food intake is a complex interaction between special senses and action of intake. The appearance of the food, its colour, its consistency, and its temperature are perceived by the sensory systems which recognize and translate the stimulus into an electrochemical message to the brain. The hypothalamus is thought to be the main integrator of these signals. Both the brain and gastrointestinal tract release a variety of hormones, of which insulin is a primary hormonal factor to regulate the food intake and

utilization (Bray et al 1980). Hyperinsulinemia are characteristics of obesity which may reflect the high levels of nutrient intake and hypothalamic resistance to insulin action. Insulin resistance is frequently observed in obese patients which may result in a cluster of metabolic aberrations in obesity.

2.3. Treatment of Obesity

A large number of therapeutic approaches have been used in the treatment of obese patients. These include behavioral modification (Foreyt and Goodrick 1991), exercise (Wilmore 1983), diets of various types (Bray 1991; Brownell 1987) and surgery (Halverson and Koehler 1981; MacLean et al 1981; Yale 1989). As a rule, losing and maintaining body weight are extremely difficult. Dietary restriction is successful in a limited number of patients, but rarely helps obese patients maintain long-term weight loss. Other forms of behavioral modification have yielded similarly poor results (Brownell 1987). Pharmacological preparations either do not work or have unacceptable side effects (Foreyt and Goodrick 1991). An approach for treatment of morbid obesity which has shown promise in producing and maintaining weight loss is surgical intervention (Andersen et al 1984; Halverson and Koehler 1981; Kral 1992).

Approximately 30 surgical techniques have been described for treating obesity. Of these, intestinal bypass has been described as one of the most acceptable procedures. Patients both lose weight and maintain reduced weight produced by intestinal bypass during long-term follow-up (Kral 1992). Unfortunately, the original jejunoileal bypass (JIB) procedure

was fraught with complication rates that exceeded 40%. These complications included liver failure, nephrolithiasis, chronic electrolyte abnormalities, and persistent diarrhea (Bray et al 1977). In order to overcome some of these complications, alterations in the procedure have been developed. The procedure of ileogastrostomy (Figure 1) was developed to produce weight loss and reduce complications created by JIB such as hepatitis and arthritis (Cleator et al 1988; Gourlay et al 1989). In this procedure, the standard end-to-end jejunoileal bypass was performed. However, the ileal end of the bypassed segment was drained into the stomach in which hydrochloric acid suppresses bacterial overgrowth in the bypassed segment. Previous studies (Cleator et al 1988,1991) found that the procedure induced significant weight loss which was unaccounted for by reduced energy intake and malabsorption. Therefore, the exact causes of weight loss following ileogastrostomy are still unknown. Further understanding the mechanism of weight loss following this procedure will have potential applications for safer and more effective treatment of obesity.

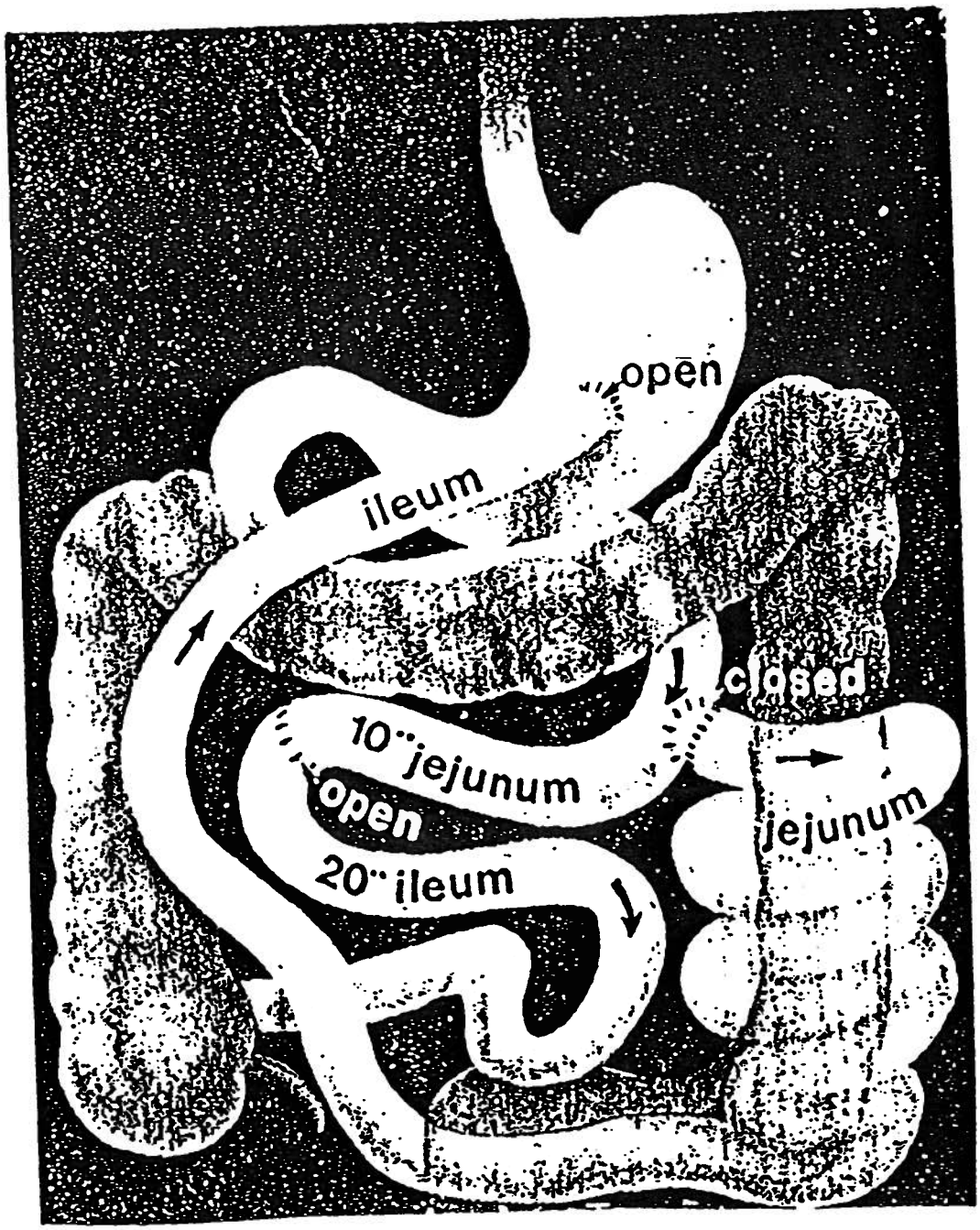

Figure 1. Operative model for ileogastrostomy. In this procedure, the standard end-to-end jejunoileal bypass was performed. However, the ileal end of the bypassed segment was drained into the stomach in order to suppress bacterial overgrowth in the bypassed segment.

2.4. Mechanisms of Weight loss Following Intestinal Bypass Surgery

Intestinal bypass surgery has been found effective in producing weight loss in the morbidly obese since the procedure was introduced more than 20 years ago (Weisman 1973). However, presently there remains controversy regarding what fraction of the weight loss stems from shifts in energy intake and malabsorption as well as from other factors. Figure 2 shows the proposed four factors which may be associated with weight loss following intestinal bypass procedures.

2.4.1. Reduction in Energy Intake

Clinical and experimental studies have shown a significant reduction in food consumption following intestinal bypass surgery (Bray et al 1978,1979; Brewer et al 1974). Bray et al estimated energy intake in 14 female patients over a 4-day period in the hospital before JIB surgery, and 3 weeks and 6 months after surgery. They found a decline from 4766 $kcal.d^{-1}$ preoperatively to 2965 $kcal.d^{-1}$ at 3 weeks, and 3389 $kcal.d^{-1}$ at 6 months postoperatively. The distribution of calories consumed as protein, fat, and carbohydrate was not different before and after surgery. Based on the daily reduction in energy intake and daily weight loss during the study period, they concluded that reduced energy intake accounts for most of the weight loss produced by JIB surgery (Bray et al 1978,1979). Somewhat similar results were reported by Robinson et al (1979), who investigated the role of reduced food intake and fat absorption in weight loss in 31 bypass patients. Energy intake declined from 2425 $kcal.d^{-1}$ preoperatively to 1115 $kcal.d^{-1}$ at 2

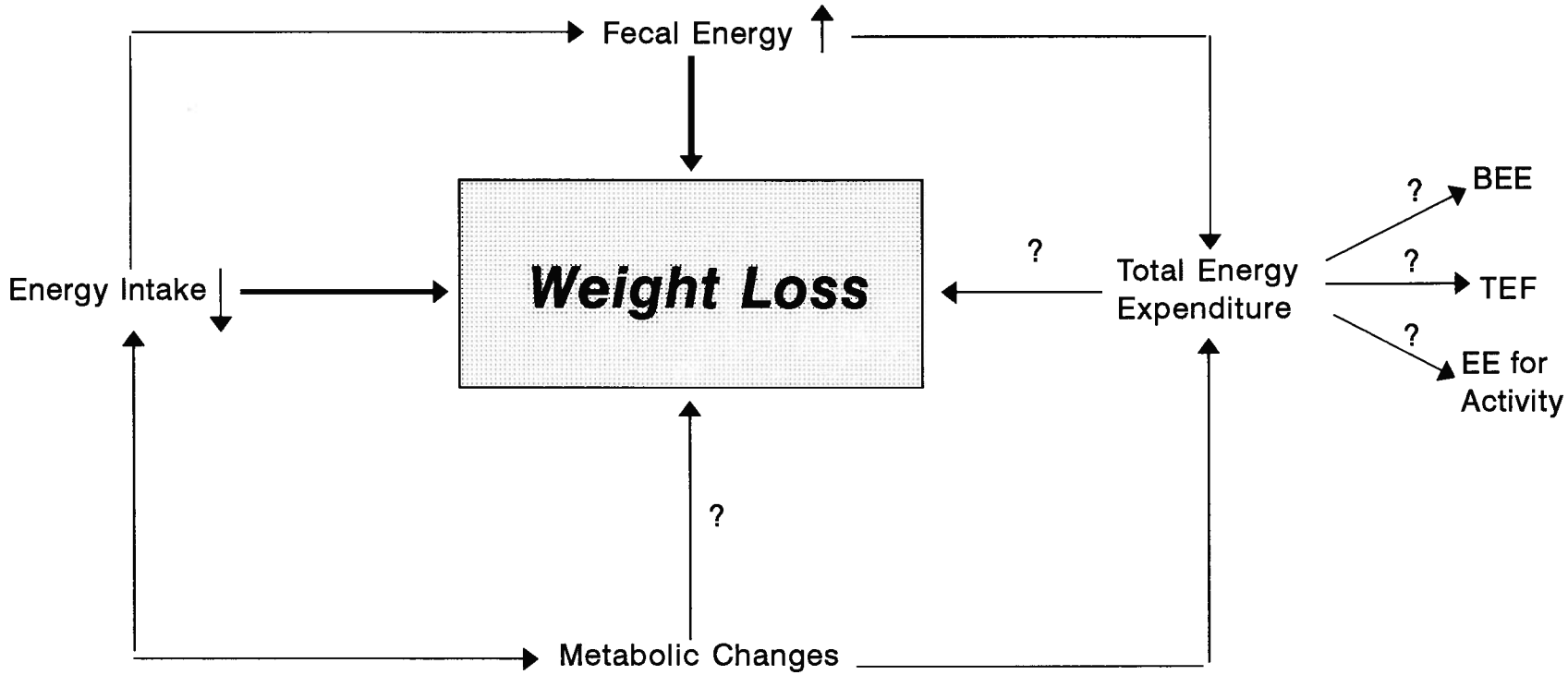

Figure 2. A diagramatic model of weight loss following intestinal bypass surgery. The central component represents weight loss. Fecal energy loss (malabsorption), energy intake, energy expenditure and metabolic changes are presented in the peripheral components. Arrows returning to the central part indicate effects on the weight loss after intestinal bypass procedures. The interrelationship of each factor is also demonstrated in the figure. BEE=basal energy expenditure, TEF=thermic effect of food and EE for activity=energy expended for physical activities.

weeks, and 1904 $kcal.d^{-1}$ at 4 months after surgery. Also, the degree of reduction of energy intake was closely related to postoperative weight loss ($r=0.95$). Fat malabsorption at 4 months was also correlated with weight loss ($r=0.89$). This study accounted for the weight loss primarily on the basis of the reduction in energy intake with malabsorption playing a secondary role.

Condon et al (1979) reported on the pre- and postoperative energy intakes of 65 bypass patients. The mean energy intake decreased significantly from 3261 kcal to 2595 kcal after surgery. In agreement with Bray et al (1978, 1979), energy consumed as carbohydrates, fat and protein decreased evenly compared with that presurgically. However, the authors reported that there was no definite relationship between the changes in energy intake and weight loss in JIB patients. Of these 65 patients, 48 decreased whereas the remaining 17 patients increased their food intake after surgery. The difference in weight loss between the two groups was not significant. They concluded that alterations in energy intake as well as malabsorption are important factors determining the rate of weight loss 1 to 9 months after bypass surgery. The relative importance of these factors in the cause of weight loss in the first operative month or two may be different. Marked decrease in energy intake and striking steatorrhea often occur early, but both problems resolve partially with the passage of time (Condon et al 1979).

With ileogastrostomy, food intake decreases somewhat, and there is some malabsorption, however, these alterations have been found insufficient to account for the energy loss

associated with body weight loss. In a preliminary study of 12 subjects undergoing ileogastrostomy, subjects lost a total of 23 kg body weight mostly as fat over the 90 day period, with about 1300 calories per day unaccounted for using energy balance calculations (Cleator et al 1991). It was suggested that other routes of energy loss may play a role in the weight loss following ileogastrostomy.

In addition to energy intake changes, eating behavior was also reported to be altered after intestinal bypass surgery (Mills and Stunkard 1976; Rodin et al 1976). Bypass patients increase food intake in the morning and decrease it at night (Bray et al 1978; Brewer et al 1974). Pleasantness rating to highly concentrated sugar declined following surgery. In general, bypass surgery has been described as normalizing appetite behavior (Mills and Stunkard 1976).

There is a considerable variability in the degree of decreased energy intake and the relationship between postoperative undereating and weight loss (Benfield et al 1976; Condon et al 1979; Robinson et al 1979). This variability can be attributed, at least in part, to differences in energy intake measurement procedures and sampling periods used in the various studies. Shortcomings in the methodology of dietary intake assessment may therefore have resulted in potentially misleading data. Recently, there has been a growing awareness that measuring food intake may be the most challenging problem faced in these studies, especially in studies of energy balance and obesity. The quality of dietary intake data in both normal-weight and obese subjects has been questioned (Block and Hartman 1989; Schoeller et al 1990).

Energy expenditure, as measured by DLW method, has been used to evaluate the accuracy of reported energy intake (Schoeller et al 1990). Energy is conserved, and therefore metabolizable energy intake must equal expenditure plus the changes in body energy stores. Energy expenditure and changes in body energy stores can be used to measure metabolizable energy intake. Researchers have found that the obese tend to more greatly underestimate their energy intake compared with normal-weight subjects (Acheson et al 1980; Schoeller et al 1990). The magnitude of this underestimation in bypass patients is still unknown. Therefore, the role of reduced food intake in weight loss following intestinal bypass needs to be further investigated.

2.4.2. Malabsorption

The original rationale for intestinal bypass was that a shorter intestine would produce malabsorption and thus facilitate the loss of body weight (Kremen et al 1954; Scott et al 1971). Many authors have concluded that malabsorption accounts for most or all of the weight loss after JIB (Corso and Joseph 1974; Scott et al 1971; Weisman 1973). There is a decrease in the intestinal absorption of fat, nitrogen, carbohydrate, calcium, potassium and vitamins (O'Leary et al 1974; Scott et al 1971). Scott et al (1971) reported pre- and postoperative measurements of fat absorption in 7 patients. Postoperative fecal fat levels were significantly higher in all patients than those preoperatively. Other studies have likewise found steatorrhea after intestinal bypass surgery (Benfield et al 1976; Bray et al

1976b). Preoperative fecal fat averaged 7.8±1.3 $g.d^{-1}$ in the stools. Four to six weeks after operation, fecal loss of fat rose to an average 44.4±6.6 $g.d^{-1}$. With the passage of time, there was a reduction in the quantity of fat appearing in the stools (Benfield et al 1976; Bray et al 1976b).

The increased excretion of fat in the stools probably results from decreased ileal absorption of bile acids (Wise and Stein 1976). The pancreatic exocrine function was also reported to decline after bypass surgery (Dano and Lenz 1974; Sorensen and Krag 1976). These changes reduce the intestinal digestion of triglyceride and thus absorption of fatty acids (Moore et al 1969). In response, the liver increases the production of bile acids from cholesterol, and plasma cholesterol level decreases (Scott et al 1971). Scott et al (1971) found that plasma cholesterol levels fell rapidly within the first one to five months and then tended to stabilize. There was no tendency to rise with time, even though the absorption of fecal fat increased.

Malabsorption of carbohydrates has been documented (Bray et al 1976b). Segmental absorption of glucose in the jejunum was reported to decline after surgery in one study (Barry et al 1977), but in another study was unchanged (Fogel et al 1976). The loss of calories in the stools rose from 131 $kcal.d^{-1}$ preoperatively to a maximum of 593 $kcal.d^{-1}$ postoperatively, and this no doubt increases the rate of weight loss (Crisp et al 1977). Scott et al (1971) also reported that the energy content of the stools rose from 100 $kcal.d^{-1}$ preoperatively to 500 $kcal.d^{-1}$ postoperatively.

2.4.3. Changes in Energy Expenditure

It is well established that energy expenditure falls in response to diminished energy intake (Apfelhaum et al 1971; Welle et al 1984), and it is generally recognized that this energy conserving phenomenon is counter-productive to the effectiveness of low energy diets in treating obesity (Bray et al 1969; Miller and Parsonage 1975). There are, however, conflicting views concerning whether this adaptive reduction in EE results from a loss of FFM or an increased efficiency of energy utilization by cellular metabolic processes.

Very few data are available on energy expenditure after intestinal bypass surgery (Pilkington 1980). The contribution of changes in energy expenditure to weight loss is unknown at the present time. Kopelman et al (1981) have found that a significant rise in serum 3'5'3' triiodothyronine (T_3) and a significant fall in 3'3'5 triiodothyronine (rT_3) concentration between 15 and 20 weeks after bypass surgery. They concluded that this increase in T_3 after bypass may contribute to the substantial weight loss seen at this time. It is not known if there are any associated changes in metabolic rate, therefore, the role of increased energy output remains speculative.

Total daily energy expenditure can be divided into three major components: BEE, TEF, and the energy cost of physical activity. Most studies have shown that BEE or sleeping energy expenditure (SEE) in obese subjects is significantly higher than that of normal-

weight subjects (James et al 1978; Ravussin et al 1982). A decrease of SEE after weight loss was reported by Geissler et al (1987), where SEE was 10 percent lower in post-obese women compared with lean controls. Dale et al (1990) found a comparable decrease in SEE in subjects just after dietary induced weight loss and the decrease in SEE persisted over years.

An impaired TEF has been suggested as a factor contributing to the development of obesity (Jequier 1984). However, studies on postprandial thermogenesis in obesity have shown conflicting results. Some studies demonstrated reduced postprandial thermogenesis in obese compared to lean subjects in response to a mixed meal (Segal et al 1987a; Shetty et al 1981; Swaminathan et al 1985), whereas others could not find a different thermic response to a mixed meal (Cunningham et al 1981; Felig et al 1983). Bessard et al (1983) found a significantly lower postprandial thermogenesis in obese subjects after weight loss when compared to lean subjects in response to a liquid mixed meal. There are no available data for the changes in TEF after intestinal bypass surgery.

Total energy expenditure has also been shown to be elevated in the obese state (Ravussin et al 1982; Welle et al 1992). However, little is known about changes in TEE after weight loss. Controversies exist in changes in TEE after weight loss induced by various strategies. Some investigators (Bradfield and Jourdan 1972; Westerterp et al 1990) reported no changes or increase in TEE, whereas others (Bessard et al 1983; Ravussin et al 1985) found that TEE declined after weight loss.

2.4.4. Changes in Hormonal Response and Nutrient Partitioning

The gastrointestinal tract is an important component of the diffuse endocrine system. There are good reasons to believe that the anatomical changes induced by intestinal bypass surgery alter the patterns of gut hormone release (Besterman et al 1978). Reductions of the upper small intestinal hormones such as gastric inhibitory polypeptide (GIP) were found (Sarson et al 1981). Conversely, the ileal hormones such as neurotensin, enteroglucagon and cholecystokinin (CCK) were elevated following surgery (Buchan et al 1993; Chan et al 1987; Sarson et al 1981). It is possible that other regulatory peptides such as somatostatin, enkephalins and pancreatic polypeptides, as well as unknown intestinal peptides also participate as hormones or neurotransmitters in the regulation of satiety and metabolism, and consequent weight loss. At present, changes in these hormones and their physiological roles are not well understood, thus, any commentary on their effects on weight loss falls into the category of speculation.

Morphological and functional alterations to a sub-group of regulatory peptides have been found after ileogastrostomy (Buchan et al 1993). Quantification of the endocrine cell populations in the jejunum in continuity three months after ileogastrostomy demonstrated a hyperplasia of cholecystokinin-, secretin-, gastric inhibitory polypeptide- motilin- and somatostatin-containing cells . In samples of the ileum taken from within the bypass loop the neurotensin- and somatostatin-containing cells were unaffected while the

enteroglucagon-containing endocrine cells were significantly increased in numbers. The most significant alterations were the decreased circulating insulin and increased CCK levels. The physiological roles of these hormonal changes were not addressed in this study. Whether the dramatic decline of insulin level following surgery influences the metabolism of glucose and other energy-containing nutrients needs to be addressed.

In conclusion, reduced energy intake as the primary determinant inducing weight loss following intestinal bypass procedures needs to be further clarified due to the limitations of dietary intake assessment. The role of energy expenditure in weight loss following surgery needs to be investigated. The difficulties in clarification of the relationship between weight loss and factors associated with this weight loss may lie in the methods available. Fully understanding the principles and limitations of each method is fundamental for researchers to interpret the results.

2.5. Methodological Studies

2.5.1 Assessment Of Body Composition

Assessment of body composition is important in order to describe metabolic consequences of clinical interventions producing changes in body weight. The most commonly used methods for obtaining estimates of body composition are hydrodensitometry, IDS method, anthropometry, and ^{40}K counting. When used individually, each of these methods can only crudely partition body weight into FM and FFM based on various assumptions. Hydrodensitometry and anthropometry are not applicable for these bypassed obese subjects due to difficulty in measurement and inaccuracy of the method. ^{40}Potassium counting is based on the same priciple as the IDS method. Recent advances in body composition methodology can expand body composition analysis from a two-compartment model to four or more body weight fractions and validate old methods. Dual energy x-ray absorptiometry is one of these advances in body composition research and was chosen to compare with BIA and IDS methods on the basis of availability. This section reviews the methods we used in the study.

2.5.1.1. Bioelectrical Impedance Analysis

The BIA method for determining body composition is based on the nature of the conduction of an applied electrical current through the organism under study. Electrical conduction in living organisms is related to water and electrolytes in the biological conductor. Because FFM contains virtually all the water and conducting electrolytes in the human body, conductivity is far greater in FFM than in FM of the body (Lukaski 1987). The electrical volume is inversely related to impedance (Z), resistance (R), and reactance (Xc) where $Z=(R^2+Xc^2)^{0.5}$. Determination of resistance and reactance are made using a four terminal impedance plethysmograph. Estimation of FFM is obtained from an arithmetic calculation using a previously validated predictive equation.

The first investigations to develop mathematical models to predict TBW and its distribution in humans using the impedance approach were performed by Thomasset et al (1962). Since then, investigators have demonstrated significant relationship between TBW, estimated as isotope dilution space, and Z, R, and Xc in 37 men (Lukaski et al 1985) and in a group of 26 children and adolescents (Davies et al 1988). These preliminary findings indicated the potential of the tetrapolar method to assess compositional variables. Cross-validation studies were also undertaken to determine the validity of BIA method to assess TBW and FFM. Kushner and Schoeller (1986) tested the validity of an impedance model for the prediction of TBW derived in a sample of 40 nonobese adults by applying it to 18 obese patients. The model successfully predicted TBW ($r=0.95$) with differences between measured and predicted values of only 0.6 to 1.0

liters. In another study, it was shown that the prediction equation developed in the men was capable of estimating FFM accurately in the women (Lukaski et al 1986). This approach has also been used to demonstrate that impedance estimates of percentage body fat are similar to those determined using appropriate densitometric procedures.

The application of BIA method to assessment of body composition in obese individuals indicates an obesity-dependant bias in predicting FFM determined densitometrically in a large cross-validation study (Segal et al 1988). The controversies still exist in the application of BIA method to assessment of body composition during weight loss. Gray (1988) reported a significant correlation between TBW and Ht^2/R before and after a 2-week fast in 6 obese women who lost 10 kg. However, Deurenberg et al (1989) reported that estimates of FFM were significantly less than those determined by densitometry in a group of 13 obese women whose body weight decreased 10 kg after an 8-week weight reduction program. The apparent lack of consensus about validity of the BIA method to estimate the composition of weight loss indicates the need to conduct controlled studies in which a multicompartmental assessment of body composition is employed.

The BIA method offers a wide variety of potential applications for noninvasive assessment of human body composition, because it is safe, convenient, and easy to use. Experimental findings from cross-validation studies demonstrate that the BIA method is valid and accurate for estimation of FFM, TBW and BMC in healthy individuals. However, the

validation of BIA method in patients with abnormal water and electrolyte distributions needs to be evaluated.

