RESTING METABOLIC RATES IN CHILD-ONSET AND ADULT-ONSET OBESE WOMEN

by

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ABSTRACT

Title of Dissertation: RESTING METABOLIC RATES IN CHILD-ONSET AND ADULT-ONSET OBESE WOMEN

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This study investigated differences in resting metabolic rate (RMR) between obese and nonobese females and between females with adult and childhood onset of obesity. Subjects were 18 healthy, Caucasian women, ages 20-38 (M = 28.16 years), 6 from each of 3 groups: nonobese with no history of obesity (M = 18.53% fat), child-onset obese (COO) (M = 41.00% fat), and adult-onset obese (AOO) (M = 37.80% fat). Subjects were nonsmokers, weight-stable for at least 3 months prior to the study, and not following a low-calorie diet. All obese subjects had lower-body obesity (waist/hip girth ratio < .80).

Subjects underwent three measures: RMR by indirect calorimetry, residual lung volume, and hydrostatic weighing. In addition, a questionnaire elicited information about weight history, educational level, occupation, frequency of exercise, and activity level.

When data from the 12 obese subjects were combined, RMR per kg body weight (RMR/BW) was significantly lower in

the obese (18.47 kcal/kg/day) than the nonobese (22.94 kcal/kg/day). The obese subjects also had significantly lower RMR per kg fat mass (RMR/FM) than the nonobese. When data from COO and AOO subjects were analyzed separately, COO were found to have significantly lower RMR/BW (17.00 kcal/kg/day) than the nonobese. The difference between AOO and nonobese subjects in RMR/BW was not significant. Both AOO and COO had significantly lower RMR/FM than the nonobese. COO and AOO subjects did not differ statistically in absolute RMR, RMR/BW, RMR/FM, or RMR/FFM, although COO had lower values on all measures.

Multiple regression analysis indicated that, in all groups, more of the variance in RMR was explained when the variables, activity and exercise, were used in addition to the variables, FM and FFM. However, the effect of activity and exercise on explained variance in RMR was much smaller in COO women.

These results indicate that obese women, especially COO, may be more metabolically efficient than nonobese women. Future research is needed to determine if COO women are less able to benefit metabolically from the addition of exercise and physical activity to their daily regimen.

DEDICATION

This dissertation is dedicated to my family: to my parents, who encouraged their children to think; my sister, who made sure that I thought often about chemistry; my husband, who never complained when I didn't think about him; and my daughter, who never let me forget to look out the window once in a while.

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I would like to express my deep gratitude to Dr. Patricia Mann who guided me through 5 years of study with enthusiasm and good humor. I am also grateful to my employers at Marymount University, in particular Dr. Martha John who not only provided release time but encouragement and support.

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LIST OF ABBREVIATIONS

ACM	active cell mass
AOO	adult-onset obesity
BMR	basal metabolic rate
BW	body weight
cm	centimeter
COO	child-onset obesity
ERV	expiratory reserve volume
FFM	fat-free mass
FM	fat mass
FRC	functional residual capacity
kcal	kilocalorie
kg	kilogram
LBM	lean body mass
$\underline{M}$	arithmetic mean
RMR	resting metabolic rate
RMR/BW	resting metabolic rate per kg body weight
RMR/FFM	resting metabolic rate per kg fat-free mass
RMR/FM	resting metabolic rate per kg fat mass
WHR	waist/hip girth ratio

CHAPTER 1 INTRODUCTION

Introduction

Estimates of the incidence of obesity in the United States vary from 12 to 26% of the adult population, depending upon whether obesity (excess fat) or overweight (excess weight) is the criterion being measured. The 1977 National Health Interview Survey found 26% of the population to be overweight, defined as weighing more than 120% of the 1959 Metropolitan Life Insurance Company's recommended weight-for-height (Forman et al., 1986). More recently, the Rand Health Insurance Experiment found 22% of the population surveyed to be overweight, 10% to be moderately overweight, and 12% severely overweight, using body mass index (weight divided by the square of height for men and weight divided by the 1.5 power of height for women) as criteria (Stewart & Brook, 1983). Van Itallie (1985) estimates that 13% of the adult U.S. population is obese, defined as overfat.

Obesity is widely considered to be a disorder of energy balance, where either energy in exceeds energy out or the reverse occurs (Bray, 1983; Danforth, 1985). The early experiments of Atwater and Benedict (1903) and of Rubner (1883; cited in Keys et al., 1973) established that the Law of Conservation of Energy, the First Law of Thermodynamics, could be applied to humans. That is,

energy balance in humans could be represented by the following equation:

Energy Intake = Energy Expenditure +/- Energy Storage

The treatment of obesity would therefore seem simple: to upset one side of the energy balance equation so that energy stored in the body is lost and a reduction in body fat occurs. However, despite this apparent simplicity, decades of study have failed to identify a uniform method of treatment for obesity that is safe, effective, and long-lasting.

Several reasons for this may be postulated. Most importantly, there has probably been an overemphasis on dietary intake. The term obesity is thought to derive from the Latin ob, meaning "over," and edere, meaning "to eat" (Sims, 1982). Yet, studies of food intake of obese individuals do not consistently support the notion that the obese consume more food than the nonobese (Bray, 1983; Curtis & Bradfield, 1971; Horton & Danforth, 1982; Maxfield & Konishi, 1966). In those studies in which caloric insufficiency has been induced, the obese have been found to demonstrate a rapid reduction in metabolic rate which offsets any decrease in the "energy in" side of the energy balance equation (Bray, 1969). Studies of the post-obese have indicated that fewer calories are required by the formerly obese than by the nonobese to maintain the same level of body weight (Geissler et al., 1987; Leibel &

Hirsch, 1984). Further, a recent study by Ravussin et al. (1988) reported a significant correlation between low resting metabolic rate (RMR) and subsequent weight gain among 95 southwestern American Indians, which suggests that the development and maintenance of obesity may be more closely related to "energy out" than to "energy in".

If "energy out" is more critical to the maintenance of obesity than "energy in," the question becomes one of trying to determine which aspect of energy expenditure is at fault. Some researchers have found the obese to be less active than the nonobese, which would result in less caloric expenditure in physical activity per day (Bloom & Eidex, 1967b). Others suggest long-term after-effects of dieting may permanently reduce metabolic rate in the obese (Donahoe et al., 1984). Also the idea of greater metabolic efficiency in the obese has been explored (Ravussin et al., 1982).

Activity Levels of the Obese

Tryon (1987) had lean and obese subjects wear a gravity-activated switch sensitive to changes in knee angle which would occur when a subject went from standing to sitting or sitting to lying. The 7 obese subjects spent 21.7% of the day standing, compared with 6 lean subjects, who spent about 36% of the day standing. The obese spent significantly more time lying down than the lean -- up to one hour per day. As a result of less time

standing or even sitting, the authors concluded that the obese may spend more time at the basal level than the nonobese. In time, this difference could have significant impact on caloric expenditure.

In a study of housewives where subjects self-reported activity, Durnin et al. (1957) found obese women to spend 5% less time in moderate activities than their normal-weight counterparts and 5% more time in sitting and light activities than the nonobese. Because moderate household activities and walking would result in a greater caloric cost for the obese than the nonobese, lack of such activities was thought to contribute to maintenance of the obese state in these subjects.

Not all authors have found the obese to expend less energy, however. Bloom and Eidex (1967a) categorized male and female college students of various weights as underweight or overweight. Subjects wore actometers on all four limbs 24 hours per day for 14 consecutive days. All groups were found equally active, although as degree of overweight increased above 18% in women and 20% in men, activity level began to decrease. Prentice et al. (1986) found average daily energy expenditure for the obese and lean to be very similar -- 9.3 kcal/kg body weight/day for the lean and 9.6 kcal/kg body weight/day for the obese. The amount of discretionary activity performed by each group was identical.

Dieting Effects on Energy Expenditure

Reduced caloric intake is perhaps the commonest treatment for obesity. The Rand Health Insurance Experiment provides a variety of demographic and health care information on almost 6,000 nonobese and obese Americans ages 14 to 61. Slightly less than one-fourth of these individuals were under a physician's care for weight loss, and 91% of that number were using "dieting" (Stewart & Brook, 1983). Yet, reduced caloric intake, even in the lean, will have a suppressive effect on RMR, typically slowing attempts at weight loss (Keys et al., 1950).

Drennick and Dennin (1973) found that a 500 kcal per day diet lowered 24-hour energy expenditure from a mean of 3,600 kcal per day during the control period to 2,500 kcal per day after a 3 week fast in obese men. Similar findings have been reported with obese women. For example, 14 moderately obese women showed a slight but significant loss of lean body mass after a 9 week 800 kcal per day diet, but their RMR decreased significantly throughout the diet (Henson et al., 1987).

If the RMR is reduced due to dieting, weight loss can be elusive. Apfelbaum et al. (1971) put 41 obese men and women on a 220 kcal/day protein diet. BMRs of subjects dropped approximately .9% per day, so that after the 15 day diet, 24 hour oxygen consumption was 15-35% below its pre-diet level. The authors calculated that 170 grams of

fat (equivalent to 1,530 kcal) was lost each day during the 2,100 kcal per day deficit diet. Lowered metabolic rate hindered greater fat loss.

Interestingly, Miller and Parsonage (1975) found no significant correlation between BMR and duration of previous dieting in 29 obese women. Yet, the authors could have predicted which women would reduce body weight on a 1,500 kcal per day diet, based upon pre-diet BMR. This suggests that, at least in some instances, the reduced BMR of obesity has other causes.

Metabolic Efficiency and the Resting Metabolic Rate

Basal metabolism has been studied for over 100 years. The first experiments in calorimetry were conducted by Atwater and Benedict (1903) in the United States and by Rubner (1883; cited in Keys et al., 1973) in Germany.

Current knowledge about metabolic rate, however, is based largely on three extensive studies carried out during the early part of this century. Early in 1900, DuBois and DuBois (1916) began measuring the body surface area of humans, which resulted in development of a formula for calculation of body surface area based on height and weight. This formula was used almost half a century later in estimation of basal caloric expenditure from surface area. At approximately the same time, Harris and Benedict were studying 136 men and 103 women by indirect calorimetry. Their classic work, published in 1919,

established resting metabolic rates of healthy males and females based upon height, weight, age, and gender. Boothby and Sandiford began reanalyzing the Harris and Benedict data in 1922 using over 1,500 men and women from the Mayo Clinic, and, after almost 20 years of study, Boothby et al. (1936) published a nomogram that combined the DuBois surface area estimates with RMR equations. This nomogram is widely used today.

Initially, interest in the energy needs of humans was a natural progression from interest in other nutritional needs, particularly the vitamins and minerals. Early researchers like Gulick (1922) were intrigued by the effects of weight fluctuation, and they performed overfeeding and underfeeding experiments on themselves to demonstrate the central role of caloric intake on weight gain and loss. After World War I and the "war diet" imposed in many European countries, interest shifted to the effects of undernutrition on metabolic rate, and in 1944-45 Keys et al. (1950) performed their well-controlled experiments on the effects of semi-starvation on 32 male volunteers at the University of Minnesota. Subsequently, an interest in the effects of overnutrition on metabolic rate has evolved, and a significant number of studies using obese subjects has emerged.

Typically, absolute RMR increases in obesity due to the larger cell mass created by the obese state (Ljunggren

et al., 1961). However, when expressed per unit of body weight, RMR has been found to be suppressed in the obese by some authors (Hoffmans et al., 1979; Kaplan & Leveille, 1976). In addition, Ravussin et al. (1982) found the oxygen consumption of 14 obese subjects to fall more dramatically than that of 10 lean subjects during sleep, when the RMR was used as a baseline. The implication of this may be a more metabolically efficient state.

Indeed, Sims et al. (1973) have demonstrated that the energy needed to maintain excess weight in obesity is 35% below expected, and the energy needed to maintain excess weight in overfed lean subjects is 35% above expected. In an overfeeding experiment conducted by Katzeff and Danforth (1982), 2 weeks of 1000 extra kcal per day resulted in a 7% increase in RMR by 6 lean males and no change in RMR in 6 obese males. The practical consequence of this energy efficiency may be great difficulty in losing weight and inability to maintain reduced weight over the long-term, leaving the obese susceptible to rebound weight gain (Leibel et al., 1985).

Since it is impossible to identify and study people for a prolonged period prior to obesity development, the post-obese have been studied on many occasions to provide clues to the energy efficiency of obesity. Post-obese (n = 16), obese (n = 8), and lean (n = 16) women matched to age, height, and weight were studied at three levels of

activity (Geissler et al., 1987). At all levels -- sedentary, normal activity, and aerobic exercise -- the post-obese exhibited approximately 15% lower energy expenditure than the lean, even when energy expenditure was expressed per unit of lean body mass. The post-obese had significantly lower caloric intake than the lean, although it was above 1,200 kcal per day. The authors observed that the post-obese required less than 70% of the caloric intake of the lean to maintain their weights.

Leibel and Hirsch (1984) studied 12 obese males and 14 obese females who lost an average of 52 kg. Following weight loss, the obese subjects required 24% fewer kcal than nonobese controls, while weighing 60% more than the controls. The authors likened the obese subjects' energy requirements to that of semifasted subjects, yet these obese individuals were ingesting normal and sufficient kcals.