2.5.1.2. Isotope Dilution Space Method

The finding that water occupies a relatively fixed fraction (73.2%) of fat-free mass (FFM) (Pace and Rathburn 1945) has stimulated the determination of total body water (TBW) as an index of human body composition. Some general assumptions of the isotope dilution technique are that the isotope has the same distribution as water, it is exchanged by the body in a manner similar to water, and it is nontoxic in the amounts used (Pinson 1952). Isotopes of hydrogen, deuterium and tritium, have been used to determine body water volumes in healthy and diseased individuals (Culebras and Fitzpatrick 1977; Henry and Phyllis 1985; Schoeller and Jones 1987). The extensive use of the deuterium oxide dilution technique for the estimation of TBW in mammals has demonstrated that the method is valid and accurate (Culebras and Fitzpatrick 1977; Moore 1946). This isotope is rapidly absorbed in the gastrointestinal tract and equilibrates with body water in a few hours (Schoeller 1980, 1992). This method is comfortable for patients because it requires only the ingestion of the isotope and the collection of one or more urine or saliva samples afterwards. It is the most precise method for the determination of pool sizes of body water (Schoeller 1992). This procedure has an analytical precision of 2.5% (Lukaski 1987). The technique is generally advocated as the traditional method for body composition measurement. It seems a particularly appropriate method to compare with BIA because

body fluids and electrolytes are responsible for electrical conductance (Henry and Phyllis 1985; Schoeller 1989).

Despite the high technical precision of the isotope dilution method, errors can be made in calculating FFM and FM because it is not known whether the water content in FFM remains constant in all subjects under all circumstances. Particularly, the assumption of 73.2% of body water in FFM (Siri 1956) may be violated in the bypassed patients who may experience dehydration following surgery. The validity of isotope dilution application to this group of patients has not been studied. Also, the technique provides no information concerning patterns of body fat distribution or changes in regional body composition after weight loss.

2.5.1.3. Dual Energy X-ray Absorptiometry

Dual-energy x-ray absorptiometry is a relatively new method for quantifying the skeletal and soft tissue components of body mass in vivo (Going et al 1993; Mazess et al 1990; Svendsen et al 1993). The fundamental principle of DEXA is based on the differential attenuation by tissues at two energy levels. The composition of soft tissue is given by the ratio of the soft-tissue attenuation (R_{st}) measured at the two energies. The attenuation of pure fat (R_F) and of bone-free lean tissue (R_L) are known from both theoretical calculations and human experiments. Given the subject's R_{st} and the known Rs for fat and lean, the proportion of fat and lean tissue in each pixel can be calculated. The method can

simultaneously measure bone mineral content and soft tissue for total and regional body compostion (FFM and FM).

Preliminary results suggest that this new method can be used to accurately estimate soft tissue composition with better precision (≈1-1.5%) than was possible with dual photon absorptiometry (DPA) (Going et al 1993; Johansson et al 1993). However, the cross-validation of DEXA measurements has not been extensively researched. Comparison between DEXA and hydrodensitometry estimates showed high intercorrelations between DEXA and hydrodensitometry methods (range 0.86-0.92). When DEXA was compared with skinfold anthropometry, bioelectrical impedance and total body potassium methods fot the measurement of total body fat, significant differences in total body fat were observed between DEXA and the other methods (Oldroyd et al 1993). More recently, Ryde et al (1993) compared DEXA with neutron activation method for the measurement of body fat. The results indicate that DEXA and neutron activation methods give comparable measurements of body fat in a female population. On individual basis, however, there are clear differences between the methods. Measurement of abdominal and visceral fat with computed tomography (CT) and DEXA showed that CT- and DEXA-meaused total abdominal fat were similar and highly correlated ($r=0.985$, $p<0.001$) (Jensen et al 1995). The validation of DEXA measurement in obese subjects has not been studied. Because the DEXA method is theoretically independent of compartmental assumptions, the technique may prove useful for following changes in body composition over time.

Future studies are needed to expand the subject pool by investigating obese individuals and patients with disturbed hydration. DEXA is independent of biological assumptions about the consistency of tissue densities and level of hydration. Also, DEXA is inexpensive and safe compared with the imaging techniques such as CT and nuclear magnetic resonance imaging (MRI), because the radiation dose for a whole-body scan by DEXA is <5 mrem. DEXA is rapid and easy requiring only 15-20 min and little cooperation from the subject. Disadvantages of DEXA include the limited dimensions of the scanning table, which can exclude persons too large (>300 lb) or tall. The manufacturers usually recommend an upper limit of body weight for DEXA instruments because body weight as well as tissue thickness may affect the accuracy of DEXA measurements.

2.5.2. Measurement of Energy Expenditure

Measurement of human energy expenditure is important in many areas of clinical and research investigation such as obesity, undernutrition, exercise, and a number of diseases such as trauma, infection and cancer. Both direct and indirect calorimetry have been applied to assess the metabolic rate and short- and long-term energy balance (Jequier 1981; Jequier and Schutz 1985). The relative advantages and disadvantages of both direct and indirect methods have been reviewed by Jequier (1981). A variety of measurement techniques have been applied by investigators in the study of obesity with specific consideration to the role of inadequate energy expenditure in the onset and persistence of

obesity. Conflicting results in this area of research have led to speculation about the importance of methodological differences as a possible source of some of these inconsistencies (Jequier 1981; Jequier and Schutz 1985). Several indirect methods have been used to study human energy expenditure on the basis of gas exchange analysis. It has been suggested that the ventilated hood technique is the most comfortable indirect method because subjects are able to breathe more naturally under the canopy than using a mask or a mouthpiece (Welle 1984). Furthermore, canopy systems require careful adjustment of the rate of the air flow into the canopy (Segal 1987b). However, this technique cannot measure the energy expenditure of physical activity.

The DLW method for measuring energy expenditure provides the capacity to measure total energy expenditure, including that of activity. Development of this method can be traced to a study performed by Lifson et al (1949) in the 1940s. They administered ^{18}O-labeled water to animals and demonstrated that the oxygen in expired CO_2 was derived from body water. This is now known to result from the maintenance of isotopic equilibrium between the oxygen atoms of body water and CO_2 through the carbonic anhydrase reaction. On the basis of this observation, Lifson et al (1955) reasoned that integrated CO_2 production could be measured from the differential elimination of water labeled with both isotopic hydrogen and oxygen. After a loading dose of DLW, the labeled hydrogen would be eliminated as water, whereas the oxygen isotope would be eliminated as both water and CO_2. Thus, it is theoretically possible to measure CO_2 production by measuring the isotopic hydrogen and oxygen remaining in body water after administration

of the DLW. The DLW method was used to monitor the fluxes of water and CO_2 through the body (Schoeller 1982, 1986). The principle of the DLW method is demonstrated in Figure 3.

The DLW method has been extensively validated in animals (Nagy 1980) and humans (Coward et al 1988; Jones et al 1987, 1993a; Schoeller 1987,1988). The method has an accuracy of 1% and a precision of 6% (Schoeller 1987). Moreover, replicate measures in 3 subjects over a 2-year period and in 16 subjects in consecutive weeks have demonstrated a repeatability of 6% (Schoeller and Taylor 1987; DeLany et al 1989). Thus, it appears that the DLW method can accurately measure integrated energy expenditure over periods of at least 2 weeks. Furthermore, the DLW method is noninvasive, nonrestrictive and thus ideal for the measurement of total daily energy expenditure in free-living subjects (Schoeller 1988).

The applications of the DLW method are wide, but most uses to date have taken advantage of the ability of the method to accurately measure energy expenditure in free-living subjects. A number of investigators have applied the method to the study of obesity. These studies have measured the energy expenditure of obese individuals to determine if they are energy-efficient, as some intake studies have suggested. In addition to that, DLW method has been proposed as a method to validate energy intake assessment techniques. More recently, the majority of applications of the DLW method have been

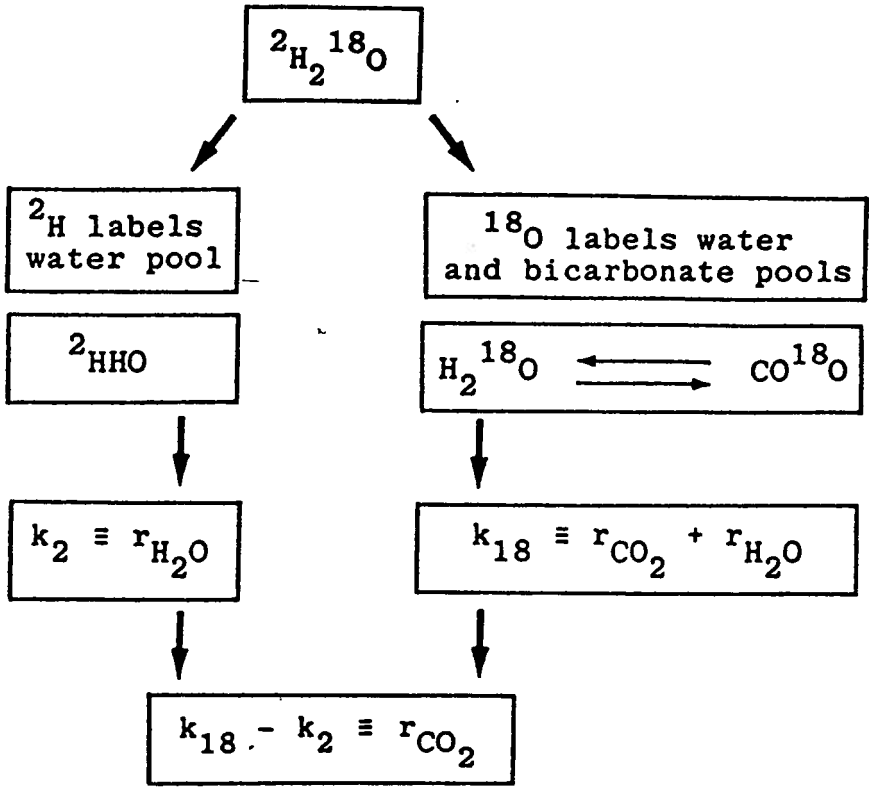

Figure 3. Principle of doubly labeled water method. k=experimentally determined rate constant. r=production rate.

aimed at determining energy requirements of healthy individuals. Current recommendations for energy requirements in adults with different levels of physical activities are based on fractional estimates of total energy expenditure TEE in which the principal components of TEE are either measured or estimated. In most cases, the values for resting energy expenditure (REE) are predicted from age- and gender-specific equations. Application of an activity factor, derived from a crude assessment of the subject's physical activity level, to a measured or estimated level of REE are the basis of current energy requirement in healthy adults (Goran and Poehlman 1992). An activity factor of 1.7 and 1.6 was used for male and female adult subjects, respectively. Because there have been no accurate methods to measure energy expended for physical activities, these factors are questionable. Many studies using the DLW method have been conducted in various age groups which include young adult men (Roberts et al 1991), adolescents (Bandini et al 1990), elderly persons (Goran and Poehlman 1992), lean and obese women (Prentice 1986), underweight adults (Riumallo et al 1989) and patients after surgery (Westerterp et al 1991). Token together, these studies provide evidence consistent with the findings that current recommendations for energy requirements may underestimate the energy needs in the healthy adults. Therefore, the activity factor should be increased to 1.8 or more to cover the actual energy requirements in healthy adults.

Clinical applications of the DLW method are currently in progress. Novick et al (1987) measured the energy expenditure of surgical patients and reported that energy expenditure increased by 18% after surgery. In order to examine the role of energy expenditure in the

weight loss following ileogastrostomy and validate the reported energy intake, the DLW method was used to determine total energy expenditure in the postsurgical obese subjects in the present study.

2.5.3. Food Intake Measurement

Various methods of dietary assessment have been used in studies of the role of diet and diseases, and their strengths and deficiencies have been reviewed by Barrett-Connor (1991). The five main methods of diet assessment used in individuals are summarized in Table 1. At present, there are no dietary intake methods to assess energy intake without errors (Beaton 1994). The nature and magnitude of the error depends on both the dietary data collection methodology and the subjects studied. This section briefly reviews the weighed food record method, because it was the method most commonly used to investigate the role of reduced energy intake following surgical intervention in the past and was chosen for energy intake assessment in the present study.

The weighed food record approach has traditionally been perceived as the "gold standard" for dietary measurement and has been used in attempts to validate other methods such as food frequency questionnaires. It is a method of diet assessment applicable to free-living populations that assures quantitative and qualitative measurement of all nutrients consumed (Barrett-Connor 1991). The weighed food record method has both merits and drawbacks. The main advantage is that the amounts

Table 1. Methods for Dietary Intake Assessment

Method	Expensive	Behavior change	Quantitative	Representative
Diet diary or record (Condon et al 1978)	Yes	Yes	Yes	?
Observation (Lansky and Brownell 1982)	Yes	No	Yes	Yes
Diet history (Burke 1947)	Yes	Yes	Semiquantitative	?
24-h diet recall (Balogh et al 1971)	Yes	No	Yes	No
Food frequency questionnaire (Robinson et al 1979)	No	No	Semiquantative	Yes

consumed can be recorded more accurately than by any other conventional methods (Pekkarinen 1970). The disadvantage of the method may be the problem of a training effect and less representiveness of usual intake. The need to weigh and record intake may lead to a reduced intake or more monotonous diet and induce behavior change. The length of the recording period is also an important methodological concern (Tarasuk and Beaton 1992). It is generally agreed that the recording period should be long enough to give reliable information on the normal food consumption (Pekkarinen 1970). However, too long a survey may result in under-representing of the actual intake, since much work and trouble is involved in the use of the method (Marr 1971). In conclusion, the collection of food records and the associated nutrient analysis comprise an extremely expensive and time-consuming aspect of dietary studies and pose a considerable burden to study volunteers.

The weighed food record method has been utilized over the decades; however, the accuracy of reported intake remains largely unknown. The vast majority of evaluations of the weighed food record instrument have not included tests of accuracy or bias, because such tests are extremely difficult to perform in a home environment. Lissner et al (1989) compared the reported intake of women with the actual intake fed these women during subsequent metabolic studies. The actual intakes were corrected for any change in body energy stores during the metabolic period. The authors found that reported intakes tended to underestimate maintenance energy intake. The degree of underestimation was related to subject's FFM. Because of this study and others (Bingham 1987; Schoeller 1990), there is

controversy about the accuracy of reported dietary intake. The obstacle to resolution of the controversy is the absence of methods to validate the accuracy of reported intake, especially for free-living subjects in which the goal is to determine habitual intake.

The doubly labeled water technique has been proposed as a reference method to validate reported energy intake (Schoeller 1990). The method has an accuracy of 1% and a precision (1 SD) of 6%. Thus, the DLW method is known to be accurate and precise enough to serve as a reference method for the validation of reported dietary intake.

Although some validation studies using the DLW method have found that reported intake agrees well with energy expenditure and hence provides an unbiased estimate of habitual intake, the majority of the studies have detected bias in reported intake. Riumallo et al (1989) observed the highest level of accuracy for reported intake. Reported dietary intake averaged 2689±284 $kcal.d^{-1}$ (mean±SD) versus measured energy expenditure of 2724±303 $kcal.d^{-1}$. Thus, in this study, reported intake was accurate. Another study in which reported intake was found to be accurate was that of DeLany et al (1989). Dietary intake averaged 2960±487 $kcal.d^{-1}$ versus an expenditure of 3230±520 $kcal.d^{-1}$. On the other hand, more and more studies have noted a large bias in reported intake. Bandini et al compared reported intake with expenditure in obese and nonobese adolescents. In the nonobese subjects, reported intake averaged 81±19% of measured expenditure (2190±620 $kcal.d^{-1}$ versus an expenditure of 2760±600 $kcal.d^{-1}$). In the obese, reported intake averaged only 59±24% of expenditure (1940±720 $kcal.d^{-1}$ versus an expenditure of 3390±

610 kcal.d^{-1}). This reported low intake could not be traced to undereating during the reporting period, because both obese and nonobese gained weight during the reporting period (0.1±0.7 and 0.4±1.0 kg, respectively). Therefore, the reported low intake in both groups probably reflects underreporting. In a similar study, Prentice et al (1986) compared reported intake with expenditure measured by the DLW method. Reported dietary intake (1880±350 kcal.d^{-1}) compared quite well with measured energy expenditure (1910±240 kcal.d^{-1}) in the lean group, but poorly (1610±430 kcal.d^{-1} versus 2440±310 kcal.d^{-1}, respectively) in the obese group. Similar to the data reported by Bandini et al (1990), bias was greater among the obese subjects. However, in contrast to the observations by Bandini et al (1990), the lean control group reported quite accurately. A third study also grouped subjects as either normal or overweight (Bronstein and King 1988). Qualitatively, the results are similar to those of Prentice et al (1986); normal and overweight groups reported very similar intakes, whereas energy expenditure was 550 kcal.d^{-1} greater in the obese group than in the lean group.

The findings presented above indicate great variation in the accuracy of reported intake. Perhaps the greatest limitation occurs in the use of dietary record for studies of energy balance, requirements, dietary intervention and obesity. The DLW technique provides a unique opportunity to identify the bias in reported energy intake and possibly improve techniques for assessing dietary intake.

3. EXPERIMENTAL DESIGN AND METHODS

The overall experimental design encompassed two parts (Figure 4). For the first experiment, 16 obese subjects were consecutively selected to participate in the measurements of body composition, food intake and energy metabolism before and after ileogastrostomy. A 14-day energy balance study was conducted during the 90-day experiment (Figure 5). The strength of our design was the use of short-term measurement of weight loss and factors associated with this weight loss.

Experiment 2 was intended to answer the question of validation of energy intake measurement in obese and normal weight subjects. Validation in obese subjects was conducted during 6-8 weeks following ileogastrostomy using the DLW method. Subjects who had completed the entire energy balance study were selected for the validation study. A supplementary study regarding validation of reported energy intake in normal-weight subjects was carried out to assure the limitations of dietary record in estimation of energy intake. The reason for selection of normal-weight group in this study was that very few obese subjects completed the energy balance study in experiment 1. Therefore, the validation of energy intake is limited due to small sample size.

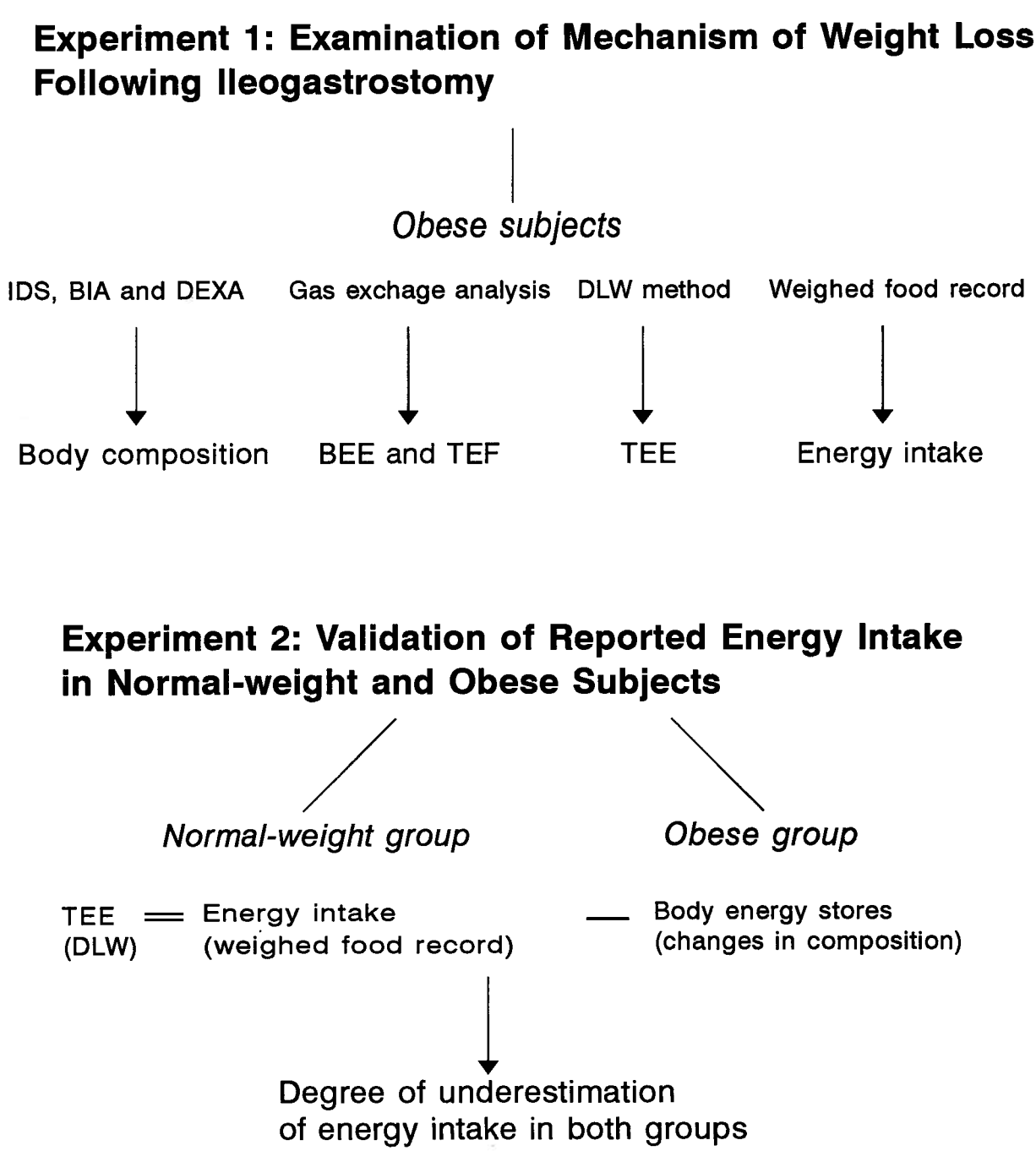

Figure 4. Experimental design: In experiment 1, obese subjects participated in pre- and postsurgical corresponding measurements. Bars indicate subjects included in each experiment. Arrows indicate measurement by corresponding methods. In experiment 2, energy balance equation was used to evaluate the degree of underestimation of energy intake in both normal-weight and obese subjects.

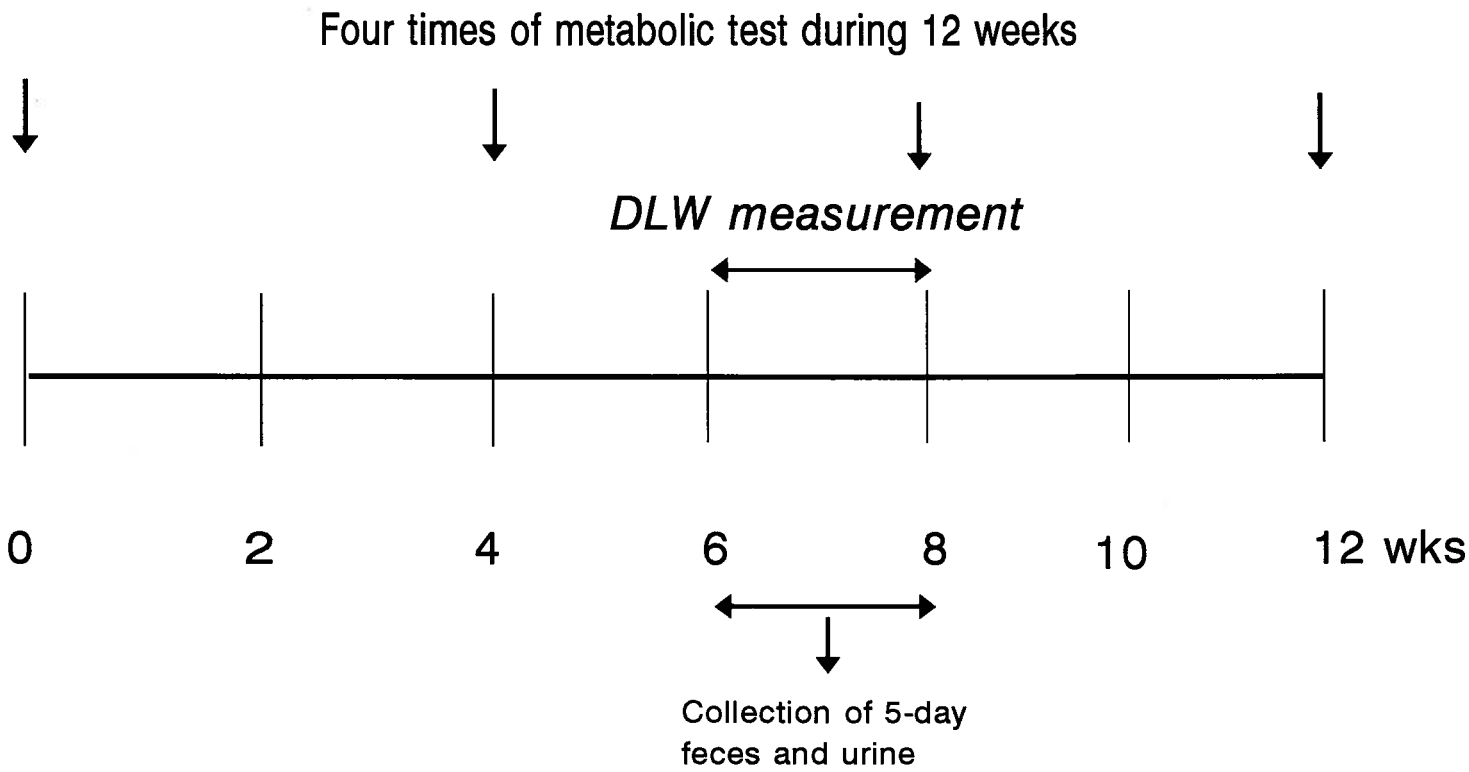

Figure 5. Protocol of overall study plan. Total energy expenditure using DLW method and collection of feces and urine were carried out during the 14-day period. Four metabolic tests were conducted before and at 4, 8 and 12 weeks after surgery.