Evidence from studies with mice suggests that differences in energy metabolism may precede development of obesity (Kaplan & Leveille, 1973; Kaplan & Leveille, 1974). Leibel and Hirsch likewise suggest that reduced energy requirements of formerly obese humans may be evidence of energy abnormalities preceding obesity.

Heterogeneity of Obesity

A very large number of factors interact in the development and maintenance of the obese state. Among the

factors known to affect body composition are genetics (Stunkard et al., 1986), composition of the diet (Bray, 1978), and the number, size, and location of adipose cells (Leibel & Hirsch, 1984). The obese thus represent a heterogenous group and, given the environmental and genetic variability within the population, one would therefore not expect metabolic sameness.

The impact of body composition differences on RMR in the obese has barely been studied. Some authors have found differences in energy expenditure between hypertrophic/adult-onset (enlarged fat cells) and hypercellular/child-onset (excessive number of fat cells) obese females (Bessard et al., 1983; Blair & Buskirk, 1987; Miller & Parsonage, 1975), suggesting that this aspect of obesity should be taken into account when studying the metabolism of obese individuals. Site of fat deposition, too, could affect RMR because of known metabolic and hormonal differences in adipocytes from different areas of the body (Vague et al., 1974). Despite this cursory knowledge, only a few studies of metabolic rate in the obese have controlled for site of fat deposition or cellularity.

Beaton (1983) says that the study of energy expenditure has not progressed very far in 75 years because, although learning has occurred, the practical implications of the Law of Conservation of Energy have not

yet been fully appreciated. Perhaps the heterogeneity of obesity is one practical implication of the energy balance equation that has not been appreciated. It is the intent of this study to explore the effect of one aspect of this heterogeneity, age of obesity onset, on RMR.

Purpose of the Study

The purpose of this study was to determine if obese females expend fewer kilocalories (kcal) at the basal level than nonobese females, and, if so, to determine what component of body composition -- lean tissue or fat tissue -- might be responsible for this energy efficiency. Further, the study considered the obese population as a heterogenous group having different patterns of fat distribution and having different durations of obesity. Only obese subjects having lower-body fat deposition were retained for the study, and resting metabolic rates of the two groups of obese subjects -- hypercellular (child-onset) and hypertrophic (adult-onset) -- were compared.

Significance of the Study

Health problems associated with obesity and overweight include hypertension, hypercholesterolemia, and diabetes (Van Itallie, 1985), and the risk of these disorders increases as the individual approaches and passes 30% overweight (Bray, 1978). Obesity is also associated with social handicaps and Low self-esteem

(Bruch, 1974). For health and social reasons, weight loss is a pressing concern of many Americans.

Successful weight loss requires prolonged negative energy balance, which can be accomplished by either reduced caloric intake or increased energy expenditure or a combination of both (Feurer et al., 1983). Reduced caloric intake, or "dieting," is by far the most common treatment for obesity and overweight (Stewart & Brook, 1987).

Dieting is considered ineffective as a treatment for obesity over the long-term. Only about 10% of obese individuals who lose weight through caloric restriction maintain the loss for more than 6 months (Bray, 1980), due to further reduction of a possibly already reduced RMR (Leibel & Hirsch, 1984). Even following jejunal-ileal bypass surgery, some patients have been found to have reduced mobilization of fat stores, when the malabsorption induced by the surgery should have precipitated greater fat mobilization (Nutritional Complications.., 1980).

Exercise is certainly indicated in the treatment of obesity, but it does not significantly increase daily caloric expenditure (Bray, 1983). Forty minutes of aerobic exercise resulted in an increase in 24-hour oxygen consumption of 220 to 250 kcal in 8 obese subjects (Geissler et al., 1987). The individuals considered the exercise uncomfortable and were unlikely to maintain the

exercise behavior on a daily basis.

By far, the largest proportion of total daily energy expenditure is the resting metabolic rate, accounting for 60 to 75% of the 24-hour energy expenditure in lean and obese individuals (Horton & Danforth, 1982; Ravussin et al., 1982). RMR is considered to be the best predictor of total daily caloric requirements (Owen et al., 1986) and is highly correlated with the 24-hour energy expenditure in obese and nonobese males and females (Ravussin et al., 1982). In addition, the caloric cost of non-basal work has been found to increase in proportion to the RMR (Dore et al., 1982). Therefore, a metabolically efficient individual would have a much more difficult time at permanent weight loss and be much more susceptible to weight gain.

Are the obese more metabolically efficient? Thirty years of study have produced a substantial number of works on the energy intake and expenditure of the obese. Most studies have shown that the obese neither consume more calories than the nonobese (Curtis & Bradfield, 1971; Horton & Danforth, 1982; Maxfield & Konishi, 1966) nor are less active than the nonobese (Prentice et al., 1986). The evidence, therefore, is somewhat suggestive of a metabolic efficiency among the obese (Garrow et al., 1978; Geissler et al., 1987).

Yet, most studies of RMR have not demonstrated a

statistically significant difference between the adjusted RMR of obese and lean individuals. Two conclusions may be drawn from this: first, there is no difference in RMR between the obese and lean; and second, that a difference does exist but that some confounding factor is preventing it from being detected. Given the evidence of metabolic efficiency already cited, it is this author's belief that the latter conclusion is valid and that age of obesity onset and site of fat deposition may represent those confounding factors.

The complexity of human obesity suggests that overeating and inactivity are too simplistic to be the primary causes of obesity. It is hoped that by controlling for onset of obesity and site of fat deposition this study will provide insights into the resting energy metabolism of the obese female. This insight may subsequently suggest effective remedies for the obese state and further the concept of obesity as a disorder of energy balance, rather than a disorder of gluttony and sloth.

Statement of the Problem

The literature is suggestive, although inconclusive, of a metabolic efficiency in the obese. This study looked at one potential explanation for this metabolic efficiency by investigating the differences that exist in resting

metabolic rate between obese and nonobese females and between females with adult and childhood onset of obesity.

Research Hypotheses

1. Obese females will have a lower resting metabolic rate (RMR) per unit of fat-free mass, fat mass, and body weight than nonobese females.

2. Child-onset obese females will have a higher RMR per unit of fat-free mass, fat mass, and body weight than adult-onset obese females.

3. Child-onset and adult-onset obese females will have a lower RMR per unit of fat-free mass, fat mass, and body weight than nonobese females.

Delimitations

1. Subjects were restricted to 18 Caucasian females, ages 20-38 years old, who were less than or equal to 26% fat (nonobese) or who were greater than 30% fat (obese). Obese subjects had predominantly lower-body fat deposition.
2. Subjects were not in the active stages of weight gain or weight loss and were not on low calorie diets.
3. Subjects were apparently healthy nonsmokers who had no reported history of thyroid dysfunction, hypertension,

heart disease, diabetes, or chronic lung disease and who were not taking any metabolism-altering medications.

4. Obese subjects were classified as child-onset obese if they or others characterized themselves as having been moderately or extremely overweight before menstruation onset and if they continued to meet obesity criteria now.

5. Obese subjects were classified as adult-onset obese if they characterized themselves as having been underweight or normal weight at menstruation onset.

Assumptions

1. Obesity can be categorized on the basis of adipose cellularity. Some research indicates that child-onset obese individuals tend to have an excessive number of adipose cells (Salans et al., 1973; Sjostrom & William-Olsson, 1981) and that adult-onset obese individuals tend to have a normal number of enlarged fat cells (Bray, 1978).

2. It was assumed that subjects truthfully responded to the questionnaire.

3. It was assumed that subjects followed instructions for the 24-hours prior to measurements (no food for 12-14 hours and no exercise for 24 hours).

Limitations

1. The sample size was smaller than expected due to the difficulty in finding subjects who met the criteria for inclusion in the study.

2. Adipose cellularity (hyperplasia or hypertrophy) was inferred from onset of obesity.

Definitions of Variables and Terms

Active Cell Mass (ACM or BCM) -- The component of body composition containing the oxygen-exchanging, potassium-rich, glucose-oxidizing, work-performing tissue (Moore et al., 1963). This includes the intracellular part of fat-free mass (Bernstein et al., 1983). This term is used synonymously with the term body cell mass (BCM).

Adult-onset Obesity (AOO) -- Obesity having its onset after age 17, or more than 2 years after onset of menstruation (Blair & Buskirk, 1987). Obesity having its onset in adulthood is associated with hypertrophy and a normal number of fat cells (Bray, 1978).

Basal Metabolic Rate (BMR) -- The sum of the oxygen consumption of the active cell mass of the body (Grande, 1984), measured upon first waking (Goldman & Buskirk, 1961) in a resting supine subject, 12 to 14 hours after a moderate meal (Keys et al., 1950) in a thermoneutral environment (Felig et al., 1983). The BMR is usually considered to be slightly lower than the resting metabolic rate (Horton & Danforth, 1982).

Body Weight (BW) -- The sum of fat mass and fat-free mass (Behnke & Wilmore, 1974).

Body Weight to the three-fourths power ($BW^{.75}$) -- A method of expressing body weight which is thought to reflect the active tissue component of weight (Kleiber, 1975). As weight increases, active tissue increases exponentially, not in fixed proportion.

Centimeter (cm) -- A metric unit of length corresponding to .3937 inches (McArdle et al., 1981). There are 2.54 cm in an inch.

Child-onset Obesity (COO) -- Obesity having its onset before menarche (Blair & Buskirk, 1987). Obesity having its onset in childhood is associated with hypercellularity and, in morbid obesity, with hypertrophy as well.

Expiratory Reserve Volume (ERV) -- The amount of air that can be forcefully expired from the lungs following a normal exhalation (McArdle et al., 1981).

Fat-free Mass (FFM) -- The non-fat portion of body weight, consisting of body water, body minerals, and non-fat portions of organs and muscle (Behnke & Wilmore, 1974). Not synonymous with lean body mass (Garrow, 1980), although for practicality, the two terms are often used interchangeably (Bakker & Struikenkamp, 1977).

Fat Mass (FM) -- The lipid portion of body weight, which

includes the fat in adipose tissue and the essential fat (Garrow, 1980). This aspect of body composition has the greatest variability (Johnston & Bernstein, 1955).

Functional Residual Capacity (FRC) -- The volume of air remaining in the lungs following a normal exhalation (Miller et al., 1987). The sum of the residual lung volume and expiratory reserve volume (McArdle et al., 1981).

Hypercellular Obesity -- Obesity associated with an increased number of fat cells (Bray, 1978; Salans, 1981).

Hypertrophic Obesity -- Obesity associated with increased lipid content of the fat cells, typically greater than or equal to .8 micrograms per cell (Vasselli et al., 1983).

Kilocalorie (kcal) -- The amount of heat required to raise the temperature of 1 liter of water 1 degree Centigrade, from 14.5 to 15.5 degrees Centigrade (McArdle et al., 1981). An expression of both the energy value of food and the energy value of activity.

Kilogram (kg) -- A metric unit of weight corresponding to 2.2046 pounds (McArdle et al., 1981).

Lean Body Mass (LBM) -- The fat-free mass (FFM) plus a small amount of essential lipid (Bakker &

Struikenkamp, 1977). Not synonymous with FFM (Garrow, 1980), although for practicality, the two terms are often used interchangeably (Bakker & Struikenkamp, 1977).

Obesity -- In women, a body fat content that exceeds 30% of total body weight (Bray, 1978).

Residual Lung Volume (RV) -- The volume of air remaining in the lungs which cannot be exhaled following a maximal exhalation (McArdle et al., 1981).

Resting Metabolic Rate (RMR) -- The sum of the oxygen consumption of the active cell mass of the body, when an individual is sitting or lying quietly several hours after a meal or physical activity (Danforth, 1985). RMR, not BMR, is the most common measure of metabolic activity today, because it is measured under less stringent conditions (Horton & Danforth, 1982).

CHAPTER 2 REVIEW OF THE LITERATURE

This chapter is divided into five sections: general concepts of energy expenditure, contribution of body composition to the variability in resting metabolic rate (RMR), metabolic rates in obesity, effects of adipose cellularity on RMR, and effects of fat deposition on RMR.

Energy Expenditure: General Concepts

This section of the literature review presents information on some of the factors that affect the rate of metabolism.

Total daily energy expenditure can be thought of as having four principal components: resting (basal) metabolic rate (RMR), thermogenesis following exercise or physical activity, adaptive thermogenesis, and thermogenesis following the ingestion of food (Danforth, 1985). Of these components, RMR accounts for an estimated 65-75% of the total daily caloric output in most people (Danforth, 1985; Owen et al., 1986; Ravussin et al., 1982). Hence, the RMR is widely considered to be the best predictor of total daily caloric requirements, making its accurate estimation extremely important when energy balance is examined.

Body Size. Absolute RMR is elevated in obesity due to the greater cell mass of the obese individual (Ljunggren et al., 1961). Greater muscle mass, larger

heart, greater number of blood cells, and, in obesity, enlarged fat mass, contribute to this elevation. Contrarily, following weight loss, absolute RMR has been found to decline in nonobese (Keys et al., 1950) and obese individuals (Bessard et al., 1983; Dore et al., 1982), much of which is attributable to the decrease in body mass.