3.1. Examination of Mechanism of Weight Loss in Obese Subjects Following Ileogastrostomy

3.1.1. Selection and Screening of Subjects

Sixteen obese subjects who were scheduled for the ileogastrostomy were selected for a 90-day study. Subjects who had been obese for over 5 years and failed at other strategies had been selected at the Division of Internal Medicine at St. Paul's Hospital. Subjects who had previously diagnosed with diabetes or coronary heart disease were excluded. Eligible subjects were sent a description of the research project protocol (Appendix 1) and subsequently contacted by telephone to further discuss the study. The consent form (Appendix 2) was signed at the presurgical test. The surgery performed in this study was ileogastrostomy (Figure 1) carried out by Dr. Cleator's group and described elsewhere (Cleator et al 1988). Anthropometric measurements were determined by the same investigator at each of the 4 measurement points. Weight was determined to the nearest 0.01 kg by the same scale with the patient dressed only in light underwear and without shoes. Body mass index was calculated dividing body weight (kg) by height squared (m^2). Figure 6 outlines the protocol of each metabolic test. The protocol used at the other time points was nearly identical. The experimental protocol was approved by the Ethical Committee of UBC and St. Paul's Hospital.

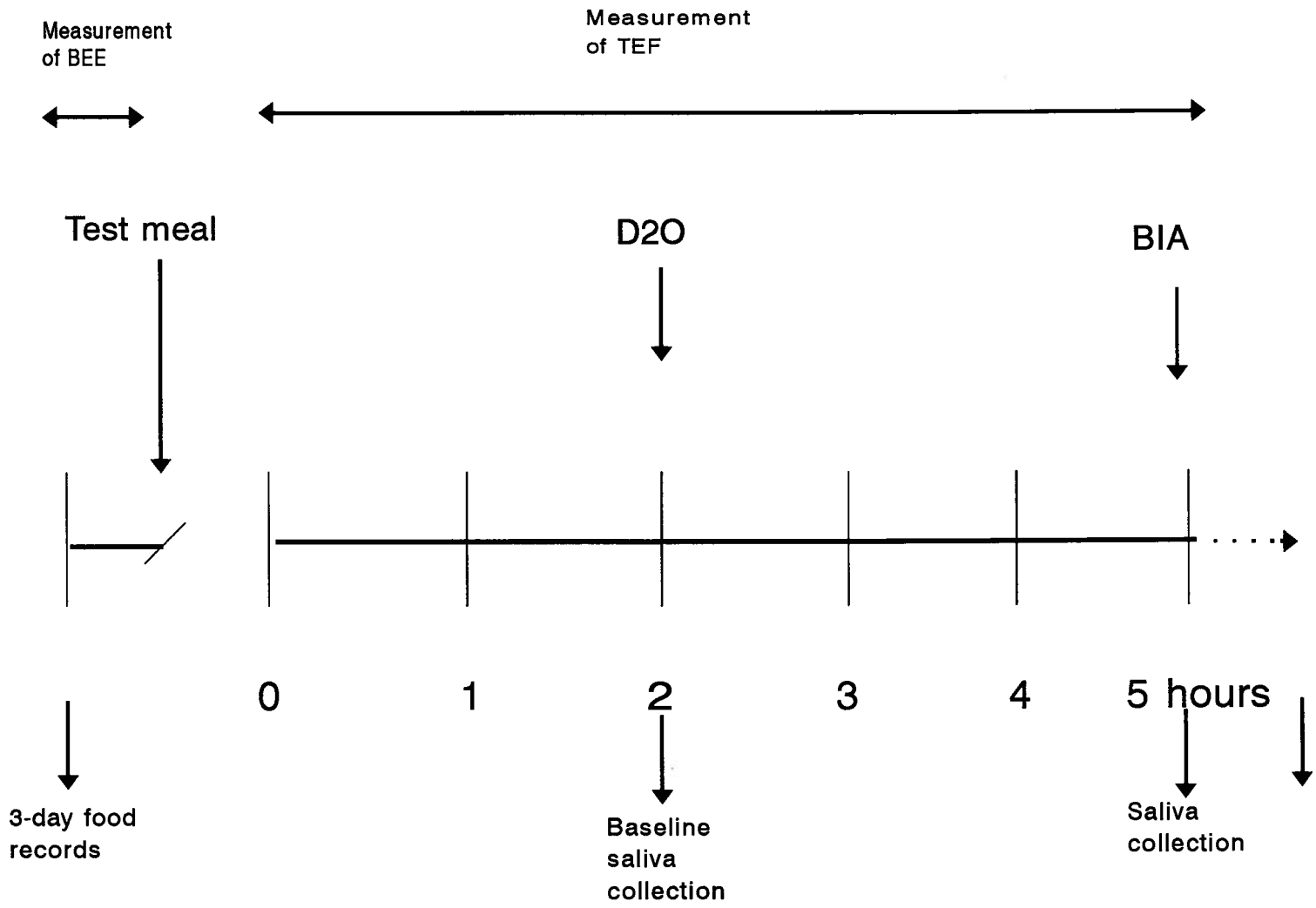

Figure 6. Measurements of each metabolic test. Deuterium oxide (D2O) was administered at 2 hours after meal and BIA measurement was performed at the end of each test. 3-day food record was kept by each subjects 3 days before the test. BEE measurement lasted for 30 minutes and TEF continued for 5 hours.

3.1.2. Measurement of Energy Intake

Energy intake was determined by weighed food record method. Subjects were provided with an instruction sheet (Appendix 3), food record (Appendix 4) and a dietary scale to measure food weight. The dietary food record was kept by each subject over 3 days before each of the metabolic tests. On the presurgical assessment, each subject was trained for measuring food weight using a dietary scale and the instruction sheet was explained. The subjects were requested to specify the brand names for commercial products or type of ingredients used in preparing recipes. All items of food were weighed and recorded separately. Leftover foods were also weighed and recorded. Some uncertainties about the food records were clarified and corrected on the metabolic test days to ensure accuracy. The nutrient composition and energy intake of the records were analyzed using Food Processor II program (ESHA Research, Salem, OR, 1987). Consumption of energy, macronutrients and some micronutrients can be analyzed on the basis of food items and amount of food records.

3.1.3. Basal Energy Expenditure and Thermic Effect of Food

Subjects were tested prior to, and at 1, 2, and 3 months following surgery in the Nutrition Metabolism Unit at St. Paul's Hospital. All gas exchange measurements were performed by use of a ventilated-hood system (Deltatrak; Sensormedics, Anaheim, CA). This metabolic cart system was validated by directly measuring CO_2 production and O_2

consumption model in a previous study (Phang et al 1990). The overall errors for VCO_2 and VO_2 were 1.5% and 1.9%, respectively. The subjects were not hospitalized. After a 30-minute rest, BEE was continuously measured between 7:00 and 7:30 a.m. After the BEE measurement, a test meal (Appendix 5) was served at about 7:35 a.m. and was eaten within 20 minutes. The energy level of the test meal was calculated to cover 30% of daily energy expenditure estimated from IBW, using Mifflin's equation of energy expenditure (Mifflin et al 1990). This meal contained 15% kcal derived from protein, 35% kcal from fat and 55% kcal from carbohydrates (CHO). The TEF was then continuously measured for 300 consecutive minutes while subjects remained at rest.

3.1.4. Body Composition Measurement

On the four tests of BEE and TEF, an oral dose of non-radioactive deuterium oxide (99% APE, 0.06 $g.kg^{-1}$ estimated TBW) was consumed at 2 hours after the test meal. Saliva samples were collected predose and at 3 and 4 hours post dose. The deuterium enrichment was determined using mass spectrometry. Bioelectrical impedance analysis was also performed as a comparative indicator of composition on each occasion. Bioelectrical impedance was measured with the subject supine as described by Vazquez and Janosky (1991) with a body composition analyzer (RJL System, Detroit, MI). FFM was calculated using the equation of Segal et al (1988).

$$\text{FFM (kg)} = 0.00091186\times(\text{height})^2 - 0.01466\times(R) + 0.29990\times(\text{weight}) - 0.07012\times(\text{age}) + 9.37938 \qquad \text{(Eqn. 1)}$$

Dual-energy x-ray absorptiometry was performed in some of subjects presurgically and at 6 weeks postsurgically. DEXA measurements were made with a total-body scanner (model DPX: Lunar Radiation Corp., Madison, WI) that uses a constant potential x-ray source to achieve a congruent beam of stable dual-energy radiation with effective energies of 40 and 70 keV. The scanner was calibrated daily against standard calibration block to control for possible baseline drift. Subjects lay supine on a comfortable table while the scintillation counter moved across the body from head to foot. A series of transverse scans were made in ≈20 minutes at 1 cm intervals. DEXA directly measures three principal chemical components of the body: total fat mass (TFM), total lean mass (TLM) and total bone mineral content (TBMC) (Appendix 6). Fat-free mass by DEXA is the sum of TLM and TBMC. The fat percentage of the body is calculated as TFM divided by the sum of FFM and TFM. DEXA also provides measurements of these three components in different parts of the body (Appendix 6).

3.1.5. Measurement of Total Energy Expenditure

Total energy expenditure in obese subjects was measured between 6 and 8 weeks following ileogastrostomy (Figure 5). On day 0 of the study, subjects reported to the Metabolic Lab in the fasting state. Subjects were weighed and the baseline urine and saliva samples were obtained. A single oral dose of ^{18}O and deuterium labeled water (Appendix 7) (0.25 g $H_2O^{18}.kg^{-1}$ estimated TBW from ideal body weight (IBW), 0.1 g $D_2O.kg^{-1}$ estimated TBW) was followed by about 100 ml tap water. Two urine samples (one in the

morning and the other in the afternoon) were collected on day 1 at the patient's home. On day 7 and 14, approximately at the same time, further urine samples were collected. On the morning of day 15, subjects reported to the Metabolic Clinic at St. Paul's Hospital and a further dose of labeled water (0.06 g D_2O kg^{-1} estimated TBW) was administered to detrmine TBW at the end of the DLW period. All samples were frozen at -50^{0}C in airtight parafilm wrapped plastic containers until use.

3.1.6. Measurement of Fecal and Urinary Energy Losses

Additional routes of dietary and metabolic energy loss were investigated. During the period of TEE measurement, subjects were requested to comprehensively collect fecal materials and urine into containers provided for 5 days. The entire fecal and urine materials for each subject were weighed, homogenized, pooled and freeze-dried. After grinding and mixing of freeze-dried samples, feces and urine samples were subjected to gross energy content determination by bomb calorimetry (Miller and Payne 1959). Measurements were performed in duplicate on approximately 1.0 g of the dried samples using benzoic acid as standard. Metabolizable energy was calculated for individual subjects as the difference between energy consumed and energy loss in feces and urine.

3.2. Validation of Recorded Energy Intake Using Doubly Labeled Water Technique in Normal-weight and Obese Subjects

3.2.1. Selection and Screening of Subjects

Validation of reported energy intake in obese group was conducted during 6-8 weeks following ileogastrostomy. The subjects who had completed the energy balance study were selected for the validation study. Twenty-six normal-weight subjects were recruited from all women who had participated in a low dietary fat trial for the prevention of breast cancer in the Toronto area. All women were sent a letter and information sheets describing the validation study. Participants who reported current use of diuretics or who had a history of an eating disorder were excluded. Eligible subjects were contacted to further discuss the DLW project. The consent form was signed at the beginning of the first clinic visit. The study protocol was approved by the University of Toronto Review Committee on the Use of Human Subjects.

3.2.2. Measurement of Energy Intake Using Weighed Food Records

The collection and analysis of food records in the obese and normal-weight groups were conducted by different researchers using different computer programs in Toronto and Vancouver areas. Each subject in the obese group was requested to complete weighed food records as described above (Appendix 3,4) for 5 days during the 14-day DLW

period. The records were reviewed and analyzed using the Food Processor II (ESHA Research, 1987). Normal-weight subjects were asked to record a 7-day weighed food intake during the DLW period. Subjects were asked to weigh and record all food and beverages consumed in the similar manner as the obese subjects had been instructed (Appendix 3). The nutrient composition and energy intake of the records were reviewed and analyzed using the nutrient data-analysis system (NDS, Nutritional Coordinating Center, Minnesota, 1993).

3.2.3. Measurement of Total Energy Expenditure Using Doubly Labeled Water Technique

The obese group included subjects who were participating in the examination of weight loss and energy metabolism following ileogastrostomy. The validation study in this group was conducted during 6-8 weeks following ileogastrostomy. The procedure of TEE measurement was described above.

Normal-weight subjects were instructed to maintain their normal daily activities and to make no conscious attempt to lose or gain weight during the study period. On day 0 of the study, subjects were weighed and baseline urine (10 ml) and saliva (5 ml) samples were obtained. A single oral dose of 0.17 g H_2O^{18} and 0.07 g D_2O per kg body weight was administered and followed by 100 ml of tap water. Saliva samples were collected at 3 and 4 hours and a urine sample was collected at 4 hours post dose for measurement of TBW.

A urine sample was also collected by the subject at home on the morning of day 1. On the morning of day 14, subjects returned to the Clinic in the fasted state. A urine sample was obtained and a further dose of labeled water (0.06 g D_2O per kg body weight) was administered. Saliva samples were collected at 3 and 4 hours post dose for the determination of final body water volume.

3.3. Analytical Procedures

Urine and saliva samples obtained for body composition and TEE measurements were prepared for isotopic analyses using a vacuum system and analyzed by an isotope ratio mass spectrometer (VG Isomass, 903D, Cheshire, UK).

3.3.1. Purification of Deuterium and Carbon Dioxide

A vacuum line was used for the preparation of hydrogen gas from the aqueous phase of biological fluids and working standards. Preannealed 6-mm-OD Pyrex tubes containing 60 mg of zinc (Indiana University, Bloomington, IN) were attached to a vacuum inlet system and dried of moisture for 10 minutes. A 2-µl microcapillary filled with urine or saliva samples was added to each tube before reattachment to the inlet system. Tubes were immersed in liquid nitrogen for 5 minutes, residual gases evacuated ($<10^{-2}$ Torr) over 2 minutes, and tubes flame-sealed. Reduction of samples was carried out at 540^0C for 30 minutes before mass spectrometric analysis.

^{18}Oxygen was purified as CO_2. Urine was aliquoted (1.5 ml) into vacutainer tubes. Carbon dioxide (1 ml) was added by injection, and then samples were agitated for 1 hour and incubated at 25^0C for at least 48 hours. The CO_2 collection line was evacuated to less than 100 millitorr. The sample tube was immersed in liquid nitrogen for 5 minutes. The

contents were transferred to N_2/methanol bath for 5 minutes. Then, CO_2 was collected in a tube placed in an N_2 bath. The collecting tube was flame-sealed.

3.3.2. Mass Spectrometric Determination

Isotope ratio mass spectrometry permits an accurate isotopic enrichment analysis for a number of low molecular weight compounds. The deuterium and ^{18}O were measured through the determination of $^{2}D/^{1}H$ and $^{46}CO_2/^{44}CO_2$. Sample tubes were manually inleted into the mass spectrometer and analyzed against Vienna standard mean ocean water (SMOW). For deuterium measurements, the mass spectrometer was set up and calibrated daily using SMOW standard and two working standards (GISP and V-Std). Regression analysis of observed enrichment values of standards indicated good linearity of response at both high and low enrichments ($r>0.999$). Appropriate standards, baseline and all samples for a given subject were analyzed in triplicate against an identical set of standards within a 12-hour period. Isotopic data was expressed as δ per mil (δ‰) abundance relative to SMOW. Measurements were repeated in cases where replicate value differences exceeded the maximum acceptable tolerance for low and higher (>500 ‰) enrichment samples of 2 and 5‰, respectively. As with ^{2}D analyses, ^{18}O was analyzed as CO_2 against SMOW and calibrated tank standards (-30‰). Maximum enrichment difference between replicates was 0.5‰. Linearity of response was checked periodically with Vienna ^{18}O standards enriched at 250 and 500‰.

3.4. Data Calculation

3.4.1. Calculation of Total Body Water and Energy Expenditure

Total body water was determined from deuterium dilution space (DS) calculated as follows:

$$DS\ (kg) = (dose \times APE \times 18.015)/(MW \times R \times \Delta\ Enrichment) \qquad \text{(Eqn. 2)}$$

where dose (g) is the amount of label given, APE is the atom percent excess of the dose, 18.015 (g) is the molecular weight of water, MW (g) is the molecular weight of the dose, R is the known ratio of the heavy to light isotopes in a reference standard and Δ enrichment is the observed isotopic enrichment over baseline enrichment. TBW is defined as DS of ^{2}D divided by 1.04 (Schoeller et al 1980). Body water was assumed to comprise 73.2% of FFM, so that FFM equals TBW divided by 0.732, and fat mass equals body weight minus FFM (Culebras and Fitzpatrick 1977; Moore 1946; Pace and Ruthburn 1945).

The calculation of energy expenditure was based on the assumptions of DLW techniques using Schoeller's equation (Schoeller 1982,1986,1988). Mathematically,

$$rCO_2\ (mole{\cdot}d^{-1}) = 0.46 \times TBW\ (1.01K_{18} - 1.04K_2) \qquad \text{(Eqn. 3)}$$

where rCO_2 is the rate of carbon dioxide production (mole·d^{-1}), TBW (mol) is the average of TBW volume determined from deuterium dilution space during 14 days, and K_{18} and K_2 are the calculated elimination rates (pool.d^{-1}) of ^{18}O and deuterium, respectively. Respiratory quotient (RQ) is estimated by food quotient (FQ) derived from 5-day food records (Black et al 1986). Energy expenditure (kcal.d^{-1}) (Jones and Leitch 1993a) was calculated from the CO_2 production rate using the FQ (Black et al 1986).

$$EE\ (kcal.d^{-1}) = 3.9 \times rCO_2 / FQ + 1.1 \times rCO_2 \qquad \text{(Eqn. 4)}$$

3.4.2. Estimation of Basal Energy Expenditure, Thermic Effect of Food and Substrate Utilization

Gas exchange data were corrected as computed values for oxygen and carbon dioxide exchange at standard temperature, pressure and humidity. The respiratory quotient (VCO_2/VO_2) was calculated with subtraction of gas exchange with protein oxidation and results were converted to kilocalories by the Weir formula (Weir 1949). Similarly, carbohydrate and fat oxidation rates were determined each minute. A constant protein oxidation rate of 0.7 g protein kg $FFM^{-1}.d^{-1}$ was assumed, and non-protein energy expenditure and macronutrient utilization rates (per minute) were calculated (Jones and Schoeller 1988a). Energy expenditure and macronutrient oxidation data were expressed as 30-minute averages during the BEE period and as 60-minute averages during TEF

measurement. Postprandial thermogenesis was calculated as (i) the net increase over BEE; (ii) the percentage of increase relative to BEE and (iii) the percentage of increase relative to ingested energy of the test meal. The latter approach (iii) used calculations as follows:

$$\text{TEF (\%)}=[\Sigma(\text{postprandial EE-preprandial EE})/\text{EI}]\times 100 \qquad \text{(Eqn. 5)}$$

where postprandial EE and preprandial EE ($kcal.h^{-1}$) represent the mean energy expended postprandially and preprandially over 1 hour. The sum of the difference during 5 hour measurement divided by ingested energy was the percentage of meal energy production.

3.4.3. Evaluation of Postsurgical Energy Balance

The following equation was used to evaluate the energy balance in each obese subject.

$$\text{EE} = \text{EI}-[\text{Body Stores}+\text{Fecal and Urinary Energy}] \qquad \text{(Eqn. 6)}$$

The data obtained from the DLW measurement was used to estimate energy expenditure. Energy intake was assessed using 5-day weighed food records. Body stores were determined by changes in body composition over a 2-week period divided by the numbers of days. The fecal and urinary energy levels were assessed by bomb calorimetry.

3.5. Statistical Analyses

Results were analyzed using a statistical software package (Systat, Version 4.0, Evanston, IL, 1989). Results were expressed as means±SEM. Differences with $p \leq 0.05$ were considered to be significant.

Repeated measures ANOVA with the subsequent Bonferroni multiple comparison was used to compare energy intake determined by food records, BEE, TEF, and body composition data over the presurgical and 3 postsurgical periods (Ott 1988). Comparison of isotopic technique, BIA and DEXA measurement of body mass were performed using linear regression analysis and pairwise comparisons between corresponding variables from the three different methods.

The evaluation of reported energy intake and adjusted energy intakes using changes in body weight and composition was described by the following equation:

$$(EI/EE)\times 100 \text{ and } (EE\text{-}EI)EE\times 100 \qquad \text{(Eqn. 7)}$$

The mean of reported energy intake from the food records was compared to the mean of energy expenditure measured by DLW method using a paired t-test and correlation coefficient. Relationships between underestimation and body weight as well as other

related variables such as height and age were assessed using simple and multiple linear regression analysis.

4. RESULTS

4.1. Examination of the Mechanism of Weight Loss in Obese Subjects Following Ileogastrostomy

Table 2 showed subjects' overall completion of the study protocol in the obese subjects' study. Of the 16 obese subjects participating in the study, 10 subjects (1M, 9F) completed the presurgical metabolic tests and 7 subjects (7F) finished the tests over the 3 postsurgical time points. The other 3 subjects did not undergo metabolic measurements after the first observation due to discomfort under the hood and time involved. From then on, metabolic tests and 3-month body composition measurement were stopped to ensure the completion of TEE measurement. The DLW method was performed in 10 subjects postsurgically. Of these 10 subjects having completed TEE measurement, six finished the collection of fecal and urine materials. Nine subjects took part in the presurgical total body scan using DEXA and eight completed the postsurgical measurement.

Physical characteristics and body composition in the obese subjects before surgery are shown in Table 3. The average age was 36±2 years with a range of 20 to 49. We accepted patients with a BMI above 35 $kg.m^{2-1}$ and many were much heavier. Their mean body weight and BMI were 121.9±4.1 kg and 45.6±1.1 $kg.m^{2-1}$, respectively. FFM and FM determined by IDS method were 62.9±2.2 kg and 59.0±2.8 kg, and FM represented about 48% of body weight in this group of subjects.

Table 2. Participation in Study Protocol in Obese Study

Subjects	BEE and TEF	IDS for body composition	BIA for body composition	EI	TEE	FE and UE measurement	DEXA
1	yes	yes	yes	yes	yes	yes	
2	yes	yes	yes	yes	yes	yes	
3	yes	yes	yes	yes	yes	yes	
4	yes	yes	yes	yes	yes	yes	
5	yes	yes	yes	yes			
6	yes	yes	yes	yes	yes	yes	
7	yes	yes	yes	yes	yes	yes	
8		yes*	yes*				yes*
9		yes*	yes*				yes*
10		yes*	yes*		yes		yes*
11		yes*	yes*		yes		yes*
12		yes*	yes*		yes		yes*
13		yes*	yes*		yes		yes*
14		yes*	yes*				yes*
15		yes*	yes*				yes*
16		yes*	yes*				yes*

The first seven subjects completed corresponding measurements prior to and at 1, 2 and 3 months following surgery.

*Subjects only participated in the comparison of IDS and BIA methods with DEXA in assessing body composition before and at 6 weeks after surgery.

"Yes" represents participation in the corresponding measurements. Symbols used are BEE, basal energy expenditure; TEF, thermic effect of food; EI, energy intake; EE, energy expenditure; FE, fecal energy; UE, urinary energy; DEXA, dual energy x-ray absorptiometry.

Table 3. Physical Characteristics of Presurgical Obese Subjects

Subjects	Sex	Age (ys)	HT (cm)	BW (kg)	BMI ($kg.m^{2-1}$)	FFM (kg)	FM (kg)	FM/BW (%)
1	F	48	155	115.5	48.1	63.49	52.01	45.03
2	F	28	163	100.5	37.8	51.82	48.68	48.44
3	F	22	157	118.5	48.1	54.10	64.40	54.35
4	F	26	152	101.1	43.8	55.32	45.78	45.28
5	F	36	165	116.5	42.8	61.08	55.42	47.57
6	F	48	157	105.5	42.8	59.44	46.06	43.66
7	F	40	168	120.0	42.5	73.63	46.37	38.64
8	M	49	184	172.0	50.8	87.62	84.38	49.06
9	F	29	169	133.5	46.9	64.22	69.29	51.90
10	F	38	157	108.5	44.2	54.31	54.19	49.95
11	F	34	171	127.0	43.4	61.29	65.71	51.74
12	F	40	166	125.5	45.7	64.55	60.95	48.56
13	F	36	171	120.0	41.0	67.37	52.63	43.86
14	F	40	156	119.0	48.9	56.59	62.41	52.45
15	F	42	161	121.5	47.1	61.43	59.57	49.03
16	F	20	161	146.0	56.3	69.54	76.46	52.37
Mean		36	163	121.9	45.6	62.86	59.02	48.24
SEM		2	2	4.4	1.1	2.22	2.80	1.03

FFM and FM are the data derived from IDS method.

The postoperative complications occurred in this group of subjects are presented in Appendix 8. The most common complications were nausea, diarrhea and infection. Diarrhea was reported in virtually all patients in the early postoperative period, but thereafter usually subsided.

4.1.1. Changes in Body Composition Following Ileogastrostomy

4.1.1.1. Weight Loss

All patients lost weight following surgery. Approximately 15% of preoperative body weight was lost during the 3-month period for the 7 subjects having completed the 3-month measurement ($p<0.0001$). Mean body weight decreased monthly by 5.2, 4.2 and 7.8 kg at 1, 2 and 3 months postsurgically. However, the weight reduction in each month was not statistically significant.