Body Composition. In the nonobese, lean body mass is the aspect of body composition having the greatest influence on RMR (Cunningham, 1980; Keys et al., 1973; Tzankoff & Norris, 1977). Some research shows it to have a similar influence on RMR in obesity (Halliday et al., 1979; James et al., 1978; Ljunggren et al., 1961), since, as obesity develops, there typically is an increase in FFM (Forbes, 1987).

Conversely, a reduction in LBM is associated with a decrease in RMR. Bessard et al. (1983) studied body composition changes in 5 obese women who lost an average of 12.1 kg after 11 weeks and found that 25% of the weight lost was LBM. This corresponded with an approximate 14% decline in BMR.

Preceding Level of Nutrition. Undernutrition by starvation, fasting or low-calorie diet for a period of days or weeks will reduce the metabolic rate in the nonobese (Apfelbaum et al., 1971; Keys et al., 1950) and the obese (Bray, 1969; Danforth, 1985; Hill et al., 1987;

Warwick & Garrow, 1981). This may be due to the body's attempt to conserve energy in the face of caloric insufficiency, or to a reduction in LBM.

An 8.4% decrease in RMR was reported by Donahoe et al. (1984) in 8 overweight women (112-178% ideal body weight) who consumed 800 kcal/day for 6 weeks, while body weight decreased only by 4%. Hill et al. (1987) even found significant decrements in RMR among 8 dieting (800 kcal/day) obese women who were also exercising during food restriction, as did Warwick and Garrow (1981) in their study of 3 obese women ingesting 800 kcal/day. Twenty-four-hour energy expenditure has also been shown to decrease after 10-16 weeks on a low calorie diet among 5 obese women and 2 obese men (Ravussin et al., 1985a). On the other hand, experimental overfeeding will elevate metabolic rate to levels that exceed that which one would expect from the simple addition of excess tissue (Katzeff & Danforth, 1982; Welle & Campbell, 1983).

Exercise. Metabolic rate is elevated immediately following physical activity. To what extent it remains elevated is questionable. No sustained effect of exercise on RMR beyond 100 minutes was found in 10 male and 13 female nonobese subjects (Freedman-Akabas et al., 1985), or 16 lean, 16 post obese, 8 and obese women (Geissler et al., 1987) who participated in moderate or vigorous cardiovascular exercise lasting 10-20 minutes per session.

Bielinski et al. (1985) found a 9% increase in BMR for 4 hours following very strenuous exercise, and a 4.7% increase in BMR the morning after exercise; caloric intake among subjects was unfortunately different on exercising and non-exercising days, making conclusions about the study difficult. Pacy et al. (1985) found only a short-term thermic effect of exercise on RMR in 2 males and 2 females. However, Hermansen et al. (1984) observed that 12 hours after exercise, BMR of 1 subject remained almost 20% higher than the values obtained on non-exercising days. Donahoe et al. (1984) observed RMR to be elevated in obese subjects for 8 to 10 hours after 30 minutes of pedaling a bicycle ergometer at 80% of maximum heart rate two times per week. Furthermore, a 6-week program of exercise reversed the decrease in observed RMR per kg body weight that was induced by diet alone.

Menstrual Cycle. Metabolic rate fluctuates with the menstrual cycle, being at its lowest point during menstruation and immediately thereafter (Snell et al., 1920; Solomon et al., 1982; Wakeham, 1923; Webb, 1986). Cyclic estrogen release produced changes in core temperature and BMR in 10 women ages 20-40 years having different body compositions (Webb, 1986). Changes in progesterone levels are also theorized to affect BMR, perhaps more so than estrogen (Solomon et al., 1982). Progesterone levels are elevated just prior to ovulation

and are at their lowest levels immediately following menstruation. The BMR follows a similar pattern, reaching levels 11 to 16% higher just before the start of the menstrual period than during menstruation (Solomon et al., 1982; Webb, 1986).

Endocrine System. The thyroid gland and its hormones are the components of the endocrine system having the greatest effect on metabolic rate. The thyroid gland has both a rich blood supply, which permits high levels of thyroid hormone to be circulated rapidly, and rich sympathetic innervation, which permits rapid change in the rate of hormone secretion (Hadley, 1984).

Using dietary iodine, the follicular cells of the thyroid produce the thyroid hormones thyroxine (T4) and triiodothyronine (T3). After release from the thyroid gland, 33-40% of T4 is converted to the active form, T3 (Norris, 1985). The thyroid hormones, and T3 in particular, affect most physiological functions, including calorigenesis or thermogenesis (Forbes, 1987; Hadley, 1984). Excessive secretion of thyroxine results in the condition called hyperthyroidism, characterized by an accelerated metabolic rate. Absence or insufficiency of thyroid hormone secretion is called hypothyroidism and may be accompanied by obesity if BMR and activity levels are depressed (Norris, 1985). All forms of thyroid disease are more common in women than men (Cooppan, 1986).

Drugs. Any drugs that affect production or secretion of the thyroid hormones could have an indirect effect on metabolic rate. Among the antithyroid drugs are iodide in large doses (Hadley, 1984) and some iodide-containing medicines, such as expectorants that contain iodide salts (Gilman et al., 1985). Drugs that inhibit iodide transfer into the thyroid gland include thiocyanate, perchlorate, chlorate, periodate, the thionamides, sulfonamides, and sulfonylureas (Hadley, 1984). Thiourea, propylthioracil, and other thiocarbanide derivatives block the formation of active iodide (Norris, 1985).

According to Gilman et al. (1985), the following are among drugs that can affect BMR: salicylates, including aspirin and indocin; the anticoagulant, dicumarol; and lithium salts. Estrogen and contraceptives have been found to increase levels of a thyroxine carrier in plasma, but this probably does not result in a significant change in levels of circulating T4 (Tepperman, 1980).

Caffeine, found in colas, coffee, tea, chocolate, and some cold preparations, and nicotine, found in tobacco, are among widely consumed drugs that can accelerate RMR. Caffeine is a xanthine derivative that stimulates heart rate, contractile force, and cardiac output and, in high doses, catecholamine release (Caro & Walker, 1982). Nicotine stimulates catecholamine release and has an

acceleratory effect on oxygen consumption, heart rate, blood pressure, and respiration (American Hospital Formulatory Service, 1987).

Age. Age itself has been estimated to account for a reduction in BMR of 1 to 3% per decade in men between ages 20-75 years (Keys et al., 1973), suggesting an "aging phenomenon" in BMR. Other factors, such as changes in body fat and fat free mass, account for most of the reduction in metabolic rate that has been observed with aging (Cunningham, 1980). Loss of LBM due to aging in females has been shown to correspond with a decline in RMR (Young et al., 1963).

Gender. Absolute RMR has consistently been shown to be lower in women than in men (Benedict & Emmes, 1915; Elwyn et al., 1981; Harris & Benedict, 1919). When RMR is expressed per unit of active cell mass, there is no difference between males and females (Cunningham, 1982).

In summary, the RMR of a euthyroid individual, who is not taking medication known to affect RMR, will be primarily influenced by body composition. Age and gender of the individual affect RMR mainly to the extent that they affect body composition. Thus, body composition accounts for most of the variability in metabolic rate.

Body Composition and Variability in Resting Metabolic Rate

With respect to metabolic expenditure, the human body

can be thought of as consisting of two compartments: the active tissue mass and the non-active tissue mass. Non-active tissue includes those components of body composition that have relatively low metabolic activity: body fat, extracellular fluid, bone mineral, nails, and hair (Grande & Keys, 1980). Active tissue includes everything else, including the intracellular water. This mass accounts for 30-65% of body weight and virtually all of the body's oxygen consumption (Garrow, 1982; Grande & Keys, 1980). The obese and nonobese differ not only in the proportion of low-activity fat tissue but also in active tissue.

As a result, the obese often have a higher absolute RMR than the nonobese. RMR in obese women has been found to be 19% (Prentice et al., 1986) to 25% higher than that of the nonobese (Felig et al., 1983). This is quite logical, given that the obese are carrying more oxygen-consuming tissue in the form of fat, muscle, and blood (Ljunggren et al., 1961).

To make a meaningful comparison of the RMRs of obese and nonobese women, however, it is necessary to "normalize" the data, or relate the RMR to one of several components of body size or composition. These components include body surface area, weight, lean body mass, fat-free mass, active cell mass, and fat mass. If such a comparison indicated that RMR per unit of body composition

were depressed in the obese, this could help clarify the metabolic abnormalities of obesity, even in the face of an elevated absolute RMR.

In addition, it is useful to correlate aspects of body size or composition with the RMR. When an aspect of body composition correlates highly with RMR, it suggests that this component is more involved in "running the engine" of the obese person than an aspect of body composition having a low correlation with RMR. The following section of the literature review will examine which components of body composition meet this requirement.

RMR and Surface Area

The Surface Law of Metabolism proposed by DuBois and DuBois (1916) states that the metabolic rate is proportional to the surface area of the animal, expressed in kilocalories per square meter ($kcal/m^2$), where m^2 is calculated as:

$$Weight^{.425}\ (kg) \times Height^{.725}\ (cm) \times .007184$$

The theoretical validity of relating increased metabolic rate to increased surface area is that height and weight reflect the metabolically active cells of a growing (or grown) animal. Each square meter of body surface will lose a certain amount of heat, and the larger the surface, the higher the rate of heat production required to maintain body temperature. As obesity

develops, the surface area of the individual expands in proportion to the growth of active cell mass and is reflected in an elevated RMR. These were the findings of White and Alexander (1965) in measurements taken over periods of 3 months to 5 years on 109 very obese men and women. Oxygen consumption and body surface area correlated well in men (r = 0.820; p = .001) and women (r = 0.786; p = .001). A more recent study by Felig and associates (1983) using only female subjects described similar findings, with a high significant correlation found between RMR and surface area (r = .84; $p < 0.001$) in the 10 obese and 10 nonobese. There was no significant difference in RMR per unit body surface area in obese and nonobese women in either this study or one other (Cunningham, 1982).

In fact, the relationship between oxygen consumption and surface area that these and others (Johnston & Bernstein, 1955) have reported is probably due to the relationship between surface area and lean body mass. In a study of seventeen 21-59 year old women ranging from 17% to 57% fat Johnston and Bernstein (1955) found high correlations of both lean body mass and active cell mass with surface area (r = .92 for both). Miller and Blyth (1953) reported a correlation coefficient of .79 between surface area and lean body mass in 47 male and 1 female college students ages 18 to 35 years (M = 23.5 years).

However, and this is the basis for recent criticism of a surface law of metabolism, it is now thought unlikely that the active, oxygen-utilizing body tissues grow in a fixed proportion as body weight increases (Webb, 1981). Rather, in obesity any increase in surface area is more likely due to expansion of less metabolically active fat tissue.

Keys et al. (1973) observed that it is not unusual to find high correlations between RMR and body weight or surface area when a small number of subjects are used, particularly when subjects represent extreme ends of the weight continuum. Feurer et al. (1983) observed that present surface area equations may not reflect the metabolically active tissue of the morbidly obese. When Keys et al. (1973) reworked the Johnston and Bernstein data without the extremely underweight or morbidly obese subjects, the correlation of BMR and surface area went from .92 to .03.

RMR and Body Weight

Body weight consists of both lean and fat tissue. During weight gain, both fat and lean components increase. However, great individual variation in the proportion of these tissues is found. Of the weight gained from experimental overfeeding of 39 normal weight men and women, approximately 38% was found to be LBM (Forbes, 1987). After 5 nonobese male subjects consumed an extra

17,250 kcal per day over 9 days, Ravussin et al. (1985b) found that the LBM accounted for 44% of the weight gained.

As overweight and obesity develop, the proportion of body weight consisting of lean versus fat tissue appears to be influenced by several factors. First among these is the status of body weight before additional weight gain occurs. The thinner an animal (or human) is before weight gain, the greater proportion of gained weight that will be in the form of LBM; the fatter an animal is before additional weight gain, the greater will be the accumulation of fat (Forbes, 1987). In his studies of women ages 14-40 years who were at ideal body weight, anorexic, or obese, Forbes (1987) found a curvilinear, not a linear, relationship between LBM and fat in weight gain.

Age is another significant factor influencing the proportion of lean or fat tissue accumulated in weight gain. Younger animals and humans will deposit a larger proportion of excess weight as lean tissue; adult weight gain consists of proportionately more fat tissue (Forbes, 1987). This is no doubt related to cell hyperplasia and hypertrophy discussed elsewhere in this review.

Animal studies have demonstrated that younger animals respond to overfeeding by increased fat cell number and therefore proportionately more non-fat tissue in the form of cell walls, whereas older animals respond by hypertrophy (Winick & Noble, 1967). Even in humans,

children with obesity starting in infancy have slightly greater LBM than children who develop obesity later in childhood (Cheek et al., 1970; Forbes, 1964). In rats, these body composition differences are retained into adulthood (Widdowson & Dickerson, 1960). No longitudinal studies in humans are available. The factors mentioned above may help to explain some of the variability found in the following studies.

Thirty-one percent of weight gained was made up of LBM in 5 obese adult women who had gained an average of 10 kg over several years (Sjostrom, 1980). Forbes (1987) examined six studies of spontaneous weight gain and reported that an average of 29% of excess weight in obese men and women was comprised of LBM. This was also the finding of Butte and associates (1985), who studied 37 women having no prescribed diet or activity program for 3 months postpartum. Whether the women gained or lost weight, the average tissue gained was 29% LBM and 71% fat. Webster et al. (1984) found the excess weight of 104 females having varying degrees of obesity to be 70-78% fat and 22-30% lean.

A relationship between body weight and 24-hour energy expenditure has been demonstrated in the 8 day whole body calorimeter study of deBoer and colleagues (1987). Pooled data from 29 lean and 18 overweight females showed 24-hour energy expenditure to correlate better with body weight

than with any other variable (r = .91). This is not surprising, given that the larger body mass would require more energy to move it during a 24-hour period.

Various studies have also shown significant correlations between body weight and RMR in obese subjects (Dore et al., 1982; Ljunggren et al., 1961; Miller & Parsonage, 1975; Owen et al., 1986; White & Alexander, 1965). Owen et al., (1986) studied metabolic rates of 36 lean and obese nonathletic women and 8 trained female athletes of similar ages. The lean (M = 25.5% fat) and obese (M = 44.3% fat) were considered so similar that their data were pooled. Body weight correlated as well with RMR as did other measures of body composition or size (r = .74).

Feurer et al. (1983), on the other hand, were unable to find a statistically significant relationship between weight and RMR in 112 morbidly obese (157-327% of ideal body weight) men and women. Perhaps this discrepancy can be clarified by looking at the work of Dore et al. (1982). In 140 women with varying degrees of obesity, the correlation between weight and RMR improved when total body potassium, a measure of LBM and active cell mass, was included in the analysis (r = .817) (Dore et al., 1982). Thus, as much as weight represents the active cells of the body, weight determines RMR. Perhaps as obesity increases, weight reflects active tissue less.

There is some debate as to whether the size of the active cell mass increases in direct proportion to the increase in weight. The three-fourths power of body weight ($BW^{.75}$) has been suggested as a more accurate predictor of size of the active cell mass than the absolute value of body weight (Grande, 1980; Kleiber, 1975). This is due to the fact that as body size increases, structures of low metabolic activity like the skeleton increase in size faster than tissues and organs of high metabolic rate.

In 1947, Kleiber reported a linear relationship between the logarithms of body weight and oxygen consumption. Thus, as body size increases, RMR per unit of weight should decrease. Miller & Parsonage (1975) found a significant relationship between $BW^{.75}$ and BMR in 29 obese women who were unable to lose weight (r = .47; p = .01). This was supported by Owen et al. (1986) in their study of lean and obese nonathletic women and trained female athletes. All the women showed decreased energy expenditure per kg of body weight as weight increased. Felig et al. (1983) found RMR per unit of $BW^{.75}$ to be lower by 20% ($p < 0.005$) in 10 obese females when compared to 10 nonobese, as did Cunningham et al. (1981), although in the Cunningham study subjects did not differ in RMR per unit of LBM.

In summary, weight may have different "metabolic

meanings" in obese and nonobese individuals, making it a less desirable metabolic reference standard (Keys et al., 1973). Body weight includes active and relatively inactive components. Fat contributes more to increased body weight in obesity than LBM does (Felig et al., 1983). The muscular, lean woman who weighs 150 pounds has quite a different body make-up than the obese woman of the same weight.

The degree of obesity may also affect the relationship between weight and RMR. In a study of 13 morbidly obese individuals (9 women), Zavala and Printen (1984) found a strong and significant correlation (p = .002) between degree of obesity indicated by percentage of ideal body weight and resting oxygen consumption. When Keys et al. (1973) reworked Johnston and Bernstein's 1955 data omitting the very obese and the very thin, the relationship between BMR and weight virtually disappeared. Thus, the use of body weight as a metabolic reference standard and its degree of correlation with RMR in the "average obese" is controversial.

RMR and Fat Mass

Adipose tissue has been described by Brozek and colleagues (1963) as 83% fat, 2% protein, and 15% water. More than half of the water content of adipose tissue is extracellular (Garrow, 1982). Although sometimes characterized as inert, the adipose mass does contribute

to metabolism. However, the cells in adipose tissue give it its metabolic activity, not the "plain fat" in it (Grande & Keys, 1980).

There is much more individual variation in adipose content of the body than in the FFM. Weight gain after age 25 years is, except in the case of vigorous exercisers, more likely due to an increase in fat than increased FFM (Forbes, 1987).

A few studies have found a relationship between RMR and body fat (Bray et al., 1970; Halliday et al., 1979; Miller & Parsonage, 1975). Miller and Parsonage studied a group of 29 obese women who had been unable to lose weight on a variety of prescribed diets. They found that BMR was more closely related to body fat (r = .52, p < .004) than to LBM (r = .33, n.s.). The authors acknowledged that this finding was difficult to interpret, given that fat metabolic activity is lower than muscle. In addition, they pointed out that repeated dieting, including the prescribed 1,500 kcal/day diet of the study, could have affected both BMR and LBM of the subjects.

Bray and colleagues (1970) studied oxygen consumption of 15 females, most of whom were between ages 20 to 50 years. Body fat was calculated by the formula of Pace and Rathbun (1945), which uses the variables of body weight and total body water (TBW). Oxygen consumption was measured at six to eleven intervals between 8:00 a.m. and

8:00 p.m. following a 15 minute rest. Fat was found to be significantly correlated with oxygen consumption (r = .7288, $p < .01$). Halliday et al. (1979) also used TBW to estimate body fat in a study of 22 women having varying degrees of obesity. The highest correlation in this study was between LBM determined by total body potassium (TBK) and RMR; but they also found significant correlations between fat and RMR, when percentage fat was determined by TBK (r = .623; $p < .005$) or TBW (r = .593; $p < .01$).

Both TBK and TBW have been criticized as methods for determining body composition in the obese. In obese subjects, FFM has been found to have lower than normal potassium content (Colt et al., 1981). Garrow (1982) speculated that potassium was low because much of the water in adipose tissue is extracellular and, therefore, low in potassium. Assuming a "normal" potassium in the FFM could, therefore, lead to overestimation of fat in obesity.

Total body water is accurate only insofar as FFM has a constant water content. Obese animals and humans have been found to have increased water content of fat free tissue (Garrow, 1982; Pace & Rathbun, 1945). Assuming a "normal" water content of FFM could therefore lead to underestimation of body fat in obesity.

Methodological considerations cast some doubt on the use of fat as a metabolic reference standard in these

studies. Nevertheless, these three studes do show that adipose tissue is metabolically active, contributing, perhaps significantly, to RMR in obesity.

RMR and Fat Free Mass

The FFM is approximately 19.4% protein, 73.8% water, and 6.8% mineral (Brozek et al., 1963; Womersely et al., 1976). The LBM, which is sometimes used synonymously with FFM, also contains a small amount of lipid (Bakker & Struikenkamp, 1977). As previously discussed, the FFM or LBM is not constant, and it changes in size with growth, maturity, aging, and weight gain (Wedgwood, 1963).

The inactive components of the FFM are the supporting components of body composition and do not make a significant contribution to the RMR (Shizgal et al., 1979). These include extracellular mass (bone, connective tissue, cartilage), body water, and the liquid part of blood (Bakker & Struikenkamp, 1977; Cunningham, 1982). There are no striking gender differences in inactive components of the FFM (Cunningham, 1982).

The active components of the FFM, variously termed the active cell mass (ACM) or body cell mass (BCM), include skeletal, cardiac, and smooth muscles; the visceral organs; the solid parts of blood; glands and reproductive organs; cellular components of the brain; and intracellular water (Bakker & Struikenkamp, 1977; Bernstein et al., 1983; Moore et al., 1963).

The BCM is that part of the FFM that contains potassium of 92.5 meq/kg (Burmeister & Bingert, 1967) to 120 meq/kg (Moore et al., 1963). This includes primarily muscle, viscera, and brain tissue. The LBM is thought to contain 68.1 meq potassium/kg, so BCM is approximately 57% of the LBM (Forbes, 1987).

Not all cells of the BCM have equal rates of metabolism. The brain and liver, for example, make up approximately 4% of the BCM in a healthy obese or nonobese person but account for over 40% of resting oxygen consumption (Grande & Keys, 1980). Skeletal muscle, on the other hand, accounts for approximately 40% of body weight and is responsible for 16-30% of RMR (Grande, 1980).

There are gender differences in some of the active components of FFM, with males having a larger BCM than females (Cunningham, 1980). The non-skeletal muscle portion of BCM, which accounts for 60-70% of RMR, does not differ proportionately between the sexes (Cunningham, 1980). Skeletal muscle mass, however, is found in significantly larger quantities in males than in females. Muscle mass makes up approximately 29% of the body weight of a female and 40% of the body weight of a male (Cunningham, 1980). Thus a male and female of equal weight would be expected to have different RMRs due to differences in the quantity of oxygen-utilizing active

tissue.

The obese also typically have a larger LBM than the nonobese (Felig et al., 1983). Various reasons for this have been proposed, such as the need for greater circulatory volume and more blood vessels to supply blood to the larger fat mass, and increased muscle mass to support the heavier fat mass (Grande & Keys, 1980; Keys et al., 1955). In addition, obesity is accompanied by an increased size of the parenchymal cells that make up the organs' functioning parts, including an enlargement of the heart muscle (Ljunngren et al., 1961).

Considerable debate surrounds the question of whether FFM or BCM is the best indicator of RMR and, therefore, the best reference standard for comparison of RMR between subjects. The first published discussion of this point was made in 1902 by Voit (translated in Lusk, 1906, pp. 42-44), who stated that the cell mass determines the metabolic rate. Later authors have supported this view (Cunningham, 1980; Keys & Brozek, 1953; Moore et al., 1963).

The problem with using the BCM as a reference standard is primarily one of practicality: Its measurement via total body potassium requires sensitive equipment and even then represents an indirect measurement (Garrow, 1982). Furthermore, it is difficult to determine which of the more easily measured variables accurately reflect the

active tissue (Owen et al., 1986).

To the extent that it reflects the BCM, the more directly measured FFM is a practical standard for RMR assessment. Because the FFM incorporates the BCM, various researchers have stated it to be a good reflection of the BCM (Benedict, 1915; Miller & Blyth, 1953; Shizgal & Forse, 1980). In lean subjects FFM has been reported to have the greatest influence on RMR of any body compartment (Cunningham, 1980; Keys et al., 1973; Tzankoff & Norris, 1977). Grande and Keys (1980) stated that RMR could be estimated from LBM: 1.3 kcal/hour/kg LBM in men and women. Webb (1981) has also found good correlations (r = .95) between LBM determined by underwater weighing and 24-hour energy expenditure in pooled data from 15 lean and obese men and women ages 22-55 years. The 8 females in this study ranged from 13-45% fat. Cunningham's (1980) reanalysis of the Harris and Benedict data on 223 nonobese, healthy adults found LBM to be the most predictive variable for BMR, accounting for 70% of the variability in BMR.

Strong correlations have been found between the higher absolute RMR in obesity and the added LBM of the obese (Cunningham, 1982; James et al., 1978; Kaplan & Leveille, 1976). Cunningham and associates' 1981 study of 10 obese and 10 lean women found RMR to correlate directly with LBM (r = .84, $p < .001$). Similar findings have been

reported by Ravussin et al. (1982). For 20 obese and 10 nonobese males and females, FFM (determined via skinfolds) correlated best with 24-hour energy expenditure and RMR.

This is not to say that researchers unanimously support the FFM as a reference standard for RMR. The relationship may be less straightforward in obesity. Bray et al. (1970) found a low correlation between exchangeable potassium, a measure of the BCM, and BMR in 14 obese women and between total body water, a measure of the LBM, and oxygen consumption measured at 6 to 11 intervals throughout the day and evening. Miller and Parsonage (1975) studied 29 obese women who had been unable to lose weight on prescribed diets and found a weak and insignificant relationship between BMR and LBM calculated from skinfolds at four sites (r = .33).

Methodology may in part explain these discrepancies. In the Bray et al. study (1970) neither BMR nor 24-hour energy expenditure was measured, but rather the researchers measured oxygen consumption at intervals. In the Miller and Parsonage study (1975), dieting both before and during the study may have affected RMR and LBM.

However, the highest correlations found in Halliday et al.'s 1979 study of 22 obese women were between RMR and LBM determined by total body potassium (TBK) (r = .844, p < .001). Similar correlations between LBM and RMR were obtained in 10 women who had been obese since childhood

(Felig et al., 1983), although in this case LBM was estimated from the equation of Moore et al. (1963). Likewise, Bernstein et al. (1983) found significant correlations between RMR and body cell mass and FFM determined by TBK (r = .44) and between RMR and LBM determined by TBW in 154 obese women and 48 obese men. RMR of obese, nonobese, and athletic women in another study correlated well with LBM determined from densitometry or skinfolds (r = .75 for nonathletes; r = .96 for athletes) (Owen et al., 1986). Collective data from 29 lean and 18 obese females yielded strong correlations between FFM and both 24-hour energy expenditure (r = .78) and sleeping energy expenditure (r = .76), although the highest correlations in this study were found between energy expenditure and body weight (deBoer et al., 1987). Schutz et al. (1984) observed a significant correlation between FFM and BMR in 20 women who were obese since childhood (r = .870, $p < .001$).