4.1.1.2. Influence of Ileogastrostomy on Body Composition Measured by Isotope Dilution Method and Bioelectrical Impedance Analysis

Both FFM and FM measured by IDS method and BIA showed a significant decline ($p<0.0001$, repeated measures ANOVA) across the 3 months (Table 4). However, multiple comparison did not show a significant difference in FFM among each month. When FFM and FM were expressed as the percentage of body weight during the 3

Table 4. Influence of Ileogastrostomy on Body Composition Determined by Isotope Dilution Method and Bioelectrical Impedance Analysis

	Presurgery	1 mo.	2 mo.	3 mo.
Body weight (kg)	111.1±3.2[a]	105.9±3.0[a]	101.7±2.4[ab]	93.9±3.1[b]
FFM-IDS (kg)	59.8±2.8	57.1±2.7	55.6±2.8	52.9±3.4
FFM-BIA (kg)	55.4±1.7[a]	51.9±1.4[ab]	50.3±1.3[ab]	48.2±1.6[b]
FM-IDS (kg)	51.2±2.6[a]	48.8±2.2[ab]	46.1±2.3[ab]	41.0±2.4[b]
FM-BIA (kg)	55.2±1.5[a]	53.5±1.7[ab]	50.7±1.3[bc]	45.9±1.5[c]
FFM-IDS/BW (%)	53.9±1.8	53.9±1.8	54.6±2.1	56.2±2.5
FFM-BIA/BW (%)	50.5±0.4	49.3±0.5	49.8±0.6	51.2±0.5
FM-IDS/BW (%)	46.1±1.8	46.1±1.8	45.4±2.1	43.8±2.5
FM-BIA/BW (%)	50.0±0.4	50.7±0.5	50.2±0.6	48.8±0.5

Values are mean±SEM (n=7). Post hoc comparison was made between columns and means in each column not sharing a common superscript letter are significantly different ($p<0.05$).

Presurgery is the presurgical measurement and 1 mo., 2 mo. and 3 mo. are the measurements at 1, 2 and 3 months following surgery, respectively.

months, these percentages of both FFM and FM measured by IDS method reached borderline statistical significance ($p=0.08$).

4.1.1.3. Differences in Body Composition Assessment by Isotope Dilution Method and Bioelectrical Impedance Analysis

There was a significant difference ($p<0.05$) in the detection of FFM and FM using IDS method versus BIA (Table 5). The FFM was lower and FM higher measured by BIA than those by IDS method throughout the study period. The differences in FM were 3.98±1.76 kg presurgically and 4.69±1.71 kg, 4.60±1.95 kg and 4.88±2.32 kg at 1, 2 and 3 months postsurgically, respectively. The differences in FFM were 4.48±1.86 kg presurgically and 5.24±1.79 kg, 5.25±2.07 kg and 4.67±2.32 kg at 1, 2 and 3 months postsurgically, respectively. Changes in FFM and FM following surgery and the percentage of these reduced FFM and FM are also listed in Table 5. The monthly reduction of FFM and FM were not significantly different between the two methods (Table 5), while the methods differed significantly in assessing the absolute amount of FFM and FM. From IDS method an average of 48.1, 64.6 and 71.0 % of weight loss was found to be body fat at 1, 2 and 3 months postsurgically. A slightly lower but insignificant loss of body fat (32.7%) by BIA method was found at the first month compared with that obtained by the IDS method. The percentages of fat loss at the second and third months were quite similar to the percentage of fat loss determined by the IDS method.

Table 5. Changes in Fat-free Mass and Fat Mass Measured by Isotope Dilution and Bioelectrical Impedance Analysis Methods

	IDS			BIA		
Time after surgery	1 mo.	2 mo.	3 mo.	1 mo.	2 mo.	3 mo.
FFM (kg)	57.1±2.7	55.6±2.8	52.9±3.4	51.9±1.4*	50.3±1.3*	48.2±1.6
FM (kg)	48.8±2.2	46.1±2.3	41.0±2.4	53.5±1.7*	50.7±1.3	45.9±1.5
Body fat (%)	46.1±1.8	45.4±2.1	43.8±2.5	50.7±0.5*	50.2±0.6*	48.8±0.5
ΔFFM (kg)	2.7±0.6	1.5±0.5	2.7±1.0	3.5±0.7	1.5±0.3	2.1±0.5
ΔFM (kg)	2.5±0.6	2.7±0.7	5.1±0.9	1.8±0.5	2.8±0.0.6	4.8±0.8
ΔFFM/ΔBW (%)	51.9±10.2	35.4±8.9	29.0±10.5	67.3±10.5	35.0±8.3	29.1±1.64
ΔFM/ΔBW (%)	48.1±10.2	64.6±8.9	71.0±10.5	32.7±10.5	65.0±8.3	70.9±1.6

Values are mean±SEM (n=7), compared between the two methods at corresponding months and statistical significance was symbolized by stars with *$p<0.05$

1 mo., 2 mo. and 3 mo. are the measurements at 1, 2 and 3 months following surgery, respectively. ΔBW, ΔFFM, ΔFM represent the changes in body weight, fat-free mass, fat mass estimated by the difference of corresponding values with the previous measurement.

4.1.2. Comparison of Isotope Dilution and Bioelectrical Impedance Analysis Methods with Dual Energy X-ray Absorptiometry Measurement

4.1.2.1. Dual Energy X-ray Absorptiometry Measurement

The individual data for the nine subjects who took part in the DEXA measurement are presented in Table 6. All subjects completed the pre- and postsurgical measurements except subject 10, due to lack of interest in the study. On average the percentages of body fat before and after surgery were 51.2 and 50.8%, respectively. Both FFM (LM+BMC) and FM declined significantly with and without the male subject ($p<0.01$) following surgery (Table 6).

4.1.2.2. Comparison of Isotope Dilution Method and Bioelectrical Impedance Analysis with Dual Energy X-ray Absorptiometry in Assessing Body Composition

Measurements of FFM and FM by the three techniques are shown in Table 7. Body weight measured by DEXA with and without the male subject correlated highly significantly with that measured by scale ($r=0.989$ and 0.991 with and without the male subjects presurgically; $r=0.984$ and 0.967 with and without the male subject postsurgically, $p<0.0001$). Significant differences in body weight estimates existed before surgery ($p=0.044$ and 0.009 with and without the male subject, respectively). Inter-method comparisons showed that FFM measured by the three methods was significantly

Table 6. Individual Data of Dual Energy X-ray Absorptiometry Measurement Before and After Ileogastrostomy

	Presurgery			6 wks		
Subjects	BMC (kg)	LM (kg)	FM (kg)	BMC (kg)	LM (kg)	FM (kg)
8	3.534	68.406	79.167	3.266	65.300	72.758
9	3.396	57.742	67.969	3.337	49.296	64.525
10	2.853	47.652	56.462			
11	3.356	53.788	65.176	3.344	46.237	58.226
12	3.352	56.024	62.897	3.465	51.999	60.768
13	3.424	63.272	52.235	3.376	55.489	45.342
14	3.313	52.263	61.717	3.246	52.798	55.392
15	3.160	58.112	60.023	3.034	54.307	53.162
16	3.161	63.989	72.349	3.060	59.416	68.280
Females & Male						
Mean	3.283	57.916	64.405	3.266	54.355**	59.807**
SEM	0.067	2.153	2.852	0.053	2.097	3.100
Females						
Mean	3.252	56.605	62.354	3.266	52.792**	57.956**
SEM	0.067	1.936	2.247	0.062	1.613	2.872

Presurgery and 6 wks represent measurement time before and at 6 weeks after surgery. Pre- and postsurgical corresponding measurements were compared with **$p<0.01$.

Symbols are BMC, bone mineral content; LM, lean mass; FM, fat mass. FFM=LM+BMC.

Table 7. Comparison of Isotope Dilution Method and Bioelectrical Impedance Analysis With Dual Energy X-ray Absorptiometry in Assessing Body Composition Before and After Ileogastrostomy

	IDS	BIA	DEXA
Presurgery			
Females & Male			
BW (kg)	130.3±6.3^{a}	130.3±6.3^{a}	125.6±4.5^{b}
FFM (kg)	65.2±3.2^{a}	63.5±3.0^{b}	61.2±2.2^{c}
FM (kg)	65.1±3.4^{ab}	66.8±3.5^{a}	64.4±2.9^{b}
FFM/BW (%)	50.1±0.9^{a}	48.8±0.6^{b}	48.8±1.0^{b}
FM/BW (%)	49.9±0.9^{b}	51.2±0.6^{a}	51.2±1.0^{a}
Females			
BW (kg)	125.1±3.9^{a}	125.1±3.9^{a}	122.2±3.3^{b}
FFM (kg)	62.4±1.8^{a}	61.0±1.9^{b}	59.9±2.0^{bc}
FM (kg)	62.7±2.8^{b}	64.1±2.4^{a}	62.3±2.2^{bc}
FFM/BW (%)	50.0±1.0^{a}	48.8±0.7^{c}	49.0±1.1^{b}
FM/BW (%)	50.0±1.0^{b}	51.2±0.7^{a}	51.0±1.1^{ab}
Postsurgery			
Females & Male			
BW (kg)	**117.2±5.3^{a}	**117.2±5.3^{a}	**117.4±4.4^{a}
FFM (kg)	*59.5±2.4^{a}	**55.7±2.1^{c}	**57.6±2.1^{b}
FM (kg)	**57.7±3.7^{b}	**61.5±3.4^{a}	**59.8±3.1^{b}
FFM/BW (%)	51.0±1.4^{a}	47.6±0.7^{b}	49.2±1.3^{ab}
FM/BW (%)	49.0±1.4^{b}	52.4±0.7^{a}	50.8±1.3^{b}
Females			
BW (kg)	**113.0±3.9^{a}	**113.0±3.9^{a}	**114.0±3.3^{a}
FFM (kg)	*57.9±2.1^{a}	**54.1±1.6^{b}	**56.0±1.6^{ab}
FM (kg)	**55.1±3.1^{b}	**58.9±2.5^{a}	**58.0±2.9^{ab}
FFM/BW (%)	51.3±1.6^{a}	47.9±0.7^{bc}	49.1±1.5^{b}
FM/BW (%)	48.7±1.6^{b}	52.1±0.7^{a}	50.9±1.5^{ab}

Values are mean±SEM (n=9 with and n=8 without the male subject before surgery and n=8 with and n=7 without the male subject after surgery). Comparison was made between the methods and symbolized by different superscript letters. Comparison between presurgical and postsurgical measurements was symbolized by stars at the upper left side with *p<0.05, **p<0.01.

BW, FFM and FM are the body weight, fat-free mass and fat mass presurgically and at 6 weeks postsurgically. Body weight for DEXA are the sum of LM, FM and BMC.

different ($p<0.05$) before and after surgery, when the male subject was included. The significant differences in FFM estimates before surgery were observed between the IDS and the other methods, when the male subject was excluded (Table 7). Estimates in FFM between the IDS and BIA methods still persisted after surgery, while the estimates in FFM by DEXA did not showed significant differences from those by the IDS and BIA methods postsurgically.

Presurgical %BF determined by IDS method was significantly lower than that obtained by DEXA ($p=0.033$) and by BIA ($p=0.007$). However, the postsurgical %BF measured by IDS method was similar to that obtained by DEXA, but significantly different from that by BIA method ($p=0.029$). The estimates in %BF described above were the results when the male subject was included. The significant differences in %BF estimates persisted between the IDS and BIA methods before and after surgery ($p=0.017$ and 0.016, respectively), when the male subject was excluded. The pre- and postsurgical estimates in %BF by DEXA were not significantly different from those by the BIA and IDS methods. All methods for determination of FFM and FM including the male subject correlated significantly with each other before and after surgery ($p<0.001$ for FM and $p<0.01$ for FFM. There were stronger correlations between body fat determined by the three methods before surgery than that after surgery (DEXA vs IDS: presurgical $r=0.858$, $p=0.003$, postsurgical $r=0.769$, $p=0.043$; DEXA vs BIA, presurgical $r=0.889$, $p=0.001$, postsurgical $r=0.822$, $p=0.023$; BIA vs IDS, presurgical $r=0.963$, $p<0.0001$, postsurgical $r=0.861$, $p=0.006$). The similar correlations in body fat estimates by the three methods were

observed, when the male subject was excluded (DEXA vs IDS: presurgical r=0.981, p<0.0001, postsurgical r=0.891, p=0.017; DEXA vs BIA, presurgical r=0.965, p<0.0001, postsurgical r=0.948, p=0.004; BIA vs IDS, presurgical r=0.996, p<0.0001, postsurgical r=0.939, p=0.002).

4.1.2.3. Regional Changes in Body Composition Following Ileogastrostomy

The distribution of BMC, LM and FM prior to and after ileogastrostomy is shown in Table 8. There were no significant differences in BMC in other parts of the body before and after surgery except in the trunk, where BMC declined significantly (p=0.015) after surgery. LM dropped significantly in the head (p=0.022), the trunk (p=0.004) and the legs (0.001). There was a significant decline in FM in the head (p=0.032), the trunk (p<0.0001) and the legs (0.016) but not in other parts of the body. The similar results were observed when the male subject was excluded (Table 8).

4.1.2.4. Changes in Body Composition Measured by Isotope Dilution Method, Bioelectrical Impedance Analysis and Dual Energy X-ray Absorptiometry

The changes in body composition and the percentage of the reduced FFM and FM following surgery were compared among the three methods. The changes in body weight (ΔBW) assessed by DEXA were not significantly different from those determined by the

Table 8. Changes in Regional Body Composition Measured by Dual Energy X-ray Absorptiometry

	Presurgery			Postsurgery		
	BMC	LM	FM	BMC	LM	FM
Females & Male						
Head	0.54±0.02	3.80±0.12	1.13±0.07	0.55±0.02	3.57±0.14*	0.95±0.07*
Trunk	1.34±0.03	28.92±1.16	37.14±2.06	1.22±0.04*	26.98±1.32**	34.05±2.31**
Abdomen	0.61±0.02	12.92±0.67	18.88±1.39	0.58±0.02	12.48±0.79	17.45±1.31
Arms	0.23±0.03	3.93±0.29	5.09±0.39	0.30±0.01	3.95±0.18	5.05±0.33
Legs	1.19±0.04	21.27±0.94	20.87±1.38	1.20±0.03	19.86±0.66**	19.75±1.27*
Females						
Head	0.54±0.02	3.73±0.11	1.09±0.07	0.56±0.02	3.47±0.11*	0.90±0.06*
Trunk	1.33±0.03	28.24±1.07	35.86±1.83	1.23±0.04*	26.22±1.25**	32.79±2.24**
Abdomen	0.60±0.02	12.36±0.40	17.85±1.07	0.57±0.03	11.92±0.64	16.59±1.14
Arms	0.23±0.03	3.92±0.32	4.98±0.43	0.30±0.01	3.80±0.11	4.92±0.35
Legs	1.16±0.04	20.72±0.87	20.41±1.48	1.19±0.03	19.31±0.43**	19.34±1.38*

Values are mean±SEM (n=9 with and n=8 without the male subject before surgery and n=8 with and n=7 without the male subject after surgery). comparisons were made between columns for corresponding variables (paired t-test). *$p<0.05$, **$p<0.01$.

scale with and without the male subject (Table 9). Changes in FFM and FM as assessed by IDS and DEXA were more similar to one another than they were to changes as assessed by BIA. There were no significant differences in the percentage of reduced FFM and FM determined by DEXA and IDS method. However, BIA showed a higher loss in FFM than DEXA and IDS method and a lower loss in FM than IDS method. The similar results were found when the male subject was excluded (Table 9). Linear regressions for the reduced FFM and FM by each pair of the methods showed that high intercorrelations between BIA and DEXA estimates in the reduced FFM ($r=0.938$, $p=0.006$ without the male subject) but not in FM. When the male subject was included, the relationship between BIA and DEXA estimates in the reduced FFM was not significant. Overall, poor correlations in the estimates of reduced FFM and FM by the three methods were observed in the present study.

4.1.3. Changes in Energy Expenditure Following Ileogastrostomy

4.1.3.1. Basal Energy Expenditure and Fasting Nutrient Oxidation

Basal energy expenditure and RQ prior to and at 1, 2 and 3 months are shown in Figure 7. When expressed in absolute values, BEE were 1.158 ± 0.065 kcal.min^{-1} presurgically and 1.097 ± 0.055, 1.074 ± 0.047, 1.040 ± 0.039 kcal.min^{-1} at 1, 2 and 3 months postsurgically, respectively (Table 10). As can be seen, at any time during the study, BEE tended to

Table 9. Changes in Fat-free Mass and Fat Mass Determined by Isotope Dilution, Bioelectrical Impedance Analysis and Dual Energy X-ray Absorptiometry Methods

	IDS	BIA	DEXA
Females & Male			
ΔBW (kg)	12.7±2.1	12.7±2.1	10.5±1.2
ΔFFM (kg)	5.8±1.9^{b}	7.8±1.5^{a}	4.9±1.1^{bc}
ΔFM (kg)	6.9±0.5^{a}	4.9±0.8^{b}	5.6±0.7^{ab}
ΔFFM/ΔBW (%)	38.9±8.8^{bc}	60.0±4.9^{a}	44.1±8.8^{b}
ΔFM/ΔBW (%)	61.1±8.8^{a}	40.0±4.9^{c}	55.9±8.8^{ab}
Females			
ΔBW (kg)	10.8±1.0	10.8±1.0	10.4±1.4
ΔFFM (kg)	4.3±1.3^{bc}	6.6±1.0^{a}	5.1±1.2^{b}
ΔFM (kg)	6.6±0.5^{a}	4.3±0.6^{b}	5.2±0.8^{ab}
ΔFFM/ΔBW (%)	35.1±9.2^{bc}	59.4±5.6^{a}	46.2±9.9^{b}
ΔFM/ΔBW (%)	64.9±9.2^{a}	40.6±5.6^{c}	53.8±9.9^{ab}

Values are mean±SEM (n=9 with and n=8 without the male subject before surgery and n=8 with and n=7 without the male subject after surgery) and compared between columns for corresponding variables (paired t-test). Means not sharing a common superscript letter were statistically significant.

ΔBW, ΔFFM and ΔFM are the differences between pre- and postsurgical corresponding measurements

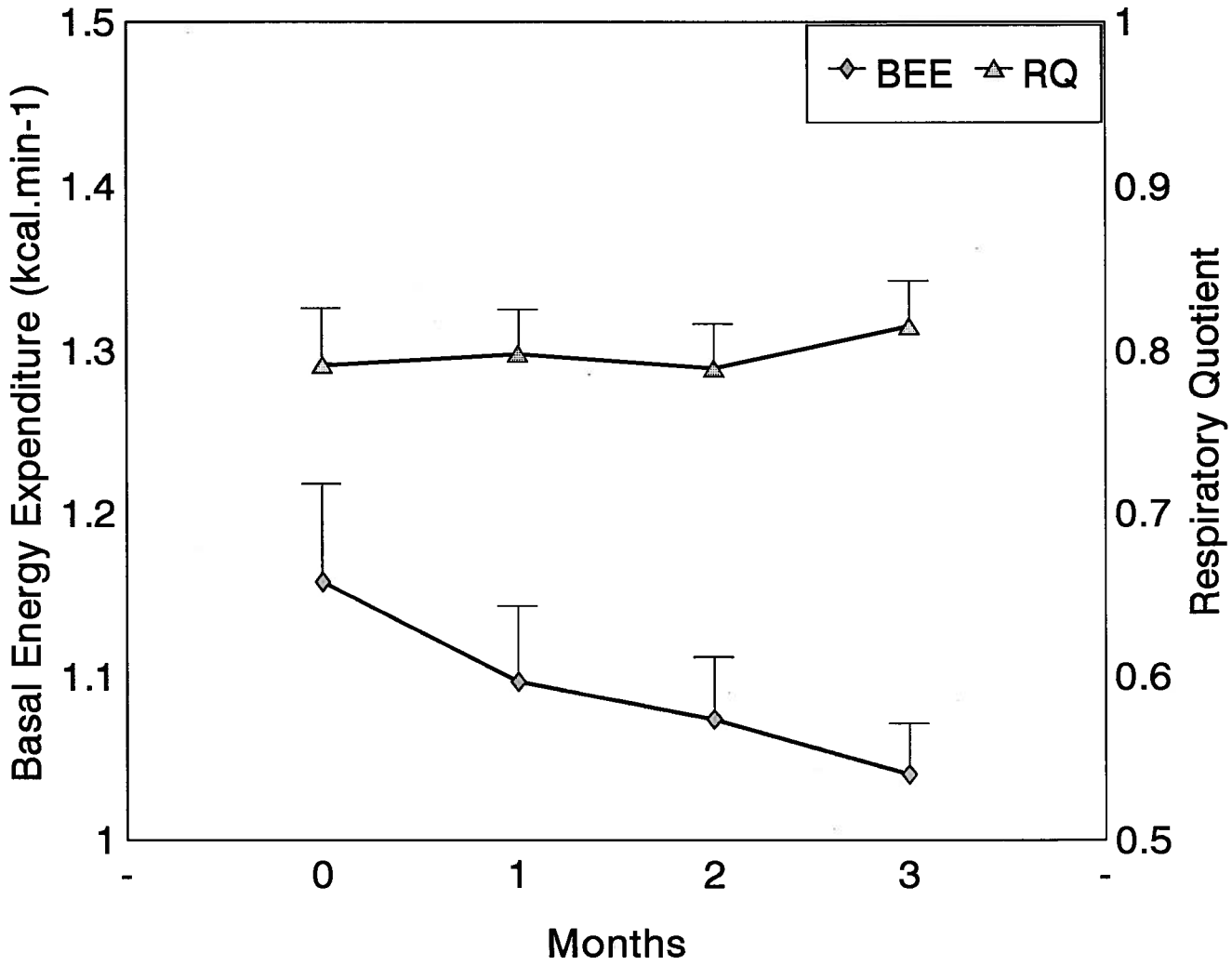

Figure 7. Basal energy expenditure and respiratory quotient presurgically and at 1, 2 and 3 months postsurgically (n=7). Error bars are +SEM. There were no significant differences between presurgical and postsurgical measurements.

decrease following surgery. The BEE declined by 0.061, 0.022 and 0.034 $kcal.min^{-1}$ during each of the first, second and third months following surgery, respectively. The decrease in BEE was in parallel to the reduction of body weight and energy intake (Appendix 9). However, the changes of BEE were of borderline statistical significance p=0.08). Because of the weight loss in this group of subjects, the changes in body weight and composition may affect the results. The analysis of covariance was applied to the BEE data with BW, FFM and FM as the covariates. The adjusted BEE was still not significantly different. The preprandial RQ level increased slightly but insignificantly following surgery (Figure 7). There were no changes in the utilization of carbohydrate (p=0.838) and fat (p=0.628) in the preprandial state (Table 10).

4.1.3.2. Changes in Thermic Effect of Food

Figure 8 shows the time course of presurgical TEF expressed as a percentage over BEE and a percentage of ingested energy in nine obese women. The net increase in energy expenditure after meal ingestion, expressed as a percentage above the BEE was 18.08± 3.19, 19.93±3.70, 21.40±3.59, 19.41±3.19 and 14.40±3.33 % at 1, 2, 3, 4 and 5 hours postprandially, respectively. The corresponding values for ingested energy were 2.08± 0.37, 2.23±0.37, 2.45±0.35, 2.22±0.32 and 1.64±0.36 %, respectively (Figure 8). The pattern of the thermic response curve showed that the morbidly obese subjects reached their peak energy expenditure in the third hour after meal ingestion. At the end of the measurement (t=300 minutes) energy expenditure was still higher than baseline values.

Table 10. Basal Energy Expenditure and Thermic Effect of Food, Expressed as Absolute Amount, Percentage of Basal Energy Expenditure and Ingested Energy

	Presurgery	1 mo.	2 mo.	3 mo.
Test meal energy (kcal)	599±13.8[a]	359±63.0[b]	424±55.0[ab]	599±13.8[a]
BEE ($kcal.min^{-1}$)	1.158±0.065	1.097±0.055	1.074±0.047	1.040±0.039
BEE ($kcal.d^{-1}$)	1668±93.1	1579±79.9	1547±68.1	1498±55.9
TEF ($kcal.min^{-1}$)	0.216±0.031[a]	0.062±0.015[b]	0.054±0.011[b]	0.066±0.012[b]
TEF ($kcal.5h^{-1}$)	64.9±9.2[a]	18.7±4.4[b]	16.1±3.3[b]	19.7±3.7[b]
TEF (% meal energy)	10.85±1.57[a]	5.55±1.38[b]	3.96±0.90[b]	3.28±0.62[b]
TEF (% BEE)	19.28±3.25[a]	5.65±1.30[b]	5.21±1.11[b]	6.22±1.23[b]
Preprandial RQ	0.791±0.026	0.798±0.021	0.789±0.023	0.815±0.023
Postprandial RQ	0.884±0.024[a]	0.811±0.018[ab]	0.765±0.027[b]	0.826±0.016[ab]

Values are mean±SEM (n=7). Comparison was made between months and the significance was symbolized by different letters.

Presurgery is presurgical measurement and 1 mo., 2mo. and 3 mo. are the measurements at 1, 2 and 3 months following surgery, respectively.

Symbols used are BEE, basal energy expenditure; TEF, thermic effect of food; Preprandial RQ is the average of RQ during 30 min BEE measurement and postprandial RQ is the average of RQ during 5 h TEF measurement.