Thus, FFM is an appropriate reference standard for energy metabolism when people are either at rest or moving about. It has a physiological relationship to the RMR, and it is measureable. Although both the FFM and BCM correlate well with RMR, Keys and Brozek (1953) noted that oxygen consumption more closely correlated with BCM than LBM when subjects of different age, sex, or fluctuating weight were compared. For a heterogenous

population, FFM is equally suitable.

Metabolic Rates in Obesity

Absolute RMR in Obesity

When expressed as an absolute value of oxygen consumption over time, RMR is typically higher in the obese than in the nonobese. Table 1 provides data on absolute RMR from 13 studies of obese and, in most instances, nonobese females. Average absolute RMR among obese females in these studies ranged from 1,210 kilocalories per day (kcal/d) (Miller & Parsonage, 1975) to 1,765 kcal/d (Ljunggren et al., 1961), with an overall average of 1,563 kcal/d in the obese. When data from studies reporting unusually low metabolic rates in the obese were dropped (Hill et al., 1987; Miller & Parsonage, 1975), the average RMR of obese women in these studies was 1,618 kcal/d.

This value is an average of 20% higher than that of nonobese females in the same studies. Mean RMR reported for the nonobese ranged from 1,209 kcal/d (Ravussin et al., 1982) to 1,454 kcal/d (deBoer et al., 1987), averaging 1,323 kcal/d.

The often statistically significant difference in RMR between nonobese and obese females is not unexpected, given the larger cell mass and supporting structures of the obese individual, as discussed in the previous

section. Low absolute RMR values are also not unexpected in certain cases. The Miller and Parsonage (1975) study included only women who had been unsuccessful in losing weight while on 1,000 to 1,500 kcal/d diets over the previous 6 months. In the Hill et al. (1987) study, baseline RMRs on 8 obese women were taken after 1 week on a "maintenance diet" (caloric composition not reported) and just before 5 weeks of 800 kcal/day. The subjects' previous dieting behavior was also unreported, but the low RMR and participation in a study involving caloric restriction suggests previous dieting.

RMR Per Unit of Body Composition in Obesity

The higher absolute RMR typically reported for obese females creates the impression that the obese have "normal" metabolism. More instructive are the studies that state RMR adjusted for body composition, such as RMR per kg of fat free mass (RMR/FFM) or per kg of body weight (RMR/BW).

A cursory examination of data from studies that express RMR per kg of FFM presents a picture of metabolic normalcy in the obese (see Table 2). In all studies listed, RMR/FFM ranges from 31.5 to 34.48 kcal/kg FFM in obese females, with an average of 32.98 kcal/kg FFM/day.

These values are, in all but one instance, statistically indistinguishable from RMR/FFM in nonobese females. Only Hoffmans et al. (1979) found a significant

Table 1

Absolute RMR in Obese and Nonobese Women

Study	N	RMR (kcal/d)	Diff Between Obese and Nonobese
Bessard et al., 1983	6 obese 6 lean	1661 1230	26% ($p < .001$)
Blair & Buskirk, 1987	16 obese 8 lean	1445 1226	15% ($p < .05$)
Cunningham et al., 1981	10 obese 10 lean	1656 1313	26% ($p < .01$)
deBoer et al., 1987	18 overweight 29 lean	1728# 1454#	16% ($p < .001$)
Felig et al., 1983	10 obese 10 lean	1656 1279*	25% ($p < .005$)
Hill et al., 1987	8 obese	1255	--
Hoffmans et al., 1979	15 obese 13 lean	1550 1421	8% ($p < .025$)
Ljunggren et al., 1961	13 obese 16 healthy	1765 1383	21% ($p < .01$)
Miller & Parsonage, 1975	29 obese	1210	--
Owen et al., 1986	12 obese 7 lean	1436.5 1256.8	12% (n.s.)
Prentice et al., 1986	9 obese 13 lean	1605 1352	19% ($p < .001$)
Ravussin et al., 1982	8 obese 3 mod. obese 5 lean	1585 1634 1209	26%
Schutz et al., 1984	20 obese 8 nonobese	1699 1267	25% ($p < .001$)

* approximate value
\# included sleeping energy expenditure in early morning.

difference between the obese and nonobese, with the 13 lean subjects in their study having a lower RMR/FFM than the 15 obese. From the standpoint of actual amounts, there was only a difference of 2.3 kcal/kg FFM/day between the two groups of subjects, a difference less than that found by Bessard et al. (1983), whose data did not reach statistical significance. In one other case, a significant difference might have been found if male and female data had been considered separately (Ravussin et al., 1982). Obese and moderately obese women studied expended in excess of 5 kcal/kg FFM/day more than their nonobese counterparts, but only pooled data from male and female subjects were tested for statistical significance.

Another study, not included in Table 1, provides additional information. Garrow and Webster (1985) studied RMR of 104 women whose percentage body fat ranged from 5.7% to 61.2%. The number of nonobese subjects was not given, and subject characteristics were not reported separately for obese and nonobese. In addition, there was great variation in percentage fat determined by total body water (the minimum percentage fat using this method was 10.6%), total body potassium (minimum percentage fat = 18%), and total body plethysmography (minimum percentage fat = 5.7%). Nevertheless, the authors reported that subjects having a higher percentage of body fat had higher RMR/FFM, regardless of the body composition method used.

After averaging FFM values obtained with the three methods, the authors found that each kg gained in FFM resulted in an increased RMR of 3.48 ml oxygen per minute. Using standard calculations, 3.48 ml of oxygen is approximately equal to 0.0167 kcal/min, or 24 kcal/kg FFM/ day (Brooks & Fahey, 1984).

On the other hand, when RMR data are expressed per unit of body weight (BW), differences between the obese and nonobese become more apparent. Both Kaplan and Leveille (1976) and Hoffmans et al. (1979) demonstrated lower rates of calorigenesis in the obese than the nonobese when expressed per kg BW. The difference is statistically significant only for Hoffmans et al.

deBoer et al. (1987) reported the same result when comparing 24 hour energy expenditure per kg BW in lean and overweight women. The lean women expended 35.1 +/- 0.6 kcal/kg BW, while the obese expended 27.6 +/- 0.5 kcal/kg BW ($p < .001$), although there was no significant difference in 24 hour energy expenditure/kg FFM, between the two groups.

Apparently the obese may have lower energy requirements per kg BW than the lean, yet the same energy requirements per kg FFM. Owen et al. (1986) commented on this phenomenon in their study. They found the energy expenditure per kg BW in athletic women and in lean and obese nonathletic women to decrease as weight increased.

It was speculated that the increased contribution of adipose to body mass as weight increased might account for this.

Table 2

Resting Metabolic Rates Per Unit of Weight or Fat-Free Mass in Obese and Nonobese Women

Study	RMR (kcal/kg FFM)		Difference
	Obese	Nonobese	
Bessard et al., 1983	32.3 +/- 1.1	29.5 +/- 0.7	n.s.
Hoffmans et al., 1979	32.9 +/- 1.4	30.6 +/- 2.4	$p < .01$
Prentice et al., 1986	32.77	33.01	n.s.
Ravussin et al., 1982	34.48 (obese) 33.95 (mod. obese)	28.77	sig. not tested
Schutz et al., 1984	31.5	30.6	n.s.

Study	RMR (kcal/kg BW)		Difference
	Obese	Nonobese	
Hoffmans et al., 1979	21.8 +/- 1.2	24.4 +/- 2.3	$p < .01$
Kaplan & Leveille, 1976	26.74	29.87	n.s.

All values are mean +/- standard deviation.

Possibility of a Metabolic Aberration in Obesity

Certain obesities are associated with a depressed RMR, usually because of decreased size of the LBM. Cushing's syndrome (Ellis & Cohn, 1975; Ernest, 1967), hypothalamic obesity (Bray & Gallagher, 1975), and Prader-Willi syndrome (Nelson et al., 1981) provide three examples from medicine of decreased LBM accounting for decreased RMR. Subjects with these disorders have been excluded from studies reviewed here. More pertinent to this study are the "average" obese, for whom the idea of metabolic efficiency is still controversial.

Some research has examined the formerly obese in an attempt to identify metabolic differences between those who have successfully reduced body fat and the never-obese lean. A recent study matched 16 post-obese and 16 lean women to age (+/- 5 years), weight (+/- 3 kg), and height (+/- 5 cm); body composition assessed by skinfolds was similar between the two groups (Geissler et al., 1987). Eight of the post-obese had maintained target weight for 6 months; the other eight were closely approaching target weight. At all levels of activity -- sedentary, normal, and aerobic exercise -- the post-obese expended significantly less energy than lean controls ($p < .001$). Even during sleep, the post-obese expended 10% fewer kcal than the lean. The post-obese consumed an average of 1,298 kcal/day, while the lean consumed an average of

1,985 kcal/day. This significant difference confounds interpretation of the data and makes it difficult to interpret whether reduced energy expenditure preceded development of obesity or was a consequence of dieting.

Others have taken caloric restriction into account when interpreting RMR data. It has already been reported in this review of literature that the RMR of obese or nonobese individuals will decrease after days or weeks on a low-calorie diet. This decrease, however, is usually greater than one would expect simply from the loss of lean body mass alone (Leibel & Hirsch, 1984). Investigators have attributed 35% (Keys et al., 1950) to 65% (Grande et al., 1958) of this reduction to a lower rate of metabolism per unit of FFM. Thus, the possibility of greater metabolic efficiency in some tissues as a precedent to obesity does exist.

Schutz et al. (1984) reported interesting findings suggestive of a metabolic abnormality in obesiy. Repeated measures of energy expenditure at zero activity (not the same as RMR) taken while subjects were in a calorimeter over 24 hours showed significantly depressed energy expenditure in obese women. When energy expenditure at zero activity was expressed per kg FFM, the 20 obese subjects expended 37.6 kcal/kg FFM/day; the 8 nonobese expended 41.39 kcal/kg FFM/day. This is particularly interesting because RMR/kg FFM/day was the same between

the groups studied. A similar finding was demonstrated by Bloom and Eidex (1967a) in a study of 8 obese and 4 lean men and women. A 250-pound obese male walking on a treadmill had a lower oxygen consumption than a 150-pound lean male who was carrying 100-pounds of bricks in a backpack. The lean subject expended 5.75 kcal/min on the treadmill, while the obese subject expended only 5.34 kcal/min.

Methodological problems contribute to difficulties in interpreting studies of RMR of obese women. In no study of women, for example, have obese and lean been matched to lean body mass, and in only one study (Geissler et al., 1987) have subjects been matched to body weight.

In a study involving 8 lean and 8 obese male subjects who were matched to age, height, and FFM, Segal et al. (1987) found no difference in absolute RMR or maximal oxygen consumption per kg FFM. However, there was a significant difference between lean and obese when maximal oxygen consumption was expressed per kg of body weight. Resting oxygen consumption was 3.88 +/- .10 ml/kg/min in the lean men and 3.19 +/- .10 ml/kg/min in the obese ($p < .01$). This led the authors to conclude that a thermogenic defect in obese men might be related to elevated body fat content. Similar studies must be conducted with female subjects.

Methodological Problems in Studies of RMR in Obesity

Metabolic rate studies typically involve a small number of subjects due to the time required to carry out measures of metabolism. Low subject number creates several problems of data interpretation. Statistical significance can be difficult to achieve with a small N, or, conversely, a finding may appear significant but not be applicable to a larger group. Whereas several large studies of nonobese individuals have been done and thereby provide data on the "healthy" population (Benedict & Emmes, 1915; Boothby & Sandiford, 1922; Keys et al., 1950), no such ambitious studies have been done on the obese population. The studies cited in Table 2 include a total of 65 obese women, and none of these studies followed the same procedures.

Oftentimes, studies have included subjects having extreme variance in personal characteristics. For example, despite the fact that age affects RMR, subjects often represent a wide age range, from 20 to 46 years (Ravussin et al., 1982), 25 to 45 years (Blair & Buskirk, 1987), 19 to 44 years (Schutz et al., 1984), and 20 to 47 years (deBoer et al., 1987). Data from women who are 20 to 30 years apart in age can be extremely difficult to interpret, given the finding of an "aging phenomenon" in RMR that has been reported (Keys et al., 1973). Of studies including obese women, only Felig et al. (1983)

and Schutz et al. (1984) considered timing of menstrual cycle in collecting RMR data.

Rarely do studies include control of subject drug use, although many drugs, including nicotine, can affect RMR. In fact, deBoer et al. (1987) permitted subjects to smoke a minimal number of cigarettes and drink tea and coffee while in the calorimeter. Prentice et al. (1986) likewise did not exclude smokers from participation in their study, and 3 lean and 1 obese subject out of a total 22 subjects were smokers.