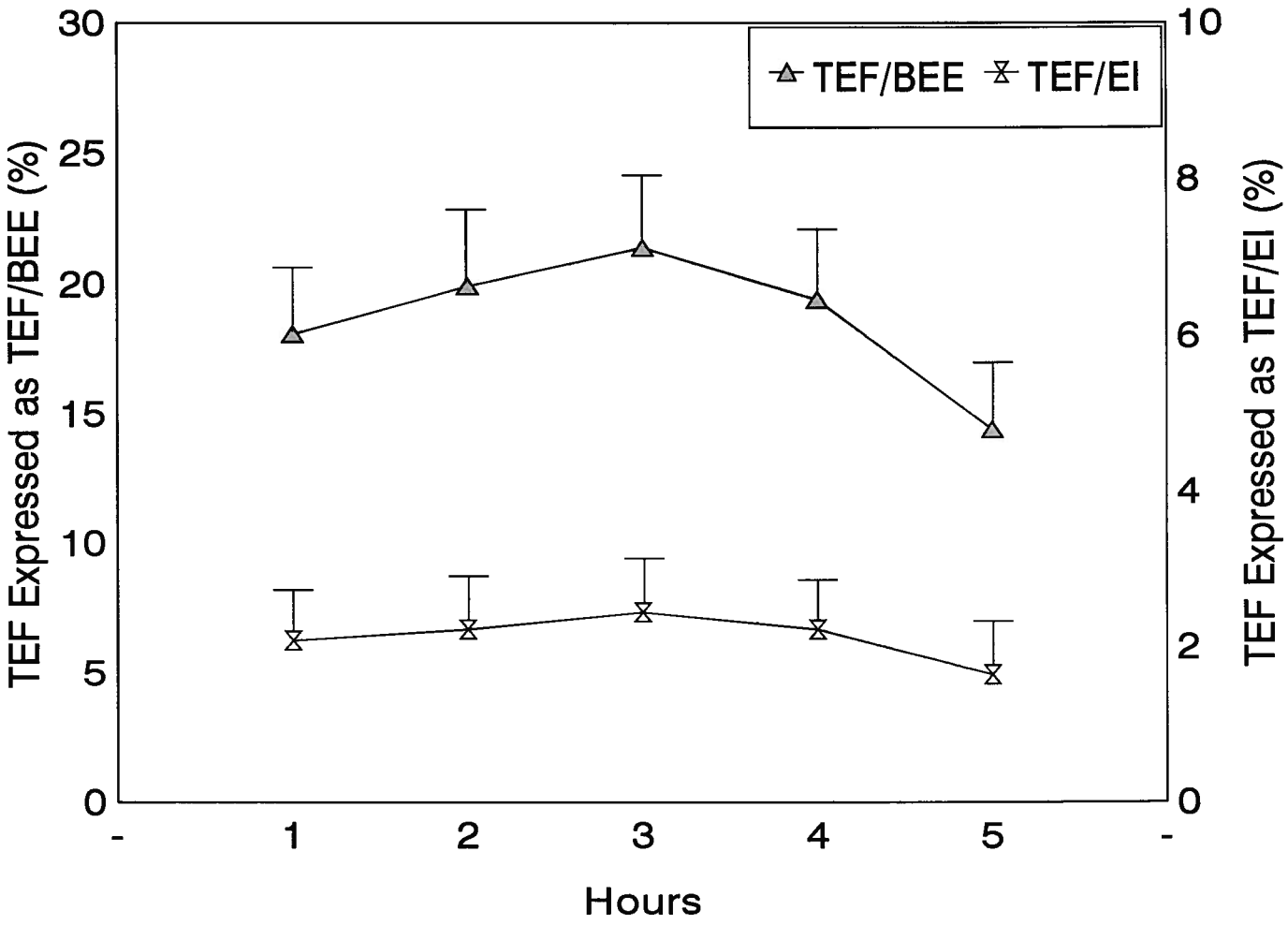

Figure 8. The time course of presurgical TEF (n=9), expressed as the percentage of BEE and ingested calories. Error bars indicate +SEM.

When TEF was expressed as absolute amount of energy over BEE, the presurgical TEF was significantly higher than those postsurgically ($p<0.0001$). Posthoc comparisons revealed that the difference between the values was limited to the presurgical determination, which was significantly greater ($p<0.001$) than each of the other measurements (Table 10). TEF values during the postsurgical study period were stabilized and were not significantly different from each other. In order to calculate the postprandial thermogenesis, the cumulative energy expenditure increment above the premeal baseline was calculated over 300 minutes. This integrated value divided by the energy content of the test meal were 10.85±1.57, 5.55±1.38, 3.96±0.90 and 3.28±0.62 % prior to and at 1, 2 and 3 months, respectively (Figure 9). Because the subjects could not consume all food items of the test meal as they did on presurgical test, the percentage of TEF was analyzed using ACOVA to adjust for the influence of meal composition. After this adjustment, presurgical TEF values were still significantly higher ($p=0.001$) than those following surgery. The thermic responses, expressed as a percentage increase over baseline energy expenditure dropped significantly following surgery ($p<0.0001$). There was no difference in preprandial RQ across the study period, however, postprandial RQ fell significantly ($p=0.001$).

4.1.3.3. Changes in Fat and Carbohydrate Oxidation

Fat and carbohydrate (CHO) oxidation rates (assuming constant oxidation for protein 0.7 g. kg^{-1} FFM.d^{-1}) during preprandial and postprandial measurements are presented in

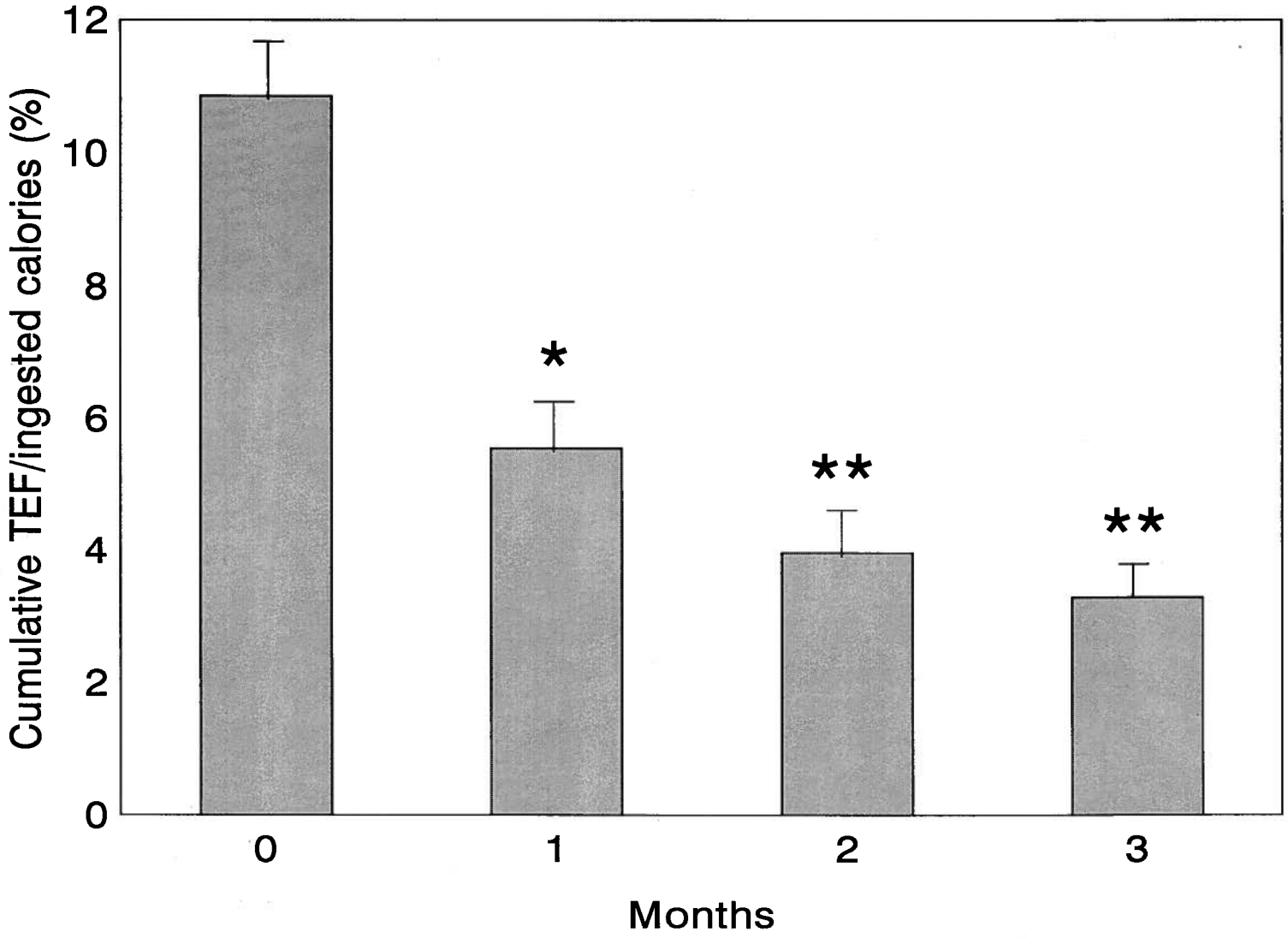

Figure 9. Cumulative thermic effect of food for 5 hours, expressed as the percentage of ingested calories (n=7). Error bars indicate +SEM. *1-mo value significantly different from presurgical value ($p<0.05$). **corresponding mo measurement significantly different from presurgical measurement ($P<0.01$).

Table 11. There were no significant changes in preprandial oxidation of fat and CHO following surgery. However, the postprandial oxidation of carbohydrate dropped off significantly ($p=0.002$) across the study period (Table 11). Because there was the confounding effect of reduced macronutrient consumption and absorption, the postprandial changes in fat and CHO oxidation could be indirect evidence of reduced intake and malabsorption of these nutrients. The relative oxidation of these two nutrients expressed as a percentage of the individual amounts ingested is also listed in Table 11. After surgery, obese women oxidized a greater proportion of the fat ingested than before surgery ($p=0.015$). The percent of CHO oxidation was significantly lower than that before surgery ($p=0.05$, repeated measures ANOVA). The difference was not observed when mutiple comparisons were performed.

4.1.3.4. Total Energy Expenditure in Bypassed Obese Subjects

The isotopic and TEE data for obese subjects are summarized in Table 12. The means of ^{18}O and ^{2}D elimination rates were 0.0927 ± 0.0058 and 0.0708 ± 0.0058 ($pool.d^{-1}$) respectively. Total body water volumes on day 0 and day 14, measured by deuterium dilution method, were 41.21 ± 1.45 and 40.44 ± 1.47 kg, respectively. The body water pool dropped by 0.77 kg during the 14-day study period. Carbon dioxide production rates varied considerably, ranging from 17.41 to 28.14 ($mol.d^{-1}$) which resulted in large differences in TEE among subjects. Similarly, a considerable difference in energy

Table 11. Pre- and Postprandial Fat and Carbohydrate Oxidation in The Obese Subjects Before and After Ileogastrostomy

	Presurgery	1 mo.	2 mo.	3 mo.
Preprandial				
Fat (g/min)	0.091±0.017	0.080±0.008	0.088±0.009	0.074±0.008
CHO (g/min)	0.075±0.025	0.084±0.019	0.065±0.018	0.088±0.018
Ingested Meal				
Fat (g)	23.30±0.54	13.97±2.45	16.51±2.14	23.30±0.54
CHO (g)	82.38±1.89	49.41±8.67	58.36±7.57	82.38±1.89
Postprandial				
Fat (g/5h)	24.34±9.12	23.98±2.67	30.14±2.81	20.29±1.19
CHO (g/5h)	60.66±8.28[a]	29.80±5.24[b]	24.43±9.95[b]	32.44±5.67[ab]
Oxidized/Ingested				
Fat (%)	105.56±40.50[b]	208.91±46.36[a]	199.44±28.82[a]	87.48±5.88[b]
CHO (%)	74.01±10.56	64.58±13.16	44.42±14.49	39.61±7.12

[1]Values are mean±SEM (n=7). Comparison was made between columns and means in each column not sharing a common superscript letter are significantly different ($p<0.05$).

Presurgery is the presurgical measurement and 1 mo., 2 mo. and 3 mo. are the measurements at 1, 2 and 3 months following surgery, respectively.

Preprandial fat and CHO are the average of oxidized fat and carbohydrates during 30-minute BEE measurement and postprandial fat and CHO are the cumulative oxidized fat and CHO during 5-hour TEF measurements.

Table 12. Individual Data of Total Body Water, Elimination Rates and Total Energy Expenditure in Obese Subjects

Subjects	K_2 ($pool.d^{-1}$)	K_{18} ($pool.d^{-1}$)	TBW-0 (kg)	TBW-14 (kg)	FQ	rCO_2 ($mole.d^{-1}$)	TEE ($kcal.d^{-1}$)	TEE/FFM ($kcal.kg^{-1}$)	TEE/BW ($kcal.kg^{-1}$)
1	0.0647	0.0903	42.50	42.86	0.842	28.17	3618	62.04	33.50
2	0.0525	0.0816	37.12	35.88	0.872	27.42	3423	68.65	35.55
3	0.1096	0.1325	39.50	38.32	0.861	23.02	2903	54.61	26.36
4	0.0494	0.0684	37.09	35.94	0.903	17.84	2165	43.41	22.71
6	0.0899	0.1081	39.69	38.66	0.858	18.44	2332	43.57	24.13
7	0.0709	0.0908	48.44	47.37	0.845	24.65	3154	48.20	28.89
10	0.0811	0.1073	35.73	35.22	0.891	23.96	2939	60.66	30.26
11	0.0599	0.0811	39.01	38.43	0.860	21.15	2669	50.46	23.57
12	0.0609	0.0830	47.90	47.09	0.797	27.02	3626	55.88	30.50
13	0.0687	0.0838	45.12	44.58	0.885	17.41	2148	35.06	20.15
Mean	0.0708	0.0927	41.21	40.44	0.861	22.91	2898	52.27	27.56
SEM	0.0058	0.0058	1.45	1.47	0.009	1.28	178	3.20	1.58

Symbols used are K_2 and K_{18}, elimination rates of deuterium and ^{18}O, respectively; TBW-0 and TBW-14, total body water at the begining and end of the 14-day experimental period; FQ, food quotient; rCO_2, rate of CO_2 production; TEE, total energy expenditure; FFM, fat-free mass; BW, body weight.

expenditure per FFM and BW existed in this group of subjects. Energy expended on the basis of FFM and BW were 52.27±3.20 and 27.56±1.58 kcal.kg^{-1}, respectively.

4.1.3.5. The Components of Total Energy Expenditure in Obese Subjects Following Ileogastrostomy

Of the 7 subjects completing metabolic tests, one could not conduct the TEE measurement using DLW method, due to the inconvenient transportation. The TEE was carried out just before the second month metabolic test. The BEE and TEF at the second month were used to estimate the percentage of energy cost for physical activity during this period (Figure 10). The physical activity index calculated from the total energy expenditure divided by resting energy expenditure (BEE+TEF) was 1.79±0.14 (mean± SEM) at the second month after ileogastrostomy.

4.1.4. Changes in Energy Intake

Energy intakes based on 3-day food records fell significantly ($p<0.0001$). Presurgically, the energy intake averaged 2022±295 kcal.d^{-1} and there was a marked drop in reported energy intake by 629, 772 and 842 kcal.d^{-1} during each of the first, second and third months following surgery, respectively. The postsurgical energy intakes at 1, 2 and 3 months were relatively stable (Table 13). The decrease in food consumption after surgery was also shown by the substantial reduction in the intake of different energy-containing

Percentage of Total Energy Expenditure for Basal Energy Expenditure, Thermic Effect of Food and Energy Cost of Physical Activity

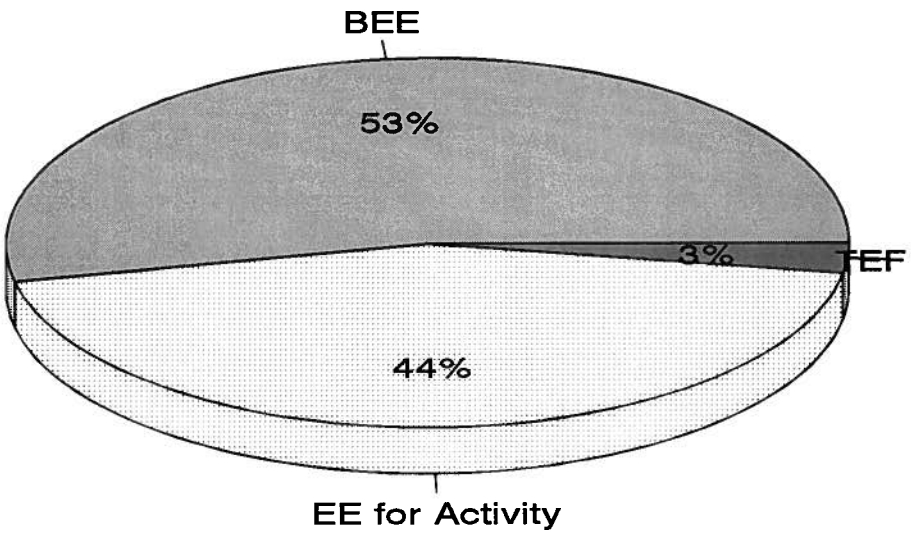

Figure 10. Hourly energy expenditure for basal metabolism (BEE), food thermogenesis (TEF) and energy expended for physical activities (EE for activity) at the second month following ileogastrostomy (n=6). Numbers are the relative percentage of each component in total energy expenditure.

Table 13. Changes in Energy Intake Following Ileogastrostomy

	Presurgery	1 mo.	2 mo.	3 mo.
Energy Intake ($kcal.d^{-1}$)	2022±295[a]	1393±201[b]	1251±257[b]	1180±174[b]
Fat (g)	85.1±20.7[a]	49.1±8.5[b]	51.9±13.5[b]	44.2±8.9[b]
Protein (g)	77.7±8.7[a]	61.6±8.5[ab]	53.5±9.0[b]	49.7±6.4[b]
CHO (g)	236.3±27.9[a]	176.2±26.7[ab]	142.5±27.7[bc]	145.8±20.4[bc]
Percentage of Energy as Fat (%)	35.8±3.3	30.9±2.1	35.1±3.0	31.8±3.6
Percentage of Energy as Protein (%)	16.1±1.3	18.1±1.3	17.9±1.8	17.4±1.6
Percentage of Energy as CHO (%)	48.0±3.2	51.0±2.1	47.1±3.5	50.8±4.0

[1]Values are mean±SEM (n=7). Comparison was made between columns and means in each column not sharing a common superscript letter are significantly different ($p<0.05$).

Presurgery is the presurgical measurement and 1 mo., 2 mo. and 3 mo. are the measurements at 1, 2 and 3 months following surgery, respectively.

nutrients There were no significant changes in the distribution of energy consumed as protein, fat and carbohydrate at the various times examined.

4.1.5. Factors Associated With Weight Loss Following Ileogastrostomy

Table 14 presents individual data for energy balance study. Energy intakes were based on 5-day food records reported by each subject who participated in the balance study. Fecal and urinary energy losses were derived from 6 subjects as described above. Total energy expenditure was determined using DLW technique between 6 and 8 weeks following ileogastrostomy. On average energy expenditure was 2898±178 $kcal.d^{-1}$ and energy intake was 1625±207 $kcal.d^{-1}$. Energy loss estimated by the changes in both FFM and FM measured by the IDS method was 929±157.2 $kcal.d^{-1}$. There was a close positive correlation between the energy loss and energy expenditure ($r=0.719$, $p=0.019$, $n=10$) during the DLW period (Figure 11A,B). On the contrary, energy intake showed a positive correlation with energy loss ($r=0.582$, $p=0.078$, $n=10$) and this relationship approached significance. There was clear evidence of malabsorption as determined by 5-day fecal energy measurement (Table 14). The amount of energy loss during the 14-day study period may have been related to the energy content in feces ($r=0.808$, $p=0.052$) but was not correlated to the urinary energy loss ($r=0.011$). The energy lost in feces accounted for 65.3% of variance in body energy loss obtained from the loss of FFM and FM during 14-day study period. However, the numbers were too small to draw justifiable conclusions. The correlation matrix for these variables in the 6 subjects who completed the energy

Table 14. Individual Data of Energy Balance in the Obese Subjects Following Ileogastrostomy

Subjects	Weight loss ($kg.14\text{-}d^{-1}$)	Energy Loss ($kcal.d^{-1}$)	REI ($kcal.d^{-1}$)	TEE ($kcal.d^{-1}$)	FE ($kcal.d^{-1}$)	UE ($kcal.d^{-1}$)
1	-2.8	-1745.1	1386	3618	404.8	109.7
2	-2.4	-525.5	1601	3423	283.3	102.4
3	-3.3	-1044.1	1475	2903	448.3	90.0
4	-1.7	-199.7	535	2165	197.1	98.3
6	-1.7	-278.8	1042	2332	289.7	115.3
7	-3.2	-1068.1	2531	3154	436.5	105.0
10	-2.5	-1036.2	1363	2939		
11	-2.5	-986.8	2305	2669		
12	-3.2	-1552.2	2564	3626		
13	-2.3	-853.7	1454	2148		
Mean	-2.6	-929.0	1626	2899	343.3	103.5
SEM	0.2	157.2	207	178	41.4	3.6

REI, TEE, FE and UE represent reported energy intake, total energy expenditure, fecal energy and urinary energy, respectively. Weight Loss was determined by scale.

Energy loss was obtained from the loss of both FFM and FM during the 14-day period. Assuming that adipose tissue consists of 20% water and that each gram of fat stored has a caloric equivalent of 9.5 $kcal.g^{-1}$and each gram of protein has a caloric equivalent of 4.23 $kcal.g^{-1}$, 1g of FM equals 7.6 kcal amd 1g of FFM equals 1.1 kcal because FFM contains 26.8% of protein.

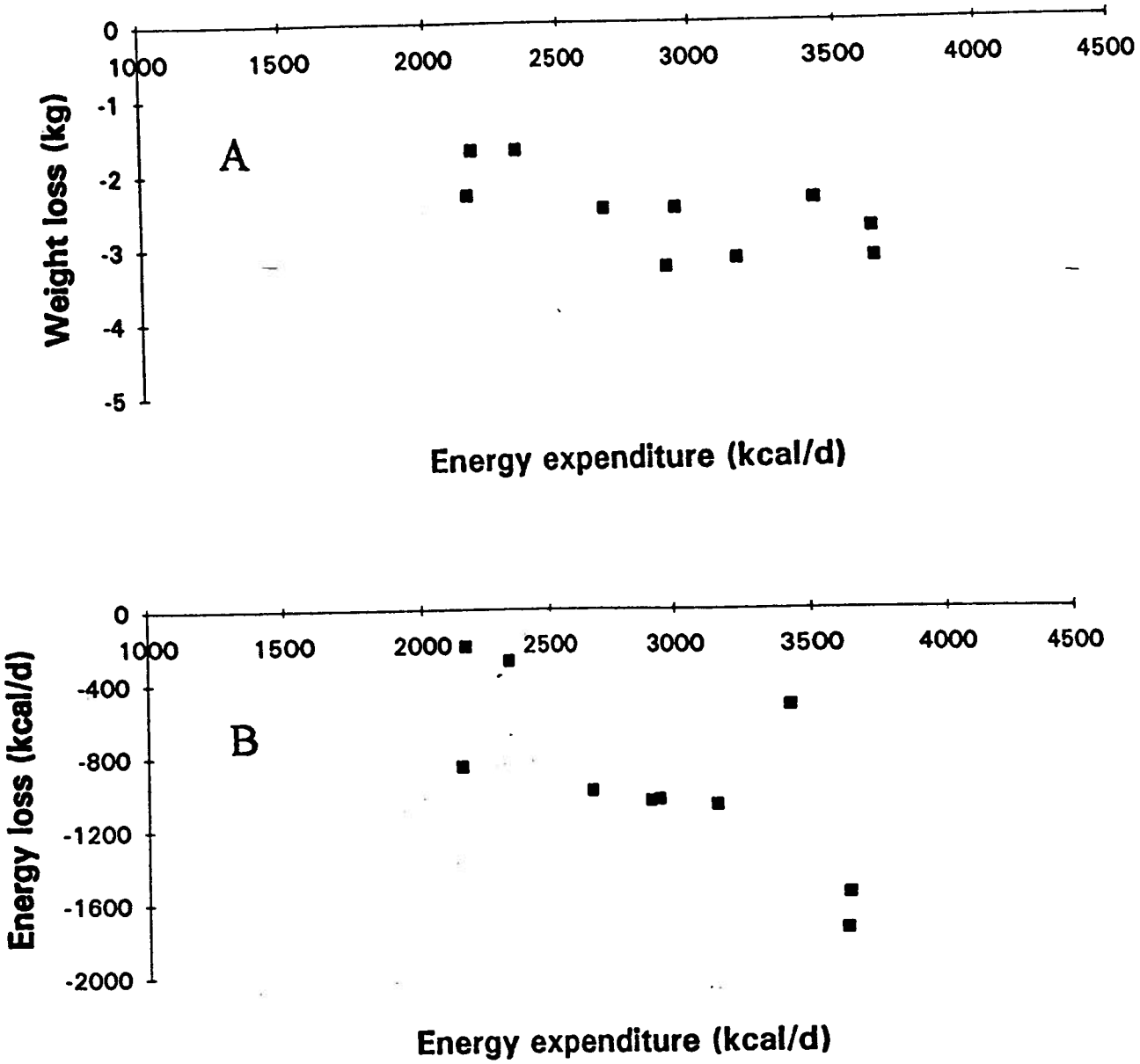

Figure 11. Correlation between energy expenditure and weight loss (11A: r=0.675, p=0.032) as well as energy loss (11B: r=0.719, p=0.019) (n=10).

balance study is presented in Table 15. There was an insignificant relationship between energy intake and energy expenditure ($r=0.628$, $p=0.168$, $n=6$) as well as fecal energy loss ($r=0.732$, $p=0.084$, $n=6$). Due to the large variability and inaccuracy of energy intake in this study, the energy intake was not closely related to the weight loss.

Table 15. Correlation Coefficients Between Energy Loss and Energy Expenditure, Fecal Energy, Urinary Energy and Energy Intake

	EE	*FE*	*UE*	*EI*
FE	0.589 (0.204)			
UE	0.054 (0.921)	-0.156 (0.763)		
EI	0.628 (0.168)	0.732 (0.084)	0.023 (0.966)	
E-loss	0.778 (0.068)	0.808 (0.052)	0.011 (0.983)	0.491 (0.323)

Numbers are correlation coefficients for corresponding variables and p values are shown in brackets (n=6).

E-loss was energy lost in FM and FFM during the 14 -day period. EE, FE, UE and EI represent energy expenditure, fecal energy, urinary energy and energy intake, respectively.

4.2. Validation of Reported Energy Intake Using Doubly Labeled Water in Normal-weight and Obese Subjects

4.2.1. Physical Characteristics of Normal-weight and Obese Subjects

The physical characteristics of 26 normal-weight and 6 obese subjects are presented in Table 16. The normal-weight subjects were 48.3±1.0 years of age, mean body weight 61.7 ±1.3 kg, BMI 23.4±0.5 $kg.m^{2-1}$, body fat 32.8±1.3%. The obese subjects were 36.0±2.8 years of age, mean body weight 105.2±2.9 kg, BMI 40.3±1.0 $kg.m^{2-1}$, body fat 47.2±1.3 %. Weight, percent IBW, and weight as fat in the obese group were all significantly greater than those of normal-weight group. The mean body weight of the obese group was 43.5 kg (70.5 %) greater than that of normal-weight group.

4.2.2. Total Energy Expenditure in Normal-weight Subjects

Table 17 presents the isotopic and TEE data for normal-weight subjects. The means of ^{18}O and ^{2}D elimination rates were 0.1158±0.0042 and 0.0903±0.0041 ($pool.d^{-1}$). Total body water volumes on day 0 and day 14 were 30.34±0.87 and 30.34±0.88 kg, respectively. On average body weight declined by 0.138 kg and the body water pool was maintained during the 14-day study period in this group of subjects. Carbon dioxide production rates ranged from 8.64 to 24.69 ($mol.d^{-1}$) with a mean value of 17.88±0.84

Table 16. Physical Characteristics of Normal-weight and Obese Subjects in the Validation Study

Subject	Age	Height	Initial BW	Final BW	MBW	BW/IBW	BMI	FM/MBW
Normal -weight	ys	cm	kg	kg	kg	%	$kg.m^{2-}$	%
1	41	166.5	71.0	69.4	70.2	110.4	25.3	38.4
2	45	162.6	61.4	61.2	61.3	98.6	23.2	29.6
3	55	163.0	54.0	54.2	54.1	87.0	20.4	36.1
4	54	149.7	61.0	61.5	61.3	113.0	27.3	41.1
5	52	170.0	61.9	61.0	61.5	92.8	21.3	31.8
6	45	165.0	66.2	65.4	65.8	103.5	24.2	35.8
7	45	166.7	61.2	60.7	61.0	96.0	21.9	30.8
8	45	160.5	57.1	56.7	56.9	93.5	22.1	35.1
9	45	166.2	56.8	58.0	57.4	90.3	20.8	26.9
10	57	166.5	64.5	64.2	64.4	101.3	23.2	45.3
11	52	164.0	57.5	57.4	57.5	92.4	21.4	38.2
12	50	177.0	70.0	69.0	69.5	100.7	22.2	16.2
13	45	155.0	62.5	62.5	62.5	107.6	26.0	28.9
14	47	165.5	70.0	69.5	69.8	109.8	25.5	31.5
15	45	158.5	59.5	59.1	59.3	99.7	23.6	19.1
16	54	162.5	59.5	60.0	59.8	96.1	22.6	25.0
17	48	162.5	52.9	53.1	53.0	85.2	20.1	26.4
18	46	157.3	71.4	71.1	71.3	122.7	28.8	40.7
19	55	170.0	75.0	74.9	75.0	113.2	25.9	38.5
20	54	155.3	48.7	48.7	48.7	83.8	20.2	32.7
21	37	161.8	58.2	58.0	58.1	95.5	22.2	29.8
22	45	169.0	57.4	57.8	57.6	88.7	20.2	29.8
23	45	153.3	58.5	57.8	58.2	102.6	24.7	42.2
24	54	153.2	52.0	52.9	52.5	92.5	22.3	37.6
25	49	159.3	63.9	63.1	63.5	106.8	25.0	34.4
26	45	165.5	75.0	75.0	75.0	118.0	27.4	30.5
Mean	48.3	162.6	61.8	61.6	61.7	100.1	23.4	32.8
SEM	1.0	1.2	1.4	1.3	1.3	2.0	0.5	1.3
Obese								
1	48	155	109.4	106.6	108.0	195.0	45.0	46.0
2	28	163	97.5	95.1	96.3	161.2	36.3	48.2
3	22	157	111.8	108.5	110.2	194.1	44.7	51.7
4	26	152	96.2	94.5	95.4	175.8	41.3	47.8
6	48	157	97.5	95.8	96.7	170.2	39.2	44.6
7	40	168	110.8	107.6	109.2	165.9	38.7	40.1
Mean	36.0	161.7	106.5	103.9	105.2	174.2	40.3	47.2
SEM	2.8	2.2	2.7	2.5	2.6	4.4	1.0	1.3

Table 17. Individual Data for Total Body Water, Elimination Rates and Total Energy Expenditure in Normal-weight Subjects

Subjects	K_2 ($pool.d^{-1}$)	K_{18} ($pool.d^{-1}$)	TBW-0 (kg)	TBW-14 (kg)	FQ	rCO_2 ($mole.d^{-1}$)	TEE ($kcal.d^{-1}$)	TEE/FFM ($kcal.kg^{-1}$)	TEE/BW ($kcal.kg^{-1}$)
1	0.0932	0.1151	32.24	31.05	0.855	15.60	1962	45.38	27.94
2	0.0704	0.0969	31.60	31.55	0.853	19.86	2483	57.57	40.51
3	0.1054	0.1322	25.47	25.11	0.864	15.46	1871	54.15	34.59
4	0.0936	0.1230	26.66	26.14	0.870	18.18	2355	65.29	38.45
5	0.0857	0.1180	30.01	31.30	0.906	23.54	2869	68.49	46.48
6	0.0861	0.1101	31.56	30.28	0.833	17.08	2086	49.37	31.70
7	0.0857	0.1176	30.86	30.88	0.899	23.37	2850	67.60	46.77
8	0.1651	0.1960	27.10	26.99	0.897	18.14	2231	60.37	39.20
9	0.0954	0.1143	30.72	30.75	0.898	12.69	1620	38.58	28.22
10	0.0810	0.1058	25.41	26.07	0.889	14.88	1895	53.91	29.45
11	0.0820	0.1061	26.09	25.91	0.848	14.49	1808	50.90	31.47
12	0.0860	0.1110	42.39	42.91	0.851	24.69	3070	52.69	44.17
13	0.1134	0.1374	32.27	32.76	0.873	17.29	2108	47.45	33.72
14	0.0998	0.1281	34.93	35.03	0.876	22.83	2807	58.69	40.21
15	0.0777	0.1071	34.83	35.41	0.898	24.56	2999	62.50	50.57
16	0.0732	0.1017	32.56	33.07	0.890	22.34	2738	61.08	45.82
17	0.0923	0.1166	28.35	28.77	0.896	15.88	2005	51.38	37.82
18	0.0955	0.1178	31.15	30.69	0.892	15.53	1937	45.86	27.18
19	0.0717	0.0970	33.67	33.78	0.860	20.15	2496	54.21	33.32
20	0.0971	0.1220	23.90	24.08	0.873	13.62	1631	49.76	33.48
21	0.0769	0.0959	29.49	30.18	0.880	12.83	1557	38.20	26.80
22	0.0709	0.0990	29.93	29.26	0.919	19.82	2428	60.06	42.16
23	0.0551	0.0800	24.69	24.53	0.903	14.79	1817	54.05	31.25
24	0.1158	0.1343	23.92	24.00	0.893	8.64	1095	33.44	20.87
25	0.1021	0.1245	30.63	30.40	0.889	15.28	1960	47.03	30.87
26	0.0766	0.1026	38.49	37.84	0.856	23.36	2913	55.88	38.84
Mean	0.0903	0.1158	30.34	30.34	0.880	17.88	2215	53.23	35.85
SEM	0.0041	0.0042	0.87	0.88	0.004	0.84	102	1.73	1.46

Symbols used are K_2 and K_{18}, elimination rates of deuterium and ^{18}O, respectively; TBW-0 and TBW-14, total body water at the begining and end of the 14-day experimental period; FQ, food quotient; rCO_2, rate of CO_2 production; TEE, total energy expenditure; FFM, fat-free mass; BW, body weight.

4.2.3. Accuracy of Reported Energy Intake in Normal-weight Subjects

Table 18 lists the individual data of reported energy intake, changes in body weight and composition during the 2 week experimental period, energy intake after adjusting for body energy stores and the intakes divided by expenditure in the normal-weight participants. Reported energy intake was significantly less than energy expenditure (-562 kcal, $p<0.0001$) and on average energy intake represented 76.8±3.4% of the measured expenditure for the whole group. The correlation between reported energy intake and expenditure was 0.504 ($p=0.009$) (Figure 12A). The results described above were not adjusted for the changes in body energy stores during the study period. The changes in body weight and composition were used to adjust for these body energy stores in the following manners:

Using the assumption of Black et al (1986) that the probable energy density of tissue lost or gained in adults under these normal conditions is 7000 $kcal.kg^{-1}$ body weight, the adjusted energy intake for body weight changes was calculated in the following equation:

$$\text{Adjusted EI } (kcal.d^{-1}) = \text{Reported EI} - (\Delta BW \times 7000\ kcal.kg^{-1})/\text{number of days} \quad \text{(Eqn. 8)}$$

On the basis of the assumptions that adipose tissue is 20% water and that each gram of fat stored has a caloric equivalent of 9.5 $kcal.g^{-1}$, the caloric equivalent of 1 g adipose tissue is 7.6 kcal (Bandini et al 1990). The caloric equivalent of 1 g protein is 4.23 kcal. The

Table 18. Accuracy of Reported Energy Intake in Normal-weight Subjects

Subject	ΔBW (kg)	ΔFFM (kg)	ΔFM (kg)	REI ($kcal.d^{-1}$)	EI_{BW} ($kcal.d^{-1}$)	EI_c ($kcal.d^{-1}$)	REI/TEE ×100 (%)	EI_{BW}/TEE ×100 (%)	EI_c /TEE ×100 (%)
1	-1.6	-1.63	0.03	1560	2360	1677	79.5	120.3	85.5
2	-0.2	-0.08	-0.12	1681	1781	1755	67.7	71.7	70.7
3	0.2	-0.49	0.69	1518	1418	1181	81.1	75.8	63.1
4	0.5	-0.72	1.22	1792	1542	1189	76.1	65.5	50.5
5	-0.9	1.75	-2.65	1938	2388	3237	67.6	83.3	112.8
6	-0.8	-1.75	0.95	2051	2489	1717	100.1	119.3	82.3
7	-0.5	0.03	-0.53	2405	2655	2688	84.4	93.1	94.3
8	-0.4	-0.14	-0.26	1790	1990	1940	80.3	89.2	87.0
9	1.2	0.04	1.16	1593	993	961	98.3	61.3	59.3
10	-0.3	0.90	-1.20	1321	1487	1898	69.7	77.6	100.2
11	-0.1	-0.25	0.15	1546	1596	1486	85.5	88.3	82.2
12	-1.0	0.71	-1.71	2355	2842	3213	76.3	92.6	104.7
13	0.0	0.67	-0.67	1409	1409	1719	66.8	66.8	81.5
14	-0.5	0.13	-0.63	1359	1609	1690	48.5	57.4	60.2
15	-0.4	0.79	-1.19	1144	1344	1728	38.2	44.8	57.6
16	0.5	0.70	-0.20	1432	1182	1483	52.3	43.2	54.2
17	0.2	0.58	-0.38	1389	1289	1547	69.3	64.3	77.2
18	-0.3	-0.64	0.34	989	1132	851	50.7	58.4	44.0
19	-0.1	0.15	-0.25	2201	2258	2330	88.4	90.4	93.3
20	0.0	0.24	-0.24	1716	1716	1829	105.3	105.3	112.2
21	-0.2	0.94	-1.14	1484	1554	1996	93.4	99.8	128.2
22	0.4	-0.92	1.32	1878	1678	1234	77.3	69.1	50.8
23	-0.7	-0.23	-0.47	1200	1553	1478	66.2	85.5	81.3
24	0.9	0.10	0.80	1115	665	647	101.9	60.8	61.5
25	-0.8	-0.31	-0.49	1826	2226	2116	93.1	113.5	107.9
26	0.0	-0.89	0.89	2280	2280	1868	78.3	78.3	64.1
Mean	-0.1	-0.01	-0.18	1653	1722	1749	76.8	79.0	79.5
SEM	0.1	0.16	0.19	76	101	122	3.4	4.1	4.4

Symbols used are the followings: ΔBW, ΔFFM and ΔFM, changes in body weight, FFM and FM during the 14-day experimental period; REI, EI_{BW} and $EI_{C,}$ reported energy intake and intakes adjusted for changes in body weight and composition, respectively.

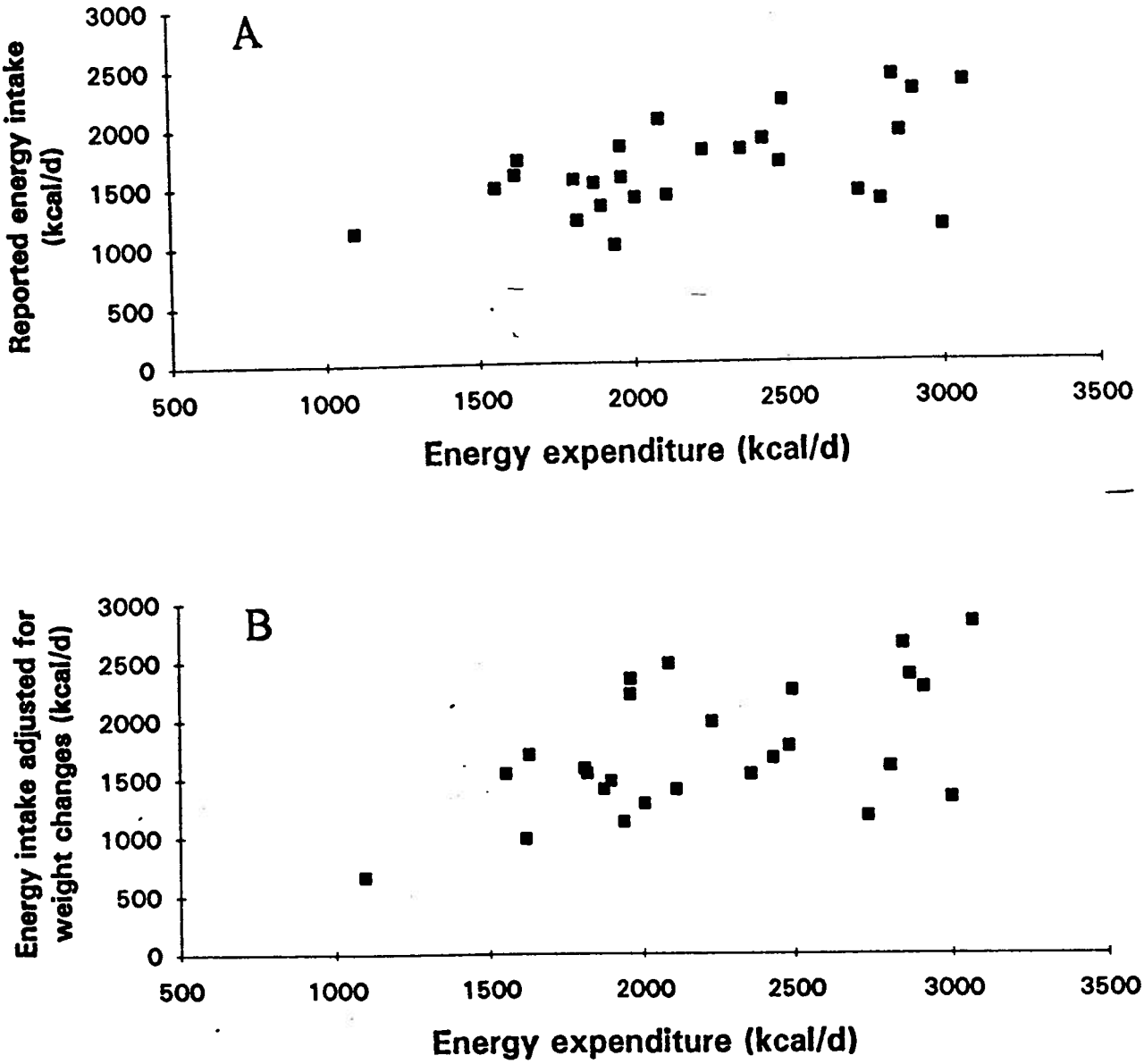

Figure 12. Plots of energy expenditure against reported energy intake (12A: r=0.504, p=0.009) as well as energy intake after adjusting for the changes in body energy stores (12B: r=0.503, p=0.009) (n=26).

following equation were used to adjust energy intake for changes in body compositions:

$$\text{Adjusted EI (kcal.d}^{-1}\text{)} = \text{Reported EI} - (\Delta FM \times 7600\ \text{kcal.kg}^{-1} + \Delta FFM \times 0.268 \times 4230\ \text{kcal.kg}^{-1})/\text{number of day} \quad \text{(Eqn. 9)}$$

On average the subjects lost only 0.138±0.116 kg. This amount of weight loss could account for a discrepancy of 69 kcal.d^{-1}. When the individual energy intakes were adjusted for the weight lost or gained, the adjusted energy intakes were not statistically different from the reported energy intakes (p=0.244) and the representiveness of adjusted energy intakes was also not different from that of reported energy intake divided by expenditure (p=0.507). This adjusted energy intake represented 79.0±4.1% of energy expenditure (Table 18) and the correlation between energy intake and expenditure was 0.503 (p=0.009) (Figure 12B). Similarly, there were no significant differences between energy intake after adjusting for the changes in body composition and reported energy intake (Table 18).

4.2.4. Accuracy of Reported Energy Intake in Obese Subjects

The individual data for reported energy intake, changes in body weight and composition and energy intake as a percent of TEE in the obese subjects are shown in Table 19. Reported energy intake was significantly less than expenditure (-1505 kcal.d^{-1}, p<0.0001). Reported energy intake represented 47.6±7.5 % of TEE measured by DLW

Table 19. Accuracy of Reported Energy Intake in Obese Subjects

Subjects	ΔBW (kg)	ΔFFM (kg)	ΔFM (kg)	REI (kcal.d^{-1})	ME_{BW} (kcal.d^{-1})	MEc (kcal.d^{-1})	REI/TEE ×100 (%)	ME_{BW}/TEE ×100 (%)	ME_c /TEE ×100 (%)
1	-2.8	0.49	-3.29	1386	2272	2617	38.3	62.8	72.3
2	-2.4	-1.69	-0.71	1601	2416	1741	46.8	70.6	50.9
3	-3.3	-1.62	-1.68	1475	2587	1981	50.8	89.1	68.2
4	-1.7	-1.57	-0.13	535	1090	440	24.7	50.3	20.3
6	-1.7	-1.40	-0.30	1042	1487	918	44.7	63.8	39.3
7	-3.2	-1.45	-1.75	2531	3590	3058	80.2	113.8	96.9
Mean	-2.5	-1.21	-1.31	1429	2240	1792	47.6	75.1	58.0
SEM	0.3	0.34	0.48	271	359	405	7.5	9.3	11.0

Symbols used are the followings: ΔBW, ΔFFM and ΔFM, changes in body weight, LBM and FM determined by the IDS method during the 14-day experimental period; REI, ME_{BW} and $ME_{C,}$ reported energy intake and metabolizable energy intakes adjusted for changes in body weight and composition, respectively.

method. Because body weight declined dramatically in this group during the 2-week period, part of the discrepancy between intake and expenditure may have been attributable to changes in body energy stores. Also, the obese subjects were patients following ileogastrostomy. There was some energy lost in feces and possibly in urine which may overestimate the metabolizable energy intake (ME). After correcting for the energy lost in feces and urine, ME fell to 982±242 kcal.d^{-1} which was significantly less than reported energy intake ($p<0.0001$). The changes in body weight and composition were used to estimate the energy stores in the same manner as we did in normal-weight subjects. The energy loss estimated from the changes in body weight and composition using equations 8 and 9 could account for 1258±145 and 810±240 kcal.d^{-1} discrepancy, respectively. The adjusted energy intakes were 2240±359 and 1792±405 kcal.d^{-1} obtained from ME and the changes in body weight (1258±145 kcal.d^{-1}) and composition (810±240 kcal.d^{-1}) (Table 19). These adjusted energy intakes represented 75.1±9.3 and 58.0±11.0 % of energy expenditure. There was significant difference ($p=0.029$) in the degree of underestimation of energy intake using both means to adjust the changes in body stores in the obese subjects, but not in the normal-weight subjects (Figure 13).

Table 20 summarizes the results of the validation study. Obviously, there were considerable differences in TEE and underestimation of energy intake, while these two groups of subjects were not comparable because TEE in the obese group was measured during weight loss. In addtion, the two groups of subjects came from two geographical areas, and the sample collection and data analyses were also slightly different between the

two groups. Obese subjects seem to have lower energy expenditure per body weight than normal-weight subjects, however, energy expended per FFM was not different.

4.2.5. The Relationship Between Underreporting of Energy Intake and Body Weight

To attempt to identify factors associated with severity of underreporting, simple correlation analyses were performed between the under-reporting of energy intake with body weight, age and height in normal-weight and obese groups. Results showed that there were no close correlations between these variables and the degree of under-reporting of energy intake in the normal-weight subjects. However, a significant negative relationship was found between under-reporting of energy intake with body weight measured during the 14-day experimental period ($r=0.868$, $p=0.025$) in the obese subjects. Multiple regression comparing degree of under-reporting of energy intake against body weight, age and height showed that there was a close relationship between these variables and the degree of underreporting in obese group, but not in the normal-weight group (Table 21).

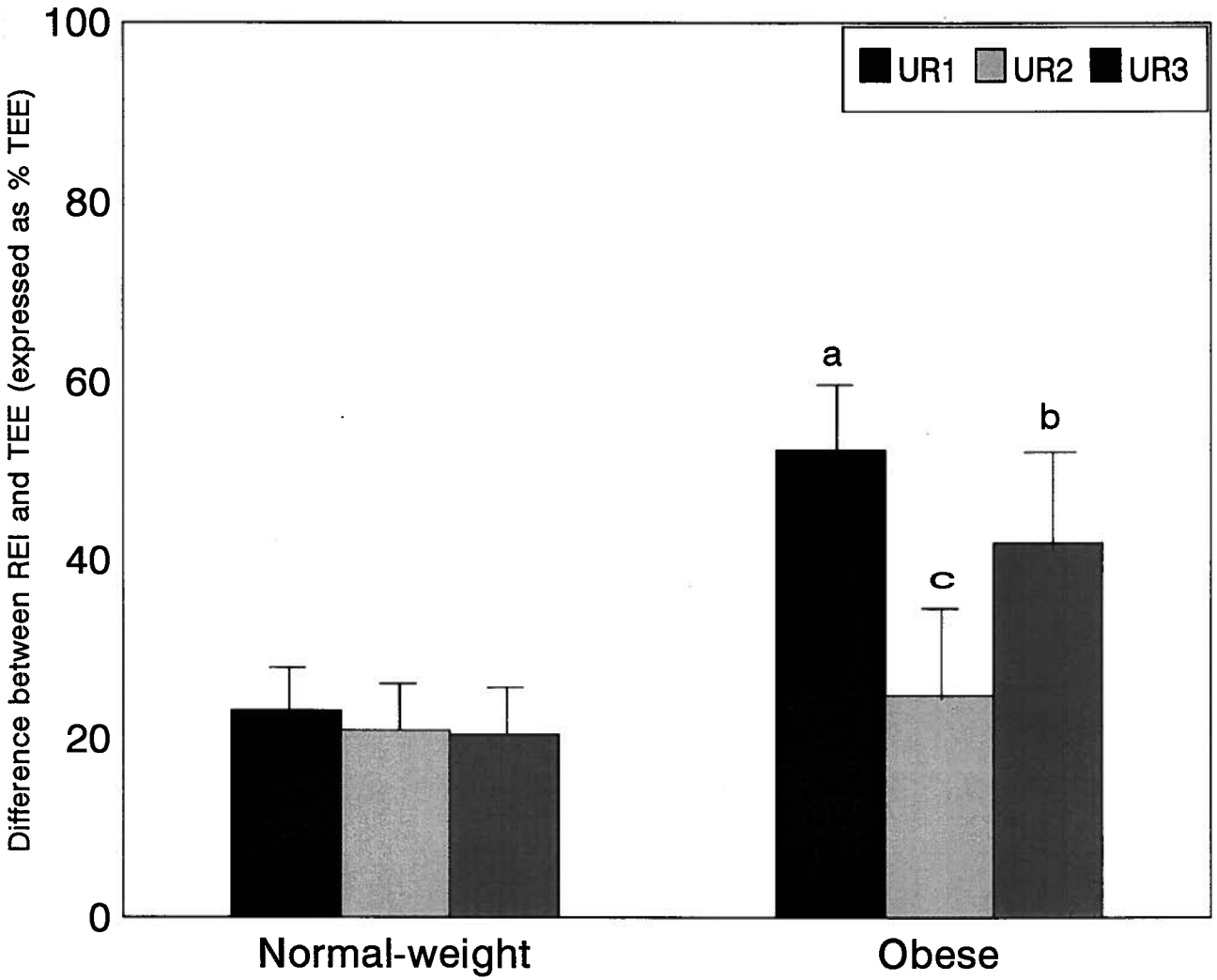

Figure 13. Difference between reported energy intakes (REI) and total energy expenditure in normal-weight and obese subjects expressed as reported energy intake (UR1) and intakes adjusted for changes in body weight (UR2) and composition (UR3) as % TEE. Statistical significance was indicated by different letters.

Table 20. Summary of Energy Intake, Expenditure and the Representativeness of Reported Energy Intake in Obese and Normal-weight Subjects

	Obese	Normal-weight
REI ($kcal.d^{-1}$)	1429±271	1653±76
TEE ($kcal.d^{-1}$)	2933±239	2215±102
REI/TEE (%)	47.6±7.5	76.8±3.4
TEE/BW ($kcal.kg^{-1}$)	28.5±2.1	34.8±1.6
TEE/FFM ($kcal.kg^{-1}$)	53.4±4.2	53.2±1.7

Values are mean±SEM. Symbols used are as follows: REI, reported energy intake; TEE, total energy expenditure; BW, body weight; FFM, fat-free mass.