Perhaps the most significant factor, in terms of the impact on the results, is the classification of subjects as obese or nonobese. There are two aspects to this: (1) method used in determination of body composition, and (2) percentage fat used as a cut-off for the definition of obesity.

Underwater weighing is considered to be the most accurate method available at this time for determining body composition, having a 3-4% theoretical error rate (Lohman, 1981). Yet, the use of hydrostatic weighing is rare among researchers studying RMR in obesity. Only four studies reviewed used hydrostatic techniques (Blair & Buskirk, 1987; deBoer et al., 1987; Hoffmans et al., 1979; Owen et al., 1986).

Skinfold measures have been more commonly used in determining body composition (Bessard et al., 1983;

Geissler, et al., 1987; Miller & Parsonage, 1975; Ravussin et al., 1982; Schutz et al., 1984). Skinfolds are thought to have, on the average, a 5% theoretical error rate, depending upon technician skill, degree of obesity, and prediction equation used (Lohman, 1981). The average lean subject in Bessard et al. (1983) was 24.2% fat; given a 5% error rate, some could have had borderline obesity. Ravussin et al. (1982) classified subjects who averaged 33.7% fat as "moderately obese." Again, considering the possibility of error in skinfolds, some could have actually been nonobese and others obese.

The overall problem of classification of subjects as obese or nonobese is troublesome. In most cases, 30% fat is used as the definition of obesity in women. Thus, subjects approaching 30% fat but not exceeding it could be classified as lean. If skinfolds are used, any lean subject having in excess of 26% fat might, through measurement error, actually be obese. Classification of subjects as obese/nonobese when hydrostatic weighing is not used must therefore be closely examined.

Effects of Adipose Cellularity on Resting Metabolic Rate

Several methodological considerations were discussed in the previous section that might affect results obtained in RMR studies with obese subjects. This section examines another aspect of body make-up that could contribute to the variability in metabolic rate and to the

interpretation of RMR data: hypercellularity and hypertrophy in obesity.

Morphology of Adipose Tissue

Adipose tissue is not composed solely of fat, although its major constituent is triglyceride. Other components include connective tissue, blood vessels, and cell walls (Grande & Keys, 1980). Fat cells are the largest cells in the body, having a mean cell diameter of 50-100 micrometers in the lean and 150 micrometers in the obese (Gurr & Kirtland, 1978). Approximately 97% of the fat in adipose tissue in males and 88% in females is thought to contain stored, readily mobilized energy and is termed "nonessential" fat. This contrasts with "essential" fat, a constituent of LBM, which the body retains even in starvation (Behnke, 1964).

Another type of tissue, brown adipose tissue, has a role in nonshivering thermogenesis. This section of the review of the literature is concerned only with white, or storage, adipose tissue.

As fat cells mature and enlarge, their proportion of lipid to protein apparently changes. Goldrick (1967) examined epididymal fat cell hypertrophy in rats and found the lipid content of the cell wall to increase 40 times (from 0.011 micrograms to 0.44 micrograms), while the cytoplasm (protein) increased just 4 times. Bjorntorp and Martinsson (1966) found little or no increase in cytoplasm

or constituents of cell membrane in adipose tissue samples taken from the abdominal wall in human fat cell hypertrophy.

Pawan and Clode (1960) analyzed samples of subcutaneous adipose tissue taken from the same area of the abdominal wall in living subjects and in deceased subjects within 24 hours of death. Ages and definition of obesity were unreported. They found substantial differences in water and lipid content of adipose tissue between the obese and lean. Water made up slightly more than one-fourth of the weight of adipose tissue in lean subjects, living or dead, but under 20% of adipose tissue in the obese. Lipid, on the other hand, made up 68% of adipose tissue composition in living lean subjects and 72% in dead lean subjects, but 79% of adipose tissue in living and dead obese.

When fat stores are depleted, as in starvation, the structural elements (active cell mass) and water in adipose tissue tend to be preserved as the triglyceride depletion is proportionately much greater (Hausberger, 1965). It is possible that this point explains some of the variance in metabolic rate seen in the obese, given that obesity could be the result of a normal number of enlarged adipocytes, a greater number of enlarged adipocytes, or a greater number of normal-sized adipocytes.

Development of Adipose Tissue

Adipose tissue is seen in the human fetus as early as 26 weeks of gestation, although young fat cells may be virtually indistinguishable from connective tissue fibroblasts in utero. Embryonic adipose cells contain almost no fat, consisting mostly of extracellular water (Hausberger, 1965).

Almost immediately after birth, fibroblasts (stem cells) change from spindle-shaped to spherical, and water is replaced by lipid (Napolitano, 1965). As white adipose cells differentiate, or mature, lipid accumulates as a large mass in the cell center.

Early in life, most growth occurs by cell division alone, with increases in cell size not contributing to growth until later (Winick and Noble, 1967). Corticosteroids (corticosterone or cortisol) have an important role in the transformation of uncommitted adipoblasts into committed preadipocytes and thereby help to regulate cell number (Hauner et al., 1987).

Several researchers believe that most fat cells are formed in utero (Leibel et al., 1983; Salans, 1981). A second surge in fat cell number seems to occur around ages 8 to 15 years (Knittle et al., 1979; Leibel et al., 1983). After puberty, increased fat deposition is typically associated with progressive hypertrophy of adipocytes. Obesity can develop due to excessive fat cell number

(hyperplasia or hypercellularity), excessive fat cell size (hypertrophy), or a combination of the two.

Hypercellular obesity is usually thought of as having its onset in childhood, and hypertrophic obesity is more frequently associated with adult obesity onset. Winick and Noble (1967) observed that increasing the caloric intake of young rats increased the rate of adipocyte division but did not change the fat cell size, suggesting that early overnutrition may at least partly account for hypercellularity.

Some researchers speculate that beyond a certain fat cell size an increase in obesity will be accompanied by formation of new adipocytes, even in adulthood (Bjorntorp, 1982; Gurr et al., 1982; Sjostrom & William-Olsson, 1981). In adulthood, the data of Hirsch & Batchelor (1976) suggests that fat cell size plateaus at approximately 170% ideal body weight and that fat gain thereafter stimulates cell replication. Sjostrom & William-Olsson (1981) studied 19 obese women from 1970-72 and again in 1979. Changes in body weight over the 7 to 9 years only correlated with changes in fat cell number (r =.59; p <.01), not changes in fat cell weight.

Possibly the corticosteroids precipitate hypercellular obesity in adult humans (Hauner et al., 1987). This has not yet been conclusively demonstrated, and not all researchers are in agreement that adipose cell

replication is possible after puberty. Karam (1982) stated that after age 21 years mature adipocytes are less able to replicate, so that obesity developing after puberty is characterized by distribution of excess fat among a normal number of adipocytes. This view is echoed by others (Bray, 1978; Bjorntorp & Sjostrom, 1971). Even authors who acknowledge the possibility of adult hypercellular obesity say that in most cases adult-onset obesity is more related to hypertrophy (Bjorntorp, 1982), or that critical size of already-existing fat cells must be achieved before cell replication will occur (Sjostrom & William-Olsson, 1981).

Salans and associates (1973) studied 99 obese and nonobese individuals, taking fat samples from three subcutaneous and three deep adipose sites. Subjects having hypercellular obesity were generally more obese and reported obesity beginning before age 5 or between the ages of 9 and 13 years. None of the subjects who developed obesity after age 20 years were found to be hypercellular in this study. In addition, the hypertrophic subjects were indistinguishable from the non-obese in fat cell number.

Hirsch and Batchelor (1976) took adipose tissue samples from the mid-triceps, abdomen, and buttocks of 68 females and 38 males having a mean percentage fat of 46% and a smaller group of nonobese controls having a mean

percentage fat of 23%. Onset of obesity was assessed by interview. They found the group having the earliest onset of obesity to have the largest number of adipocytes.

RMR in Hypercellular and Hypertrophic Obesities

Theoretically, there should be an impact of cell size and number on RMR. When an individual gains weight, there is an increase in both fat mass and FFM (James et al., 1978; Johnston & Bernstein, 1955; Keys et al., 1955). Although the less metabolically active fat mass constitutes a greater proportion of weight gain in obesity, the obese also gain active cell mass (Grande & Keys, 1980; Ljunggren et al., 1961; White & Alexander, 1965).

Keys & Brozek (1953) have termed the weight gained in obesity "obesity tissue." It consists of fat (65%), extracellular fluid (14%), and cytoplasm or cell residue, which is the metabolically active part (24%) (Brozek et al., 1963; Grande & Keys, 1980; Keys et al., 1955). The content of obesity tissue is somewhat variable, and, in fact, its composition is related to the cellularity of obesity (Grande, 1984; White & Alexander, 1965). Thus, in hypertrophy, increased weight may be composed of more lipid, and in hypercellularity, increased weight is more cell residue, and this, in theory, would affect RMR.

In what direction RMR would be affected has yet to be resolved or even thoroughly investigated. As cell size

increases, both the metabolically-active cell residue tissue and extracellular fluid have been observed to decrease in proportion to the expanding, relatively inactive lipid (Johnston & Bernstein, 1955). Further, as fat cell size increases, the extracellular space within adipose tissue diminishes, which has also been speculated to reduce metabolic capacity of adipocytes (Bjorntorp, 1982). Thus, the theoretical result of hypertrophy: lower RMR per kg of body weight.

Contrarily, if weight gain is accomplished by an expanded number of adipocytes, cell walls and accessory structures (ie, cell residue) will make up a higher proportion of weight gain than lipid does (Miller & Parsonage, 1975). The theoretical result of hypercellularity, then: higher RMR per kg of body weight.

A study of 15 obese women who were part of a larger sample of 29 obese women attempting to lose weight supports this theoretical concept (Miller & Parsonage, 1975). Adipose tissue biopsy was performed on the 15 women and, although onset of obesity was not specified, a significant correlation was found between fat cell number and BMR ($\underline{r}$ = .57; $\underline{p}$ < .025). No relationship was found between cell size and BMR.

A significant correlation between RMR and both fat cell number ($\underline{r}$ = .425; $\underline{p}$ < .0001) and fat cell weight ($\underline{r}$ = .330; $\underline{p}$ < .0001) was found by Bernstein et al. (1983) in a

study of 154 obese women and 48 obese men. Mean fat cell weight, which the authors viewed as an indicator of fat cell size, was calculated from photomicroscopic determination of fat cell diameter. The authors developed regression equations with the variables FFM, fat cell number and weight, and age that explained 66% of the variation in RMR. Their analysis indicated that hypertrophic women would have a higher absolute RMR than hyperplastic women of the same fat weight. However, because fat cell number and fat cell weight explained differing proportions of the variation in RMR, the authors speculated that RMR would be affected differently if the women lost one-half of their body fat. A reduction in half the fat weight in the hypertrophic woman would mean a loss of fat cell weight (size). Using the regression equation, this would cause a 25% decrease in absolute RMR. The hyperplastic woman losing half her fat weight would reduce fat cell size but not cell number. Therefore, the impact on her RMR would be less. The authors did not examine RMR/BW.

Some evidence of energy-sparing has been detected in child-onset obese women (Bessard et al., 1983; Blair & Buskirk, 1987; Kaplan & Leveille, 1976). Both Bessard et al. (1983) and Kaplan and Leveille (1976) found reduced oxygen consumption in response to a high protein test meal in child-onset obese women when compared with nonobese

controls, although absolute RMR was within the range that one would expect, given an average weight in excess of 200 pounds (see Table 1). Blair & Buskirk (1987) found 8 child-onset obese women to expend significantly less energy per day than 8 adult-onset obese women. Per kg FFM, the child-onset obese expended significantly fewer kcal/d than adult-onset obese ($p < .05$). The child-onset obese had a slightly higher RMR than the adult-onset obese (1483 kcal/day versus 1408 kcal/day) but the difference was not significant.

In summary, there is some theoretical basis for assuming that the hypercellular (child-onset) obese would have more active cell mass in proportion to lipid and that the hypertrophic (adult-onset) obese would have more lipid than cell material (Grande, 1984; White & Alexander, 1965). One study found absolute RMR to be higher in hypertrophic obesity (Bernstein et al., 1983). Others found that the child-onset obese had lower daily energy expenditure (not the same as RMR) per kg FFM than adult-onset obese (Blair & Buskirk, 1987). Both fat cell number (Bernstein et al., 1983; Miller & Parsonage, 1975) and fat cell size (Bernstein et al., 1983) have been found to correlate with RMR. Thus, adipose cellularity and obesity onset seem to affect energy metabolism, although the total picture of this is still unclear.

Effects of Regional Fat Deposition on Resting Metabolic Rate

The previous section explored the contribution of fat cell size and number to RMR. Recently, evidence has begun to accumulate which links the distribution of adipose tissue to abnormal glucose and insulin metabolism (Evans et al., 1983; Evans et al., 1984; Kalkhoff et al., 1983; Peiris et al., 1986). No studies have directly linked fat localization to RMR. However, this section will present suggestive evidence that the RMR of the obese may be influenced by the site of fat deposition as well as by cellularity.

Characterization of Obesity by Fat Localization

Vague (1956) characterized obesity as android, in which fat is localized on the upper body, or gynoid, in which fat is localized on the lower body. The masculine term, "android," is used because fat deposition above the waist is most often seen in men. The feminine term, "gynoid," is used to describe fat accumulation in the lower abdomen, hips, buttocks, and thighs, because this fat pattern in more commonly seen in women (Ashwell et al., 1978; Bolinder et al., 1983; Vague et al., 1974).

Two methods are used to classify obesity as predominately upper or lower body: skinfold thicknesses and the waist to hip girth ratio (WHR). As further discussed in Chapter 3, WHR is widely considered to be the

most sensitive and accurate method of making this classification (Evans et al., 1984; Kalkhoff et al., 1983; Peiris et al., 1986). The closer to one (1:1) the WHR is, the greater the degree of upper body obesity while, conversely, a lower WHR denotes lower body fat predominance (Peiris et al., 1986). Peiris et al. (1986) described as an intermediate pattern of fat distribution a WHR of 0.76 to 0.85.

Metabolic Consequences of Fat Localization: Insulin Disturbances

Insulin sensitivity diminishes as WHR increases (Evans et al., 1984; Kalkhoff et al., 1983; Kissebah et al., 1982; Peiris et al., 1986). Thus, the obese male or female who has greater fat deposition in the abdomen, chest, neck, and arms is more insulin resistant and less glucose tolerant than the obese individual who has more fat in the hips, thighs, and buttocks.

Kissebah et al. (1982) studied 25 asymptomatic obese females of similar height, weight, and age but different body fat distribution. None of the lower-body obese showed glucose intolerance, yet 10 of the 16 upper-body obese had glucose tolerance test scores in the diabetic range.

Similar findings were reported by Kalkhoff et al. (1983) in a study of 110 premenopausal women. A significant positive correlation was found between WHR and

insulin response during oral glucose tolerance tests, such that there was more insulin resistance among those with the higher WHR. This correlation was found to be independent of the degree of fatness among 80 weight stable 19-49 year old women (Evans et al., 1984) and has even been described in prepubertal girls (Legido et al., 1987).

It has been speculated that upper body fat predominance is characterized by enlarged truncal adipocytes, whereas lower body fat predominance is characterized by an increased number of normal-sized adipocytes (Evans et al., 1984). Ashwell et al. (1978) found both male and female upper-body obese subjects to have larger adipocytes in the arms, shoulders, and around the waist than lower-body obese subjects. The enlarged abdominal adipocytes have a higher rate of lipolytic activity (Arner et al., 1981; Rebuffe-Scrive et al., 1985). This can lead to elevated free fatty acid concentrations in the portal and systemic circulation, and this condition has been demonstrated to inhibit hepatic uptake of insulin and result in peripheral hyperinsulinemia (Deibert & DeFronzo, 1980; Randle et al., 1963). The effect: insulin resistance and non-insulin dependent diabetes mellitus (NIDDM). This suggests to some an explanation for the greater prevalence of NIDDM in men, who are more likely than women to have upper-body fat

predominance (Evans et al., 1984; Vague et al., 1974).

Other differences in truncal and femoral adipocytes have also been studied. Adipocytes from the thigh were not found to increase their rate of lipolysis in response to epinephrine, whereas abdominal fat cells did (Kissebah et al., 1982). Vague (1956) has found greater epinephrine secretion in the upper-body obese at all times. Therefore, greater epinephrine secretion in the android obese might result in an increased rate of lipolysis in the abdominal adipocytes with resultant insulin resistance, as previously described.

Metabolic Consequences of Fat Localization: Steroid Hormone Disturbances

Two types of steroid hormones have been described (Goebelsmann, 1986; Guyton, 1986): the sex steroids, which include the ovarian and testicular steroid hormones, and the adrenal steroid hormones. Estradiol (an estrogen), progesterone, and androstenedione are the principal ovarian steroid hormones, although testosterone and estrone (an estrogen) are also secreted. The androgen, testosterone, and estradiol, though secreted in minimal amounts, are the primary testicular steroid hormones. The mineralocorticoids and glucocorticoids are the main hormones of the adrenal cortex, with very little testosterone or estrogen being secreted by the adrenal glands.

The adrenal steroids will be discussed only briefly here, because their relationship to fat localization in the "average obese" has not been studied. However, the glucocorticoid, cortisol, plays a prominent role in the obesity associated with Cushing's syndrome. Hypersecretion of cortisol in Cushing's syndrome results in excessive upper-body fat deposition, which is described as "buffalo torso" in the medical literature (Guyton, 1986). Although subjects with Cushing's syndrome-obesity were excluded from the present study, the phenomenon does indicate how steroid hormones can influence the pattern of fat deposition.

There is also a link between the sex hormones and adipocity. In women, estrogens are the principle sex steroids. The primary estrogen prior to menopause is estrone, and after menopause, estradiol is the primary estrogen (O'Dea et al., 1979). Adipocytes are the principle site for estrogen formation after menopause (O'Dea et al., 1979), which may explain why postmenopausal estradiol and estrone levels increase linearly as the percentage of ideal body weight increases (Frumar et al., 1980).

In vivo, O'Dea and associates (1979) have found strong correlations between the extent of obesity and the conversion of plasma androstenedione to estrone. This conversion increases up to 10 times in the postmenopausal

morbidly obese. Thus, in obesity and particularly after menopause, conditions apparently exist which affect reproductive hormone dynamics.

Varying levels of sex hormones have been noted in gynoid and android obesities. Evans et al. (1983) found increased WHR in women to be associated with increased plasma androgens. The amount of circulating testosterone was not greater in these upper body obese women, but there was more unbound than bound testosterone in circulation. Bound testosterone is biologically inactive. The presence of more unbound testosterone in serum in women is usually associated with masculinization (Goebelsmann & Lobo, 1986).

Testosterone and, to a lesser extent, estradiol circulate bound to a protein, sex hormone-binding globulin (SHBG) (Gibbons et al., 1986; Lobo, 1986). In women, plasma SHBG is determined by the ratio of androgens (particularly testosterone) to estrogens in the body. A decrease in SHBG levels indicates a relative increase in androgenic action (Evans et al., 1983; Gibbons et al., 1986). In Evans et al. (1983), WHR was inversely correlated with SHBG, so that an increase in upper body fat deposition, among the 80 premenopausal Caucasian women studied, was accompanied by a decrease in plasma SHBG.

Androgenic/estrogenic balance in obese women and men may actually play a role in precipitating differential fat

localization. At puberty, upper-body fat deposition in males occurs following the onset of androgen secretion and the subsequent decline in SHBG levels (Vague et al., 1974). Women suffering from polycystic ovary syndrome have an increase in adrenal androgen secretion, and this precipitates upper-body fat deposition (Yen, 1980). Conversely, men with predominately lower-body fat deposition have been found to have increased plasma estradiol levels (Sparrow et al., 1980).

The sex steroids are more obviously related to fat localization in the "average obese" than the adrenal steroids are. The causal relationship between sex steroids and fat localization can, perhaps, be inferred from animal studies. Steingrimsdottir et al. (1980) demonstrated that androgens increased and estrogens decreased adipose tissue lipoprotein lipase levels and, subsequently, adipocyte size in rats. The previously discussed work of Evans et al. (1983; 1984) suggested that diminished glucose tolerance and insulin sensitivity were secondary to changes in androgenic activity in humans. In vitro, estrogens have been found to exert a significant effect on replication of human pre-adipocytes (Roncari & Van, 1978). So, a relative decrease in androgenic activity or a relative increase in estrogenic activity might result in an increase in femoral fat cell number (lower-body obesity), rather than an increase in truncal

adipocyte size (upper-body obesity).

Some interaction between the sex steroids and thyroid hormones has been identified. Thyroxine (T4) and, to a lesser extent, triiodothyronine (T3) are bound to thyroid-binding globulin (TBG) in the bloodstream. TBG levels are increased by estrogen action and decreased by testosterone and glucocorticoids (Gibbons et al., 1986). An additional link between the steroid hormones and thyroid hormones has been seen in thyroid dysfunction. Circulating SHBG levels have been found to be elevated in hyperthyroidism (Gibbons et al., 1986; Lobo, 1986) and depressed in hypothyroidism (Gibbons et al., 1986). Perhaps if obese subjects in RMR studies were classified by site of fat deposition, RMR differences within the obese population would become more apparent.

Theoretical Relationship Between RMR and Fat Localization

No study has attempted to make a connection between RMR and site of fat deposition. Despite lack of research in this area, several conclusions can be drawn about obese individuals having predominantly upper-body or lower-body obesity. First, abdominal and femoral adipocytes are different in their metabolism (Arner et al., 1981; Salans et al., 1968). Second, differences in glucose metabolism exist between obese individuals having upper-body or lower-body obesity (Vague et al., 1974), and this results in metabolic heterogeneity among the obese (Evans et al.,

1984). Third, levels of steroid hormones differ between the upper-body obese and the lower-body obese and may even precipitate these differences in fat localization (Evans et al., 1983). Fourth, there are links between levels of circulating sex hormones and thyroid hormones, which may affect metabolic rate. In summary, hormonal differences are present in women having upper-body or lower-body fat deposition.

CHAPTER 3 METHODOLOGY

The purpose of this study was to determine if differences in resting metabolic rate (RMR) existed between nonobese females and obese females having different ages of obesity onset. This section of the study contains a detailed description of the subjects, measurement procedures, and reliability and validity of the measurement procedures used.

Population

The population consisted of weight-stable, apparently healthy Caucasian obese and nonobese females between the ages of 20 and 38 years. To increase homogeneity and control as much as possible factors having an influence on RMR, the population was further limited to nonsmokers who had no history of thyroid dysfunction, cardiovascular disease, or diabetes. The obese population was classified as adult-onset or child-onset obese. Both obese groups demonstrated the gynoid (lower-body) pattern of fat distribution.

Sample

The sample consisted of 18 subjects, 6 from each of three groups: nonobese with no previous history of obesity, child-onset obese (COO), and adult-onset obese (AOO). Eight were students from the University of Maryland solicited from health education classes, and 10

were respondents to an advertisement in the Washington Post.

All subjects were between the ages 20 to 38 years, with a mean age of 28.16 years. There were no significant differences in age between nonobese (M = 26.50 +/- 5.92 years), COO (M = 29.83 +/- 4.35 years), and AOO (M = 28.17 +/- 6.05 years) subjects. The oldest subject in the sample was a very lean 38-year-old.

The Metropolitan Life Insurance Company's 1983 Height and Weight Tables were used for initial classification of subjects as nonobese or obese. Subjects were initially classified as nonobese or obese if their self-reported height and weight put them within the recommended weight range for a woman of medium frame (nonobese), or at greater than 20% over the recommended weight range for a medium-framed woman (obese).

Mean heights and weights of the 18 subjects may be found in Table 3 in the Results chapter. Mean height of the 18 subjects was 166.19 cm (65.4 inches), and there were no significant differences in height between the three groups. However, there were significant weight differences between the nonobese (M = 58.28 +/- 5.97 kg) and both the AOO (M = 79.02 +/- 9.98 kg) and COO (M = 94.92 +/- 27.07 kg) women.

Reference body composition values for women have shown percentage body fat to jump significantly between

age 35.1 years and 44.7 years, from a mean percentage fat of 28.74% at age 35.1 to a mean of 35.33% at age 44.7. The increment in percentage fat of reference women between ages 20.3 years and 35.1 years was small and insignificant (ICRP, 1975).

In the present study, the oldest subject was below the average percentage fat in her group. Mean percentage fat for the nonobese subjects was 18.53 +/- 6.99%, significantly lower than that of the AOO ($\underline{M}$ = 37.80 +/- 5.19%) and the COO groups ($\underline{M}$ = 41.00 +/- 9.58%). Subjects were only retained for the study if their percentage fat determined by underwater weighing was greater than 30% (obese) or less than or equal to 26% (nonobese).

The 18 subjects in the sample had a mean fat-free mass (FFM) of 50.07 kg. FFM was not significantly different between the AOO ($\underline{M}$ = 48.92 +/- 5.47 kg) and the nonobese ($\underline{M}$ = 47.22 +/- 3.49 kg). However, the COO subjects had significantly greater FFM than the nonobese ($\underline{M}$ = 54.09 +/- 7.73 kg).

Obese subjects were classified according to age of onset by using self-reported questionnaire data and a follow-up telephone interview. Subjects were classified as child-onset obese if they or others characterized themselves as "moderately overweight" or "extremely overweight" during childhood or before menarche. Subjects were classified as adult-onset obese if they characterized

themselves as "underweight" or "normal weight" during childhood and menarche. If there were inconsistencies on the questionnaire or if additional information was needed for clarification, the investigator interviewed subjects by telephone.

According to self-reported questionnaire data, the age of menstruation onset was earlier for the COO ($\underline{M}$ = 10.83 +/- 0.98 years) than for either AOO ($\underline{M}$ = 12.33 +/- 0.82 years) or the nonobese ($\underline{M}$ = 12.92 +/- 1.56 years). This is consistent with the findings of Garn et al. (1986).