Table 21. Multiple Correlation Coefficients Between Underreporting of Energy Intake and Some Physiological Variables in Obese and Normal-weight Subjects

Groups	*Obese*	*Normal-weight*
Variables	Body weight, age and height	
Underreporting[1] (%)	0.989 (0.032)	0.313 (0.508)
Underreporting[2] (%)	0.962 (0.109)	0.254 (0.682)
Underreporting[3] (%)	0.995 (0.015)	0.329 (0.463)

Numbers are multiple correlation coefficients (r) and p values are shown in brackets.

Underreporting[1,2,3] represent the degree of underestimation of metabolizable energy intake and and intakes adjusted for changes in body weight and composition, respectively.

5. DISCUSSION

This investigation expands previous studies of the energetics associated with weight loss following intestinal bypass procedures. Based on the results obtained in the present study, there is evidence that TEE was related to weight loss after ileogastrostomy. Fecal energy loss was still an important determinant in the weight loss foloowing intestinal bypass procedures. The difference between reported energy intake and expenditure was observed in both normal-weight and obese participants. This section will discuss the present findings in the context of available data from similar studies.

5.1. Influence of Ileogastrostomy on Body Composition and Methodology in Assessing the Reduction in Body Composition

We used the IDS method to measure the changes in body composition following ileogastrostomy in our first series of subjects. The results were compared with those determined by BIA in which we used the equation of Segal et al (1988) to predict FFM. We found that FFM and FM measured by IDS method were significantly different from those obtained by BIA. There were no differences in the assessment of changes in FFM and FM between the two methods after ileogastrostomy.

The difference in body composition measurement by IDS method and BIA in the present study may be due to the influence of high %BF in obese subjects on the accuracy of BIA

measurements. It was reported that obesity affected the precision of BIA (Gray et al 1989). Segal et al (1985) reported a significant relationship (r= 0.796) between residual FFM scores, calculated as the difference between observed and predicted values, and %BF. Our results showed higher FM and lower FFM determined by BIA than those by IDS method. Generally, underestimation of FFM was offset by overestimation of FM and vice versa. However, systematic errors occurring in both methods could alternatively account for the present findings.

Isotope dilution has been a traditionally used technique to investigate changes in body composition. However, it is well known that this technique has limitations. Even with high precision of TBW estimation, errors can be made in calculating FFM and FM because it is not known whether the constant water content in FFM can be applied to all subjects. Particularly, the assumption of 73.2% of body water in FFM (Siri 1956) is violated in bypassed patients who may experience dehydration following these procedures. Even in normal sujects, the assumption appears flawed: Wellens et al (1994) showed the wide range of interindividual variation in the degree of hydration, where an average 74.0% in men (range 65.8-86.2%) and 73.1% in women (range 60.8-84.5%) was observed. Other studies (Elia 1992; Fuller et al 1991) also reported an extensive range (67-78%) for the hydration fraction of FFM. This known wide range of interindividual variation in the degree of hydration can affect the calculation of body composition estimates by the isotope dilution method.

Bioelectrical impendance analysis is a relatively new method for the assessment of body composition. Because this approach is safe, noninvasive, rapid, portable, inexpensive, and easy to use, it may be amenable for laboratory, clinical, and field assessment of human body composition. Many equations predicting FFM from weight, stature and resistance have been reported (Lukaski and Bolonchuk 1988; Segal et al 1988; Vasquez and Janosky 1991). Use of these equations to measure FFM in weight-stable subjects appears valid because of the high correlation between BIA and independently measured FFM. However, controversy exists in the validity of BIA to measure changes in FFM (Deurenberg et al 1989b; Kushner et al 1990). Moreover, Vazquez and Janosky (1991) found that neither resistance nor reactance changed significantly during reduction in body weight and prediction of FFM was based on factors other than resistance. Also, they showed that all equations used recently produced high prediction errors. Forbes et al (1992) analyzed the basic equation used in the bioelectrical impedance methods. They raised doubt about the applicability of the basic equation, which forms the foundation for this technique. The validity of BIA method to estimate body composition among patients with altered fluid and electrolyte status is a critical and unsolved question. Among such individuals, the TBW/FFM and the intracellular to extracellular fluid volume may be altered. Our results showed that significant differences in estimates of FFM and FM by the two methods persisted, however, the changes in FFM and FM compartments were not different between the two methods.

In this study a mean weight loss of 17.2 kg was found during the 3 month test period. Theoretically, 70-80% of this weight loss must be due to a loss of FM (Garrow 1978, 1981). Our results showed less FM loss during the first month (48.1 and 32.7% of FM loss measured by IDS method and BIA, respectively) than the theoretical value (70-80%). The percentage of fat loss increased with the passage of time (64.6 and 71.0% of FM loss by IDS method at 2 and 3 months; 65.0 and 70.9% of FM loss by BIA at 2 and 3 months). The results indicate that ileogastrostomy induced higher loss of FFM compared with the theoretical value of 20-30% of FFM loss, especially in the first month after surgery. The loss of FFM and FM at 2 and 3 months are similar to those reported previously following JIB (Brill et al 1972; Scott et al 1975), however, a smaller loss of FM was found during the first month in this study. Regardless of the validity of IDS method and BIA, our results suggest that BIA overestimated FM and %BF compared with estimates obtained by IDS method. However, there were no differences between the two methods in assessing the changes of FFM and FM following ileogastrostomy. It appears that IDS and BIA methods are capable of estimating changes in body composition, while there were significant differences in assessment of compartment size between the two methods.

Resolution of the reliability of IDS and BIA methods in assessing body composition and changes of FFM and FM compartments may require the use of advanced technology as reference method. Use of compositional models that account for altered fluid distribution are needed to avoid reliance upon the compartmental assumptions of a relatively constant TBW/FFM.

Dual energy x-ray absorptiometry has been developed to measure body composition and it is largely independent of compartmental assumptions. The error of DEXA was reported as ≈1% in %BF and 0.8 kg in FFM (Wellens et al 1994). In addition to the high precision of DEXA measurements, the procedure provides a direct measurement of both fatty and lean elements of the body, independent of dehydration state. Because of the characteristics of DEXA, we hypothesized that DEXA would be useful for validation of the IDS and BIA methods in which the assumption of water content in FFM is questionable. However, the validity of DEXA in obese subjects has not been investigated, thus, large errors in assessing body composition may occur in the morbidly obese subjects.

Our results using DEXA showed a significant decline in both FFM and FM after ileogastrostomy. The percentage of FFM and FM after surgery was not different from that presurgically. The result was in agreement with the finding in our first series of subjects using the IDS method. As expected, the estimates of BMC were unaffected by surgery. Regional changes in body composition data showed that ileogastrostomy reduced LM and FM mainly in the trunk and legs. There was a significant difference between total body mass by DEXA and BW by scale before surgery. This difference may be accounted for by the large BW before surgery because the BW of a few subjects exceeded 300 lb that was the recommended upper level of DEXA measurement. With the reduction in BW after ileogastrostomy, there was no significant difference in assessing body mass by DEXA and BW by scale, which was an evidence that large BW before surgery can influence the

precision of DEXA measurements. It has been reported that the precision of DEXA measurements deteriorated with increasing depths of soft tissue (Laskey et al 1992). Significant effects of depths and adiposity on measurements of FFM and FM were found in their study. It was suggested that DEXA might be least accurate for obese subjects.

A significant difference in FFM and FM determined by BIA and IDS methods was observed pre- and postsurgically, however, the estimates in FFM and FM by DEXA were not significantly different from those by BIA and IDS methods. Similarly, DEXA did not differ from BIA and IDS methods in the measurement of pre- and postsurgical percentages of BF. It appears that the estimates in FFM and FM by DEXA lay between those by BIA and IDS methods. These results suggest that BIA, IDS and DEXA, as applied in this study, gave poor measurement of body composition in the morbidly obese before and after ileogastrostomy. The differences may arise from biological as well as methodological sources. For the DEXA method the potential sources include the considerable range of body thickness obseved in some of the subjects which is known to influence the ratio of the x-ray beam attenuation. For BIA and IDS methods, the limitations have been discussed at the beginning of this section.

The changes in FFM and FM obtained by IDS method was generally comparable to that obtained by DEXA and different from that obtained by BIA. Furthermore, the percentage of these reduced FFM and FM likewise showed high agreement between IDS method and DEXA. However, the reduced FFM and FM determined by the three methods were not

very well correlated with each other.The poor intercorrelations in the changes of FFM and FM between each pair of the methods may be explained by small sample size and physiological changes induced by the surgical procedures. The different effects of these changes on individual method may lower the linear relationships between each pair of the method in the assessment of changed body composition after surgery.

Our results suggest that both DEXA and isotope dilution methods may accurately assess the decrease of FFM and FM compartments induced by ileogastrostomy. There was no evidence indicating inability of the isotope dilution method to measure changes in body composition after intestinal bypass surgery. It is unlikely that IDS method underestimated FFM compartment due to dehydration in these subjects after surgery, because FFM compartment determined by IDS method was higher than that by DEXA. Also, dehydration may not be obvious at 6 weeks after this procedure. In contrast, BIA may not be a good method for assessing the changes in body composition during the study period (within 6 weeks after surgery) and its validity may improve with the passage of time after surgery.

Acceptance of a method for assessing body composition is determined by the simplicity of the method as well as by its accuracy. Our results indicate that DEXA is a first choice for assessing changes in body composition in obese research if the subject's body weight is not excessive. DEXA has many advantages (Roubenoff et al 1993) in that DEXA is nonivasive and the variance of the estimates is not affected by the subjects. It may be a

better means to estimate body composition than IDS method for individuals with altered water status.

5.2. Changes in Energy Expenditure

The level of BEE tended to decrease in obese individuals following ileogastrostomy, however, this reduction in BEE was of borderline significance. Previous studies revealed conflicting results concerning the changes of BEE in obese individuals after weight reduction. Some investigators reported that the relative BEE was unchanged with weight loss (Dore et al 1982; Warnold et al 1978). Warnold et al (1978) determined basal metabolic rate (BMR) before and after dieting. They found that despite significant weight loss after dieting, BMR declined insignificantly which is accordant with our findings. On the other hand, Leibel and Hirsch (1984) reported that the BEE of obese individuals after weight loss was less than lean subjects with comparable FFM. This finding suggests that a prolonged reduction in BEE may follow weight loss although sequential body composition and metabolic measurements were not performed in their study. McFarland et al (1989) also reported that BMR declined following gastric partition and this decrease of BMR was due to the substantial reduction in energy intake.

To our knowledge, there are very few data reported on the energy expenditure after intestinal bypass surgery. Kopelman et al (1981) found a significant rise in serum 3'5'3' triiodothyronine (T_3) and a significant fall in 3'3'5 triiodothyronine (rT_3) concentration

between 15 and 20 weeks after bypass surgery. The increase of plasma T_3 induced by intestinal bypass surgery is contrary to what has been described in the literature after weight loss induced by dieting (Froidevaux et al 1993). It is generally accepted that low-energy diets induce a decrease of total T_3 concentrations in plasma and the reduction in T_3 is due to a decreased conversion of T_4 into T_3 in the peripheral tissues. In contrast to the findings with dieting, an increase in T_3 level after bypass was observed and this may contribute to the unchanged BEE and substantial weight loss seen after these procedures. However, we did not measure the changes in plasma T_3 levels.

The current investigation, based on measurements of energy expenditure and body composition, indicates that quantitative reduction in BEE was not associated with the changes in BW and FFM. Previous studies (Bessard et al 1983; Geissler et al 1987) attributed the reduction in BEE to a loss of FFM. The following explanations may account for our findings. Firstly, BEE in our study subjects declined slightly but insignificantly after surgery. Secondly, the small sample size (n=7) and large variability in both BEE and body composition data may contribute to the results in this study. Finally, the slight decrease in BEE may result from the reduced energy intake after surgery. It is possible that BEE gradually normalizes to presurgical level with the passage of time. Nevertheless, we failed to detect a significant decline in BEE following ileogastrostomy. Further studies are needed, especially with a larger sample size, to confirm our findings.

The possibility that impaired thermogenesis, which is a blunted increase in energy expenditure in response to certain stimuli, is associated with some types of human obesity has received considerable investigative attention. The present study does not support the concept of a reduced postprandial thermogenesis in obese subjects, although we do not have TEF data for normal-weight subjects. The presurgical TEF expressed as the percentage of either BEE or ingested meal was comparable to values reported in the literature for the normal-weight subjects (Bukkens 1991; Cunningham et al 1981; Felig et al 1983), where reduced thermic responses to food were not detected. Cunningham et al compared the thermogenesis after ingestion of an 800 kcal liquid meal (45% CHO, 40% fat and 15% prot) in 10 normal-weight and 10 obese subjects. They found that energy expenditure was consequently 22-24% higher in obese than in normal weight subjects throughout the postmeal period ($p<0.01$). It appeared that obese subjects did not show impaired thermogenesis. Yet a number of other studies (Bessard et al 1983; Schutz et al 1984; Segal et al 1987a, 1990) have shown that postprandial thermogenesis is significantly smaller in obese than in lean humans.

The controversy that exists in the relationship between thermogenesis and obesity might partly be due to heterogeneity of the obese and methodological differences concerning the techniques of measuring energy expenditure. The energy content of the meal used in this study was estimated from energy requirements to maintain IBW (Shetty 1981). There were two reasons to calculate the test meal based on IBW. Firstly, food given on the basis of IBW probably related better to the individual's active mass of metabolizing tissue than

total body weight (James et al 1978), therefore, the results could be more appropriate to compare with lean controls (Shetty 1981). It has been reported that TEF increases in the same subject with an increase in the meal's energy content (Morgan et al 1982). In this study, the energy load of test meal was lower than the energy requirement of the obese subjects, because the obese subjects had more active tissue than they were at IBW. Therefore, it was not possible to overestimate the values in TEF due to the lower energy load of the test meal. Secondly, we tried to minimize the differences in meal's energy content before and after surgery, because most subjects could not complete the food we provided after surgery.

A substantial reduction of TEF corrected for the difference in energy content and macronutrient composition was observed following ileogastrostomy. The reduced TEF after surgery may be partly due to malabsorption of nutrients. However, the dramatic and continuous decline in TEF cannot be explained by malabsorption alone since the bowel rapidly adapts to the state of a shortened gut (Cleator et al 1991). With the improvement of malabsorption, TEF did not show a rise in the present study. The finding was in accordance with dieting induced weight loss. Bessard et al (1983) found a significantly lower postprandial thermogenesis in obese subjects after weight loss when compared to lean subjects in response to a liquid mixed meal.

The increase in heat production that occurs after a meal has been divided into two parts: obligatory and facultative. Obligatory thermogenesis is released in the processes of

transport, metabolism, and assimilation of metabolites absorbed after digestion. The remainder of the thermogenesis include substrate cycles (Poehlman and Horton 1987). Quantitative significance of cycles in relation to heat production in humans cannot be fully understood at the present time. The decline in TEF following ileogastrostomy may be accounted for primarily on the basis of malabsorption of nutrients with the change in substrate cycles playing a secondary role.

What is the practical importance of the reduction in TEF after surgery? The extent to which energy is saved by a reduction in TEF may contribute to slowing-down and possible difficulty in achieving weight loss. The importance of the reduction in TEF on energy balance should be assessed together with the components of total energy expenditure.

Due to the shortage of DLW, we did not conduct presurgical TEE measurements. The TEE was measured during 6-8 weeks following ileogastrostomy. For theoretical and analytical purposes, TEE can be broken down into BEE, TEF and the energy cost of physical activities. BEE is a measure of the energy expended for maintenance of normal body function and homeostasis and usually, BEE equals 60-70% of TEE. Thermic effect of food is the increment in energy expenditure above BEE after food consumption and comprises ~10% of TEE. Energy expended for physical activity is the most variable component of TEE in humans. This component varies from <100 $kcal.d^{-1}$ for inactive persons to >1000 $kcal.d^{-1}$ for those who are active. In ordinary life, physical activity comprises 30% of TEE. Quantitatively, TEF, BEE and energy cost for physical activity in

patients after ileogastrostomy were determined in the present study. The value for TEF was 3% at the second month after surgery, which is lower than the theoretical value (10%) and that (9.1%) obtained in normal-weight subjects (Weststrate et al 1989). The relative percentage of presurgical TEF is unknown due to the lack of presurgical TEE in this study. However, the findings that presurgical TEF, expressed as the percentage of BEE or ingested energy, was comparable with that reported in normal-weight subjects (Bukkens 1991; Cunningham et al 1981; Felig et al 1983) suggest a higher percentage of TEF presurgically than that postsurgically (3%). The value for physical activity (44%) in this study was much higher than the average level and quite similar to those obtained in a group of patients after gastroplasty (Westerterp et al 1991), where TEE was measured by DLW method. Before surgery, the level of energy expended for physical activity was lower than that after surgery judging from the physical activity index (1.52 vs 1.63). It was concluded that activity might rise after weight loss in their study (Westerterp et al 1991). Factorial measurements of energy expenditure showed that physical activity index for women was 1.56, 1.64 and 1.82 for light, moderate and heavy activity levels, respectively (FAO/WHO/UNU report 1973). The physical activity index was 1.79 in the present study, which implied high physical activity levels in the subjects following ileogastrostomy.

To our knowledge, there has been no work to investigate TEE after intestinal bypass procedures that would be directly comparable to the present study. Controversies still exist about the relationship between changes in TEE and weight loss. Bradfield and Jourdan (1972) have studied six grossly obese women who lost 6 kg in one and half

months after dieting, and found no difference in TEE as predicted from heart rate/EE individual regression lines. A study by Westerterp et al (1990) reported that TEE may rise after weight loss because of increased physical activities. Most other studies found that TEE declined during and after weight loss. Bessard et al (1983) reported a significant reduction in TEE after weight loss. They calculated an EE equivalent of weight loss, averaging 18 $kcal.kg^{-1}$ weight loss per day. Ravussin et al (1985) also found a reduction in TEE and reported that approximately one half of the TEE reduction was accounted for by a decrease in BEE. Most of the remaining decline in TEE was explained by a decreased TEF, and by the reduced cost of physical activity mainly due to lower body weight (Ravussin et al 1985). Although the changes in TEE after ileogastrostomy remains unknown, the findings that BEE was unchanged after surgery and the level of energy expenditure for physical activity was high in this study suggest that TEE may not significantly decline following ileogastrostomy.

Preprandial fat and CHO oxidation rates were not affected by the surgical procedure and the RQ during BEE measurement was essentially unchanged during weight loss, although the energy balance was largely negative. These results are similar to those reported by Froidevaux et al (1993). There is some theoretical evidence that individuals who are close to energy balance have an overall non-protein RQ largely influenced by the amount of carbohydrate and fat in the diet (Bessard et al 1983). If only fat was being oxidized, the RQ would be about 0.7 and if only carbohydrate was being oxidized, the RQ would be 1.0. Most humans consuming a mixed diet will have an average RQ of about 0.87. When

the individual is in negative energy balance, endogenous fat is oxidized to provide energy. Therefore, significantly lower RQ may be observed. In this study, basal RQ level increased slightly but insignificantly, however, postprandial RQ declined significantly. The results indicate that ileogastrostomy induced high postprandial fat oxidation. A significant increase in postprandial fat oxidation and decrease in CHO oxidation was found in this study. These metabolic changes may be related to hormonal alterations induced by ileogastrostomy. Increased levels of insulin are characteristics of obesity. Hyperinsulinemia may reflect insulin resistance in the obese individuals. A significant decline in plasma insulin levels has been found in a previous study (Buchan et al 1993). It was suggested that the insulin sensitivity in postsurgical obese subjects was higher than that persurgery. However, the increased insulin sensitivity could not explain the changes in fat and carbohydrate oxidation observed after ileogastrostomy. The changes in insulin level may affect the partitioning of carbohydrate and fatty acids as fuel in the body resulting in enhanced utilization of the latter for energy.

5.3. Changes in Energy Intake

A significant reduction in food consumption has been recognized as a major cause for weight loss following intestinal bypass surgery (Bray et al 1978,1979; Brewer et al 1974). Our intake data indicate that energy intake declined significantly following ileogastrostomy. Nevertheless, postsurgical energy intake was not significantly different across the first 3 months. When intake was divided into protein, fat and carbohydrate, no

significant changes were observed in the percentage of energy obtained from these macronutrients. We did not demonstrate a significant association between reduced energy intake and weight loss due to large variability and small sample size in the present study. Similarly, the amount of energy consumed on the test days was not significantly correlated with the amount of weight loss over the preceding month.

Bray et al (1978;1979) measured the energy intake of 14 female patients before JIB surgery, and 3 weeks and 6 months after surgery. They found that energy intakes fell after surgery and there were no major changes in the distribution of calories consumed as protein, fat, and carbohydrate. Our results are accordant with their findings. However, they and others (Robinson et al 1979) found a high inverse correlation between energy intake and weight loss. Therefore, it was concluded that weight loss induced by JIB was accounted for primarily on the basis of decrease in energy intake with malabsorption playing a secondary role.

In agreement with Condon et al (1978), we did not show a significant relationship between energy intake and weight loss during the 3-month and 14-day balance study. We noted that some subjects increased their intakes after surgery although their body weight declined constantly and continously. Condon et al also found an increase of energy intake in some of their subjects. They measured the energy intake of 65 bypass patients. Of the 65 patients 48 decreased their food intake after surgery, whereas the remaining 17 patients increased their food intake. The difference in weight loss was not significant in the two

groups. There was also no close correlation between weight loss and energy intake in their study.

The study by Cleator et al (1991) demonstrated that reduced food intake and malabsorption were insufficient to account for the energy loss calculated from the changes in body composition. In this study, 12 morbidly obese subjects were studied before and after ileogastrostomy. Energy intake measured by 3-day food record and the decreased energy intake was calculated from preoperative 3-day energy intake minus postoperative value multiplied by 90 study days. Similarly, malabsorption was measured using 3-day fecal collection for the determination of fecal protein, carbohydrate and fat content which were converted to energy loss. The energy loss was calculated by multipling 9.4 for FM and 4.0 for 26.2% protein in FFM compartment. Approximately 1300 calories per day was unaccounted for using energy balance calculations. However, inaccuracy of energy intake data and the indirect estimation of energy loss in feces were the main concern in their study. Also, food intake and malabsorption changed with the passage of time after surgery. Food intake and fecal nutrient contents at the final 3 days may not represent the average values during the 90-day study period. Definite conclusion could not be drawn from simple calculation of energy balance.

A considerable variability in the degree of decreased energy intake, and in the relationship between postoperative undereating and weight loss existed in the previous studies (Benfield et al 1976; Condon et al 1979; Robinson et al 1979). This variability might be

due to the differences in energy intake measurement procedures and sampling periods used in the various studies. Table 22 lists some studies describing reduced energy intake following intestinal bypass surgery and the methods they used. The inaccuracy of dietary methods is the main concern about the role of reduced energy intake in weight loss after surgery. We believe that reduced energy intake contributed to the negative energy balance following ileogastrostomy, however, its magnitude in the weight loss could not be determined.

5.4. Factors Associated to Weight Loss Following Ileogastrostomy

Data concerning fecal energy loss in the present study provide evidence that malabsorption plays an important role in weight loss although it alone probably does not account for all of the postsurgical weight loss. Moreover, the findings indicate that malabsorption depends on the amount of the food taken. Further studies are required to clarify this relationship. A justifiable conclusion cannot be drawn from these results due

Table 22. Reports of Decreased Food Consumption Following Intestinal Bypass in Humans

Study	Subjects	Methods	Time
Bray et al (1979)	14 women	self-select preferred foods	pre-, 3 wk and 6 mo.
Condon et al (1978)	48 women, 17 men	weighed food record and dietary interview	pre- and 9 mo.
Cleator et al (1991)	12 women	dietary record	pre- and 3 mo.
Pilkington et al (1976)	8 women and 8 men	prepared diets	pre-, 4,12 and 24 mo.
Robinson et al (1979)	14 women, 17 men	questionnaire	pre, 2 wk and 4 mo.

to small sample size. Increasing the size of study sample may reduce some of the effects of misclassification. However, we believe that malabsorption existed and persisted at least 2 months after surgery, and fecal energy loss certainly contributed to the weight loss after ileogastrostomy. Many authors have concluded that malabsorption accounted for all of the weight loss after JIB (Corso and Joseph 1974; Scott et al 1971; Weisman 1973). Both Corso and Scott et al suggested that weight loss after JIB occurred in the absence of a significant decrease in energy intake, although actual intake was not measured in either series. A number of investigators have noted a distinctly inverse relationship between the length of small bowel left in continuity and the degree of weight loss. Our fecal energy data were comparable with that reported in the literature (Crisp et al 1977; Pilkington et al 1976; Robinson et al 1979; Scott et al 1971). Crisp et al (1977) reported that the loss of energy in the stools rose from 131 $kcal.d^{-1}$ preoperatively to a maximum of 593 $kcal.d^{-1}$ postoperatively. Scott et al (1971) also reported that the energy content of the stools rose from 100 $kcal.d^{-1}$ preoperatively to 500 $kcal.d^{-1}$ postoperatively. In agreement with these studies, our result favors the concept that malabsorption may be the major contributing factor to weight loss in intestinal bypass procedures.

A significant correlation existed between weight loss and energy expenditure in the present study. There has been no similar study to demonstrate the relationship between weight loss and energy expenditure as we did. Energy expenditure as a factor associated with weight loss following intestinal bypass procedures was proved in our study. A close negative association between the reduction in energy intake and weight loss was not

demonstrated in this study due to the inaccuracy of reported energy intake. We found that there was a marginally positive relationship between energy intake and energy expenditure as well as fecal energy which may complicate the role of reduced intake in the weight loss following intestinal bypass surgery. The simple regression analysis was performed in this study due to the small sample size. Ideally, multiple regression analysis should be performed as weight loss was a dependent variable and factors associated with the weight loss were independent variables. The relative contribution of these factors could be assessed by their coefficients in a multivariate model to correct the interclass correlations. The data available limited this statistical analysis. As to the mechanisms of weight loss after ilegastrostomy, we believe that reduced energy intake plays some role in the weight loss, especially in the very early stage. This may be the reason for lower loss of FM at the first month observed in this study

Urinary energy loss arose from incomplete oxidation of the organic matter. Most of the organic matter in urine are the nitrogenous compounds. It was proposed that measurement of urinary nitrogen by Micro-Kjeldahl procedure could be used to predict the energy loss in urine. A wide variation in the energy:nitrogen ratio was reported. Calculation of the urinary energy from energy:nitrogen ratio were always lower than the determined values (Southgate & Durnin 1969), although urinary energy was closely correlated with total nitrogen. We measured the urinary energy determined by bomb calorimetry which was comparable with that reported in normal subjects (Southgate & Durnin 1969). Furthermore, this urinary energy loss was not closely correlated with weight loss after

ileogastrostomy and we believed that the correlation cannot be improved with the increase of sample size. The possibility of other routes of energy loss which was suggested by a previous study (Cleator et al 1991) exists but is likely very small. Its contribution to the weight loss after ileogastrostomy is probably not important.

Although this study has strengths, two limitations may have affected the conclusion we can draw. First, the inaccuracy of energy intake may have introduced significant error in the amount reported versus what they truly ate, which may underestimate the association between intake and weight loss. Second, the small sample size limits the ability to reach a justifiable conclusion.

5.5. Validation of Reported Energy Intake Using DLW Method

We found that the disagreement between TEE and energy intake after correcting for the changes in body composition was 20.5% and 42.0% of TEE in normal-weight and obese subjects, respectively. Our use of the DLW method as a reference test revealed serious discrepancies between estimates of energy intake and expenditure. Such has been the result of many other studies (Bandini et al 1990; Prentice et al 1986; Westerterp et al 1986). The discrepancy raises several important questions. Firstly, did the error occur in the estimation of energy intake or expenditure? Secondly, if it occurred in the estimation of energy intake were the results spurious or could they have general implications for

dietary research? Finally, might biased results be identifiable or related to some physical characteristics in subjects studied?

The DLW method is based on the differential elimination of ^{2}D and ^{18}O from body water subsequent to a loading dose of these stable isotopes. The difference between the two elimination rates is therefore a measure of carbon dioxide production, from which total daily energy expenditure is calculated according to the methods of indirect calorimetry. The method has been validated in small animals by comparing the method with measured carbon dioxide and the accuracy of DLW method has been reported to be 1-2%, with a relative standard deviation of 3-9% (Nagy et al 1980). The method has been validated in infants and young adults, healthy individuals and patients with gastrointestinal disorders, subjects under metabolic ward conditions, and free-living individuals under laboratory and nonlaboratory conditions (Jones et al 1978; Jones and Leitch 1993a; Livingstone et al 1990; Schoeller et al 1986, 1988). None of the studies indicated any significant bias. When data from all of these studies are combined the results suggest a small overestimation of expenditure by 2-3%.

The accuracy of the method is not significantly affected by energy balance (Schoeller et al 1986) or physical activity (Westerterp et al 1988). Schoeller et al (1986) investigated the error in the DLW method as a function of energy balance to determine whether the accuracy of the method is affected by the energy imbalance. Regression of percent error calculated from the difference with the reference method against energy balance status

(negative, zero and positive balance) was not statistically significant. The 95% confidence limit about the slope suggests that the DLW error lies between -0.21% and +0.07%. Black et al (1986) also covered most of the nutritional and physiological circumstances in which the DLW method is likely to be applied and demonstrated that errors arising from assuming an RQ of 0.85 were very small. A mean FQ value to each community can be used without incurring significant error, although the precision can be improved still further by assessing each individual's FQ. The influence of energy balance on the estimation of RQ using individual's FQ values may be large and need to be considered in clinical studies involving rapid changes in body composition. Even if such changes in body composition cannot be accurately assessed, the error for prediction of RQ from FQ should never exceed ±2 percent. The total estimated error of the DLW method can be calculated using a root-mean-square summation of the errors arising from prediction of CO_2 production and the RQ assumption. The propagation of error analysis shows that the DLW method is robust and unlikely to be biased by more than 5% (Schoeller et al 1988). In subjects in energy imbalance errors in calculated energy expenditure will rarely exceed 3-5% even if the imbalance is ignored. Therefore, DLW method is considered to be the most accurate method of assessing energy expenditure in free-living populations and valid in obese subjects during weight loss.

Previous work conducted in our laboratory entailed validation (Jones et al 1987; Jones and Leitch 1993a) and ongoing applications (Jones et al 1988,1993b; Su and Jones 1993) work in both humans and animals. Furthermore, our results of energy expenditure were

comparable to those reported in the literature (Banduni et al 1990; Welle 1992). Studies comparing TEE between normal-weight and obese subjects using DLW method are summarized in Table 23. Comparison of TEE between obese and normal-weight subjects may not be appropriate in this study since the TEE in obese group was measured during the dynamic phase of weight loss.

It is therefore reasonable to conclude that the observed discrepancies arose largely from inaccurate estimates of habitual energy intake due to conscious or subconscious changes in normal dietary patterns or underreporting, or both. It is generally accepted that the arduous task of recording food intake may contribute to the unintentional underreporting of energy intake (Block and Hartman 1989). The major factors involved in generating valid nutrient estimation include the following: (1) selection of an appropriate data collection methodology; (2) adequate level of food description; (3) appropriate techniques for quantifying amounts of food consumed; and (4) use of quality-controlled nutrient calculation system that provides an adequate level of specificity. All the nutrient calculation systems used recently are not complete and specific with the rapidly expanding number of foods available and increasing variety of foods in the diets. Difficulties in analyzing food records may also result in large errors in the nutrient calculation. Token together, bias in estimation of energy intake may underestimate or overestimate the association between energy intake and weight loss following intestinal bypass surgery. Also, this may be the reason for much of the controversies existed in the past.

Table 23. Studies Comparing Total Energy Expenditure in Normal-weight and Overweight Subjects, Using the Doubly Labeled Water Method

Reference	Group	Mean weight (kg)	Mean TEE (kcal/d)
Prentice et al (1986)	Normal weight women (n=13)	58±6	1914±287
	Overweight women (n=9)	88±14	2440±335
Bandini et al (1990)	Normal-weight boys (n=13)	56±10	3110±502
	Overweight boys (n=18)	94±26	3614±646
	Normal-weight girls (n=12)	55±9	2392±455
	Overweight girls (n=15)	99±22	3278±431
Welle et al (1992)	Normal-weight women (n=12)	60±4	2273±215
	Overweight women (n=26)	85±11	2679±431
Present study	Normal-weight women (n=26)	62±7	2215±518
	Overweight women (n=10)	104±10	2898±564

As we compared energy intake data with objective measures of energy expenditure in normal-weight subjects, underestimation of food intake was also apparent in normal-weight group. Furthermore, the errors in estimating food intake are unlikely to be specific to the current study. Studies using the DLW method, conducted among diverse age groups with a variety of health and/or disease states, confirm that self-report of energy intake tends to be lower than measured total energy expenditure (Johnson et al 1994; Lichtman et al 1992; Livingstone et al 1990; Schoeller 1990). Taken collectively, these studies found that reported food intakes underestimated habitual energy intakes.

The magnitude of underreporting (20.5% in normal-weight group, 42.0% in obese group) in the present study is comparable with other published reports (Bandini et al 1990; Livingstone et al 1990; Mertz et al 1991). Bandini et al (1990) compared reported intake with expenditure determined by DLW method in obese and nonobese adolescents. Reported intake represented 81±19 and 59±24% of measured expenditure in nonobese and obese, respectively. Livingstone et al (1990) compared energy intake as measured by 7-day weighed records and total energy expenditure measure concurrently with the DLW method and found that on average the men underreported their intake by 19% and the women by 18%. In agreement with the literature, underreporting has been found to occur to a greater degree among obese than among normal-weight subjects. Lichtman et al (1992) reported that young obese subjects underreported their actual food intake by 47% and Lansky found reporting errors that averaged 53%. To date there is a paucity of work

done in bypassed obese subjects. This study provides new information on the degree of underreporting of energy intake that occurs in bypassed patients.

The DLW method is too expensive and technically demanding to be used as a validator of energy intake measurements in large samples. It is possible that certain physiological characteristics may be predictors of the discrepancy between reported energy intake and total energy expenditure. Elucidating the relationship between these characteristics and the misreporting of energy intake could be a meaningful step toward the application of correction factors to arrive at more accurate determinations of habitual energy intake. Thus, we tried to develop a prediction equation for understanding the bias that may exist in reported energy intake data collected from both normal-weight and obese individuals using independent variables, which are easily measured in a clinical settings. In our sample, both normal-weight and obese women were likely to underreport their energy intake. We found that there was no relationship between physical variables and underreporting of energy intake in normal-weight women. Thus, research is needed to examine other non-physiological characteristics (income, marital, and educational status). However, body weight was a good predictor of underreporting of energy intake in obese women. Although the reason for this finding is unclear, it is possible that obese women purposely reduce their recording of food, which made them appear to be 'smaller eaters'.

Johnson et al (1994) examined the relationship between physical characteristics and the underreporting of energy intake in healthy older men and women. Reported energy intake

was obtained from a 3-day food diary and total energy expenditure was predicted by using a published equation (Goran and Poehlman 1992). Predicted total energy expenditure was significantly higher than reported energy intake in both men and women. On average, men underreported their intake by 12% and the women by 24%. Also, the over- and underreporting of energy intake were not significantly correlated with any of the measured physical variables in the men. Among the women, underreporting of energy intake increased as FM and %BF increased. Percent body fat explained the most variation in underreporting of energy intake ($r = -0.42$, $p=0.001$). The major findings were that older women underreported energy intake to a greater degree than did older men and increasing adiposity was an independent predictor of underreporting in older women. Due to lack of independent measurement of FM in the present study, we did not show the relationship between underestimation and %BF. However, the high correlation between underestimation and body weight in obese group suggest that %BF may be a good predictor of underreporting of energy intake.

We have defined body weight that was associated with underreporting of energy intake in obese subjects. It will be helpful to use this knowledge and begin to apply correction factors to reported energy intakes. Unfortunately, the small numbers and undefined variables in this study did not provide definitive markers and likely provided biased estimates of intake.

The future research should address the validity of the BIA, IDS and DEXA methods to estimate the changes in body composition during weight loss in patients with abnormal

water and electrolyte distributions using a multicompartmental assessment of body composition model in controlled studies. Adequate cross-validation of DEXA should be performed as has been done for BIA and IDS methods. Addition of presurgical TEE measurement would certainly strengthen the experimental design and provide valuable information about influence of ileogastrostomy on TEE. Improvement of energy intake measurement is necessary to clarify the role of reduced energy intake in the weight loss following intestinal procedures. Alternatively, further studies are needed to identify correlates of underreporting and to correct the underreporting using conversion factors.

6. SUMMARY AND CONCLUSIONS

The results of this investigation indicate that ileogastrostomy induces a significant decline in FFM and FM measured by IDS method, BIA or DEXA, while the percentage of FFM and FM was not changed significantly. Bone mineral content determined by DEXA was not affected by ileogastrostomy. From the present study, it cannot be concluded which method most accurately assesses body composition in morbidly obese subjects. Isotope dilution method and DEXA seem to be applicable to detect the changes in body composition after intestinal bypass surgery. However, BIA was not a good choice for these patients, especially during the very early stage.

Basal energy expenditure declined slightly but insignificantly, however, a substantial and continuous decline in TEF was induced by ileogastrostomy. The direction of changes in TEE is still unknown because we did not measure presurgical TEE in this study. The TEE during the short-term energy balance study demonstrated a significantly close correlation with weight loss. Therefore, we concluded that energy expenditure may be an important factor in the weight loss after intestinal bypass procedures.

Increased fecal energy loss was identified to be an important factor in the weight loss in the present study, although its relative importance cannot be determined due to the small sample size. We did not find a close relationship between urinary energy and weight loss after ileogastrostomy.The urinary energy loss was comparable with normal individuals.

Therefore, we believed that the difference existed in the energy balance equation may result from misreporting of energy intake as reported in many recent publications. The notion was supported by the validation of reported energy intake in normal-weight subjects. There were discrepancies between energy intake and expenditure observed in both normal-weight and obese subjects. Misreporting of energy intake appears to occur in both normal-weight and obese populations. The use of DLW method as an independent marker of food intake has raised serious concern about the validity of much of the food-intake data published previously and the conclusion they have drawn. Therefore, reduced energy intake as a major cause in the weight loss following intestinal bypass procedures need to be further evaluated. To a limited extent, this study has provided the data for the direction and magnitude of misreporting of actual energy intake in normal-weight and obese subjects.

These results have provided valuable information not only about weight loss and assessment of this weight loss but also about changes in energy metabolism. Energy expenditure was first proved as a factor in the weight loss after intestinal bypass procedures. The most challenging findings were to identify the serious problems in energy intake data, although our study cannot provide definitive solution to correct this bias in present dietary assessment approaches.

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Appendix 1. Invitation Letter for Obesity Study

Dear_____

I am writing to invite you to participate in a study "Examination of weight loss and changes in energy metabolism following ileogastrostomy" because you are scheduled for the surgical procedure. Obesity can be effectively corrected by ileogastrostomy. However, the mechanism of weight loss is still unknown. The purpose of this study is to help determine factors associated with weight loss following ileogastrostomy.

The study will last for 3 months after surgery. If you decide to take part in this study, you will need to:

1). have metabolic tests done at St. Paul's Hospital at 4 different times (one before surgery, the others 1, 2 and 3 months following surgery;
2). Write down everything you eat and drink for 3 days before each test;
3). Have total body scan measured by DEXA twice; and
4). Collect urine and feces completely for 5 days within 6-8 weeks following surgery.

The total time commitment is about 25 hours. You will be compensated with $100 for your participation in this study. Your participation is voluntary. You may decide not to participate or withdraw from the study at any time without affecting your normal treatment. If you are interested in the study, please call Dr. Jones at 822-6253.

Sincerely

_____

Appendix 2. Sample Consent Form

CONSENT FORM

Title: **Examination of Weight Loss and Energy Metabolism Following Ileogastrostomy**

Investigators:	Dr. Peter Jones	#822-6253
	Dr. Iain Cleator	# 681-1513
	Dr. Laird Birmingham	# 631-5269

You are being invited to participate in a study, "Examination of Weight Loss and Energy Metabolism Following Ileogastrostomy", because you are scheduled for the surgical procedure. You may decide not to participate or may withdraw from the study at any time without affecting your normal treatment.

Purpose of the Study:

Obesity can be effectively corrected by ileogastrostomy. However, the mechanism of weight loss is still unknown. The purpose of this study is to help determine factors associated with weight loss following ileogastrostomy.

Procedures:

If you decide to take part in this study, you will need to go to St. Paul's Hospital at 4 different times, once before surgery and the others at 1, 2 and 3 months after surgery, for metabolic tests. During the tests, you will lie on the bed and wear a plastic hood. Your breath will go to a monitor which can analyze how much oxygen you inhale, how much carbon dioxide you exhale and how much energy your body is using. You will be requested to drink a small amount of stable isotope (no radioactivity). We will collect a small amount of saliva sample to determine the fat mass and fat free mass in your body. Each metabolic test will require 6 hours of your time.

You will need to write down everything you eat and drink for 3 days before each test. In addition, you need to collect urine and feces completely for 5 days within 6-8 weeks following surgery. We will provide containers and deliver the freezer to your home.

DEXA (to measure the changes of fat, muscles and bone density in your body after surgery) will be done twice, once before surgery and the other at 6 wks following surgery on the same day of the metabolic test. The scan will be performed in the Department of

Nuclear Medicine at St. Paul's. The scanner will take a series of pictures to estimate your body compartments.

Total Time Commitment:
The study will last for 3 months after surgery. The total time commitment is about 25 hours.

Risks and Significant Side Effects:
There are no risks associated with the metabolic tests. During the DEXA scan, you will be exposed to a very small amount of radiation. The radiation exposure is equivalent to 10% of that a regular chest x-ray.

Potential Benefits:
There will be no direct benefit to you. However, improved understanding of the mechanism of weight loss after surgery has potential application for effecting or achieving weight loss without surgery and for maintaining weight loss after such surgery.

Monetary Compensation:
You will be compensated with $100 for your participation in the study.

Confidentiality:
All data collected for this study will be kept confidential. Only Dr. Jones, Dr. Cleator and Dr. Birmingham will have access to the data. The records will be identified by code numbers, not by patient names.

If you have any questions or concerns at any time during the study, you may contact Dr. Jones or Dr. Cleator at the numbers listed above.

****

I have read the above information. I freely consent to participate in the study and acknowledge receipt of a copy of the consent form.

_____ _____

Signature of Participant Date

_____ _____

Signature of Witness Date

Appendix 3. Food Record Instructions

PLEASE READ CAREFULLY:

1. Write down EVERYTHING you eat and drink. Be sure to include all SNACKS and ALCOHOL. Record immediately after each meal and snack to ensure accuracy.

2. Write down HOW MUCH you eat and drink using the scale provided.
   A. Try to use GRAM measures.
   B. Be specific about the TYPE OF FOOD, BRAND NAME IF APPLICABLE, HOW THE FOOD WAS PREPARED, AND CONTENT OF MIXED DISHES.
   C. For combination items, list each item separately, e.g. a cheeseburger would be described as: bun, cooked ground beef, processed cheese, butter, relish, etc.
   D. IF THE FOOD IS PREPARED BY SOMEONE OTHER THAN YOURSELF: please try to describe the contents of the dish that is served to you and estimate the amount.
   E. If you leave some foods you have weighed, please write down HOW MUCH and the TYPES.
   F. Don't forget the EXTRAS! e.g. sugar on cereal or in coffee, dressing on salad, candy, soft drinks, alcohol.

Appendix 4. Sample of Food Record

Name_____ Subject #_____ Age_____years old

Height_____cm Weight_____kg

Test #_____ Date_____

Comments_____

Meals	Types and Amounts (g)	left-over Foods
Breakfast		
Lunch		
Supper		
Others		

Appendix 5. Sample of Test Meal

Estimation of energy requirement for individual subject using Mifflin's equation:

REE(male)=10×body weight (kg)+6.25×height (cm)-5×age+5

REE(female)=10×body weight (kg)+6.25×height (cm)-5×age-161

multiplied by 1.7 and 1.6 activity factor for male and female, respectively.
Because this group of subjects was morbidly obese, the ideal body weight was used to calculate the energy requirement for individual subject

The energy content for test meal was derived from the estimated energy requirement for individual subject times 30% for breakfast. This amount of energy was distributed to fat, CHO and protein, and served to the subjects as following foods.

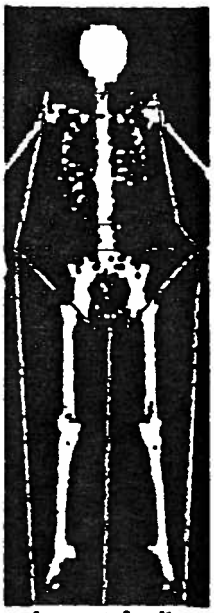
Food Item	Quantity
cereals	gram
2% milk	ml
orange juice	ml
soft sunflower margarine	gram
omelette egg whites egg yolk soft sunflower margarine	gram
whole wheat bread	gram

Appendix 6. Sample of Dual Energy X-ray Absorptiometry

St. Paul's Hospital Nuclear Medicine Dept.
1081 Burrard St. Vancouver, B.C. Ph. 631-5008

ID J3451 *Ethnic* CAUCASIAN
Age 40 *Sex* Female *Height* 160
Weight 119

L R Body 04/06/94 Sequence 1



Bone Image not for diagnosis

Total BMD (g/cm)	:	1.354
Total BMC (g)	:	3313
Total Lean Mass(g)	:	52263
Total Fat Mass (g)	:	61717
Total Fat %	:	52.6
Siri UWE Fat %	:	45.2
Brozek UWE Fat %	:	43.0
Soft Tissue Fat %	:	54.1
% TBMC/FFM	:	6.0

STD CV for Total BMD: 1.0 See Guide for other CVs.
6.5 x 13.0 mm, 180 mm/s, 61.75 cm Rev. 2.5.0 / 1.3.0 Calib. 04/06/94

COMMENTS NOTE: PATIENT'S FOREARMS ARE NOT IN THE FIELD OF VIEW

SCAN INFORMATION

Type Body
Scan Date-Seq 04/06/94 1
Analysis Date 04/06/94
Calibration Date 04/06/94
Technician RF
Physician DR. CLEATOR

Resolution 6.5 x 13.0 mm
Speed 180 mm/s
Width 61.75 cm
Host/Scanner 2.5.0 / 1.3.0
Analysis Revision 2.5.0

DETAILED RESULTS

	BMD g/cm²	BMC g	AREA cm²	LENGTH cm	WIDTH cm	LEAN MASS g	FAT MASS g
Head	2.408	580.0	240.9			3596	1057
Trunk	1.243	1349	1086			27326	36553
Abdomen	1.579	640.7	405.7			11676	16921
Arms	1.015	205.8	202.8			3103	5341
Legs	1.284	1178	917.4			18236	18766
Total	1.354	3313	2447			52263	61717

Appendix 7. Preparation of Doubly Labeled Water and Instruction Sheet for Total Energy Expenditure Measurement .

Original doubly labeled water was filtered and weighed to estimate exact amount of ^{18}O and ^{2}D in the solution. The final ratio of ^{18}O:^{2}D was 2.5:1 which was assumed as the optimal dose (Schoeller 1988).

Total Energy Expenditure Instructions

PLEASE READ CAREFULLY:

1. Fill out the information sheet in the blank.

2. Collect 3h and 4h saliva samples after administration of DLW.

3. Collect urine samples (10 ml) in the morning and afternoon at day 1.

4. collect urine samples at day 7 and day 14 as you did in day 1.

5. Select 5 days during this two-week period to COMPLETELY collect fecal and urinary materials into the containers provided. In the meantime, write down EVERYTHING you eat and drink in these 5 days using the scale as you did in presurgical test.

5. If you have any comments, please write down in the information sheet in detail such as diarrhea, vomiting.

6. On day 15, you need to visit the Metabolic Lab. and a further dose of D_2O will be given and 3h and 4h saliva samples will be collected.

Total Energy Expenditure Information Sheet

Name_____ Date_____ Initial Body Weight_____ Final Body Weight_____

Dose of DLW_____

Date and time for sample collection

Day 1_____	Comments_____	Day 2_____	Comments_____
Day 3_____	_____	Day 4_____	_____
Day 5_____	_____	Day 6_____	_____
Day 7_____	_____	Day 8_____	_____
Day 9_____	_____	Day 10_____	_____
Day 11_____	_____	Day 12_____	_____
Day 13_____	_____	Day 14_____	_____

Appendix 8. Postoperative Complications

Type of complication	*No. of patients*	*Interval (weeks)*
Wound infection	2, 6	2-3
Severe nausea and vomiting	4	7-12
Diarrhea	almost all patients except 1	throughout the study
need for antidiarrheal agent	most patients	
foul-smelling flatus	most patients	
thirst	1,5,11,15	4-12
electrolyte imbalance		
hypokalemia	2	8
Anemia	2	8
hypoproteinemia	2, 4	8
stomal ulcer	4	12
disturbances of liver functions cholelithiasis	3	7-8

Appendix 9. The Relationship Between Body Composition and Energy Expenditure

	BEE $_{-1}$ (kcal.min^{-1})	BW (kg)	FFM (kg)	FM (kg)	EI $_{-1}$ (kcal.d^{-1})	R_1 (P_1)	R_2 (P_2)	R_3 (P_3)	R4 (P4)
0 mo.	1.16±0.07	111.1±3.2	59.8±2.8	51.2±2.6	2022±295	0.49 (0.27)	0.12 (0.80)	0.73 (0.06)	0.04 (0.93)
1 mo.	1.10±0.06	105.9±3.0	57.1±2.7	48.8±2.2	1393±201	0.60 (0.15)	0.16 (0.73)	0.62 (0.14)	0.89 (0.01)
2 mo.	1.07±0.05	101.7±2.4	55.6±2.8	46.1±2.3	998±158	0.75 (0.05)	0.27 (0.55)	0.45 (0.32)	0.74 (0.06)
3 mo.	1.04±0.04	93.9±3.1	52.9±3.4	41.0±2.4	1164±201	0.82 (0.02)	0.74 (0.06)	0.01 (0.97)	0.79 0.03
	rBEE	rBW	rFFM	rFM	rEI	rR_1 rP_1	rR_2 rP_2	rR_3 rP_3	rR_4 rP_4
1 mo.	0.06±0.06	5.2±0.6	2.7±0.6	2.5±0.6	628±299	0.31 (0.49)	0.50 (0.25)	0.21 (0.66)	0.09 (0.85)
2 mo.	0.02±0.02	4.2±0.7	1.5±0.5	2.7±0.7	1023±231	0.34 (0.46)	0.34 (0.46)	0.13 (0.78)	0.30 (0.51)
3 mo.	0.03±0.02	7.6±1.2	2.7±1.0	5.1±0.9	858±141	0.04 (0.93)	0.21 (0.65)	0.31 (0.50)	0.22 (0.63)

Values are mean±SEM (n=7). BEE, BW, FFM, FM and EI represent basal energy expenditure, body weight, fat-free mass, fat mass and energy intake. rBEE, rBW, rLBM, rFM and rEI are the reduced BEE, BW, FFM, FM and EI calculated from corresponding presurgical data minus postsurgical data.

R_1, R_2, R_3 and R_4 are the correlation coefficients between BEE and BW, FFM, FM, and EI, respectively. P_1, P_2, P_3 and P_4 are the corresponding probabilities for these variables.