All obese subjects in the sample had lower-body obesity, as defined by Vague (1956). The mean waist/hip girth ratio (WHR) averaged 0.75 and did not differ statistically between COO and AOO.

A screening questionnaire was used to restrict the sample to those reporting no known medical conditions from among the following: thyroid dysfunction, diabetes, hypertension, heart disease, or chronic lung disease. None of the subjects indicated any such health impairments.

Subjects were asked to list medications regularly taken so that those taking RMR-affecting medications could be eliminated from the study. Of the 18 subjects retained for the study, six reported taking an occasional aspirin, Tylenol, or Advil for headaches or menstrual

cramps. One nonobese subject used birth control pills.

Because cigarette smoking affects RMR, only nonsmokers were retained for the study (Hofstetter et al., 1986). Six subjects in the sample were former smokers, but all had refrained from smoking for at least two years.

Finally, the sample did not include subjects on low calorie diets (below 1,200 kcal/day) (Hoffmans et al., 1979) or those who had lost more than 2.3 kg during 3 months prior to the study, as suggested by Segal et al. (1985). All but 4 subjects in the sample had experienced some weight fluctuation in the past 3 months, but the fluctuations did not exceed 2.3 kg and were not judged to be significant by the investigator.

Testing Procedures

A questionnaire and screening measure (waist/hip girth ratio) were used to determine subject eligibility for the study. Subjects meeting criteria for the study underwent three additional measures (hydrostatic weighing, residual lung volume, and resting metabolic rate) at the University of Maryland's Human Exercise Research Laboratory during the months of May and June.

Screening Questionnaire

Volunteers for the study were screened for eligibility using a questionnaire developed by the investigator and reviewed by the dissertation advisor and

University Institutional Review Board (IRB). The questionnaire collected information on: age, smoking, use of weight control diets, medical conditions that could affect metabolic rate, activity level, birth weight/length, weight history, and menstrual history. A copy of the questionnaire may be found in Appendix C. Subjects meeting eligibility requirements for the study as previously described underwent further measures.

All subjects signed an Informed Consent (Appendix D) before study procedures were carried out. Also prior to measurements, subjects were provided with Procedures for Metabolism Study Subjects, as shown in Appendix E.

Waist/Hip Girth Ratio

Measurement of the waist/hip girth ratio (WHR) was obtained to include in the study only obese subjects having predominantly lower-body fat deposition. Clothed subjects were measured in the standing position with a non-flexible measuring tape, following procedures of Evans et al. (1984). The smallest circumference around the umbilicus constituted waist girth, and the largest circumference around the gluteus constituted hip girth. Waist girth was subsequently divided by hip girth to arrive at the ratio. Subjects having WHR in excess of 0.80 were not retained for the study.

Resting Metabolic Rate by Indirect Calorimetry

Resting metabolic rate (RMR) was measured once on

each subject by indirect calorimetry with an open-circuit system, the Metabolic Graphics Corporation's Exercise System 2001 (St. Paul, Minnesota). The MGC-2001 consists of rapidly responding oxygen and carbon dioxide analyzers for data acquisition, reduction, and transfer to a CAD/Net host computer system. The CAD/Net computer consists of a color monitor for video display, electronics, keyboard, and a mass storage system running 512K of memory.

Subjects were tested in the University of Maryland's Human Exercise Research Laboratory during morning hours after an overnight fast and a 20 minute rest period (Foss et al., 1982; Zavala & Printen, 1984). Because BMR has been shown to vary during the menstrual cycle, RMR was not measured during any subject's menstrual cycle (Solomon et al., 1982; Webb, 1986). In addition, subjects were instructed not to exercise for the 24 hours preceding the RMR measurement and not to take any medications unless previously discussed with the investigator.

Upon arriving at the lab, each subject was given the opportunity to void and change into lightweight, comfortable clothes. Barefoot height and WHR (unless already obtained) measures were taken, and the subject was fitted for an air-sealed face mask having a non-rebreathing valve (Hans Rudolph 2-Way Mask) and shown the equipment to be used. Weight was measured on a balance scale which had been zero-balanced. While the

investigator calibrated the MGC-2001, the subject rested in a chair.

Calibration of the MGC-2001 was done by the investigator following standard procedures published by the company and followed by the Human Exercise Research Laboratory. The system was calibrated with a 3 liter syringe using a gas mixture of 12.1% oxygen, 4.98% carbon dioxide, and balance nitrogen. Room temperature, humidity, and barometric pressure values were updated in the system before each measurement. Dead space air for the small face mask was calculated as 175 ml and for the large face mask as 185 ml.

After the rest period, the subject put on her mask and breathed room air while a sample line brought expired gases to the MGC-2001. Respiratory gas exchange was monitored continuously for approximately 20 minutes, with oxygen consumption and carbon dioxide production computations made by the computerized system at 1 minute intervals. When five consecutive stable determinations of gas exchange occurred, measurements were stopped and the subject removed her mask. Only data collected from the last 10 minutes of the study were analyzed. The Weir (1949) formula was used to convert mean oxygen consumption and carbon dioxide production to caloric expenditure per minute.

Residual Lung Volume by Nitrogen Washout

Residual lung volume (RV) was calculated by subtracting expiratory reserve volume (ERV) from functional residual capacity (FRC). ERV and FRC were measured in the Human Exercise Research Laboratory with the Medical Graphics Corporation's Model 1070 Pulmonary Function Laboratory (St. Paul, Minnesota) a few minutes after the RMR measurement. The MGC-1070 consists of a rapid nitrogen analyzer connected to a pneumotachometer (flow sensing device) which provides breath-by-breath analysis of gas concentration in the lungs. A vacuum pump draws the gas sample into a capillary tube. An electron beam ionizes the gas sample and, as the beam passes through a magnetic field, ions of the various constituent gases separate according to their specific mass and electric charge. While the subject rested, the investigator calibrated the MGC-1070 system with standard gases and a 3 liter syringe.

For the ERV measurement, the standing subject put on a noseclip and breathed ambient air through a cardboard mouthpiece attached to a plastic breathing tube which entered the MGC-1070. Following three to four normal breaths and during an exhalation, the subject was prompted to exhale maximally. This procedure was repeated a minimum of three times with a rest between each and system recalibration as necessary. The average of the two

closest trials was used.

FRC was determined using the nitrogen washout method. The air remaining in the lungs following a maximal expiration constitutes the FRC. Of that quantity, ERV was known; the air trapped in alveolar spaces in the lungs, the RV, was not known.

When FRC is measured by the nitrogen washout technique, the FRC volume is determined by continuous measurement of the percentage of nitrogen exhaled in each breath while the subject inhales pure oxygen. At the same time, the volume of exhaled air is measured. The FRC volume is then determined by computerized multiplication of exhaled air, times exhaled nitrogen, over time.

In this procedure the seated subject wore a noseclip and breathed through a rubber sealed mouthpiece into the MGC-1070. The mouthpiece prevented air leakage around the mouth, and the noseclip prevented air leakage from the nose. After the subject had established a stable respiratory pattern and at the end of a normal exhalation, the investigator switched the inhaled gas from ambient air to humidified oxygen. This commenced the nitrogen washout procedure, which continued for 7 minutes or until less than 1% nitrogen in alveolar air remained. Nitrogen concentration was displayed on the monitor so that a breath-by-breath washout curve could be observed. Upon hearing a bell signal, the investigator switched off the

oxygen, the subject again breathed ambient air, and the procedure was ended.

The investigator flushed out the mouthpiece with the 3 liter syringe until nitrogen readings of approximately 79.6% were indicated by the computer. At least two trials were conducted for each subject, with a 5 minute rest between each. A switch-in error of less than 150 ml was considered acceptable, and only data from these trials were retained. The mean of the closest two acceptable readings was considered to represent the FRC.

Henry (1967) has observed that an individual's true score is considered to be best estimated from the average of a series of scores. Thus, RV was calculated by subtracting average ERV from average FRC.

Body Composition Assessment by Hydrostatic Weighing

Although subjects were initially classified as nonobese or obese based on height-weight chart placement, body composition was more accurately determined by hydrostatic weighing, using the densitometric method pioneered by Behnke et al. (1942). The hydrostatic weighing system in use at the University of Maryland Body Density Laboratory consists of a standard tank in which an aluminum chair is suspended from a load cell. Access to the chair is by an aluminum ladder on the side of the tank.

Prior to each underwater weighing session, the load

cell was calibrated using established procedures of the Body Density Laboratory. The water tank filter was turned off during calibration and underwater weighing. The weight of the aluminum chair and any items being used by the subject during the procedure, such as a noseclip or goggles, was then determined.

Subjects were instructed to fast overnight but to consume plenty of water throughout the evening. Prior to hydrostatic weighing, the subject's height and weight was obtained and the subject showered.

The hydrostatic weighing procedure was as follows. The subject sat in the aluminum chair, and the investigator positioned it so that the water level in the tank was between the subject's chin and lower lip. The subject got out of the chair and held the aluminum ladder, keeping the water at chin level, while the chair weight was measured. The subject returned to the chair and was instructed to exhale maximally above the water, then to lower her upper body slowly into the water, continuing to exhale as much air as possible during submersion. When the investigator observed no further expiration of air bubbles, the computerized sampling procedure was initiated. The program sampled for 2 seconds, and the investigator signalled the subject to surface. This method has been found to increase subject sense of control, to reduce fear, and to minimize water turbulence

(Goldman & Buskirk, 1961).

Three to five samples were taken on each subject, and the last and highest three to five stable weights were averaged. Behnke & Wilmore (1974) recommended using the highest obtained underwater weight if it was obseved more than twice. The subject's RV, age, height, and weight were entered into the computer. Water temperature was recorded in degrees Centigrade from a thermometer suspended in the tank. Lean body weight, fat weight, and percentage fat based on equations of Siri (1961) and Brozek et al. (1963) were generated by the Body Density Laboratory software program.

Reliability and Validity of Instrumentation

Waist/Hip Girth Ratio

The waist/hip girth ratio (WHR) is one method for differentiating between upper and lower body fat predominance (Ashwell et al., 1978). Lower-body obesity has been defined as WHR less than or equal to 0.76 (Evans et al., 1984; Peiris et al., 1986) or less than 0.73 (Kalkhoff et al., 1983). Upper-body obesity has been variously defined as WHR greater than 0.85 (Evans et al., 1984; Peiris et al., 1986), greater than 0.80 (Hartz et al., 1984), or greater than 0.83 (Kalkhoff et al., 1983).

The WHR has been found to correlate highly with multiple skinfold measures, arm-to-thigh adipose muscular

ratio, and intra- to extra-abdominal fat distribution determined by computed tomography scans for assessing body fat topography (Evans et al., 1984; Evans et al., 1983; Kissebah et al., 1982). Girth measurements have also been found to be more reproducible than measurements of skinfold thickness in the obese (Bray et al., 1978).

In addition, the WHR has been used to predict metabolic complications of obesity. Hartz et al. (1984) surveyed more than 19,000 women and found WHR more sensitive than neck, bust, waist, or hip circumference measurements to predict diabetes in women with upper-body obesity. As the WHR approaches and exceeds 0.85, insulin resistance and its metabolic consequences predominate (Evans et al., 1984; Hartz et al., 1983; Kalkhoff et al., 1983).

Hydrostatic Weighing

Hydrostatic weighing as a valid measure of body composition is based on the assumption that the body consists of two distinct components -- fat and fat-free -- and that these two components are chemically different yet relatively constant in their own make-up throughout the population. Thus, if one knows the specific gravity, or density, of each component and then measures the density of the whole body, the fat and fat-free content of the body can be calculated. The formula of Goldman and Buskirk (1961) calculates the density of the body as:

$$\frac{\text{kg wt in air}}{([(\text{kg wt in air}-\text{kg wt in water})/\text{water density}]-\text{RV}-0.10)}$$

The validity of hydrostatic weighing is predicated upon the validity of the densities of fat and fat-free components of the body. Equations presently in use for converting body density to percentage fat were developed using data from young, sedentary, adult male cadavers (Siri, 1961; Brozek, et al., 1963). These data indicated that fat has a density of 0.900 gm/cc and that fat-free tissue has a density of 1.100 gm/cc. Percentage fat is derived from body density as follows:

Siri (1961): % fat = ([density/4.570]-4.142) X 100

Brozek et al. (1963): % fat = ([4.950/density]-4.5) X 100

The correlation between these two equations was 0.995 in a study involving 54 college males (Behnke & Wilmore, 1974).

Womersley et al. (1976) examined athletic, sedentary, and obese male and female subjects of various ages and found that muscular and younger obese women had a lower density of fat-free mass compared with the young male cadavers of Siri (1961) and Brozek et al. (1963). Twelve young, muscular females ranging in age from 19 to 49 years ($\underline{M}$ = 27.2 years) had a FFM density of 1.090 gm/ml. Eight young obese females ranging in age from 27 to 44 years ($\underline{M}$ = 36 years) had a FFM density of 1.093. Only the young sedentary women studied had a FFM density equal to that

described by Siri (1961) and Brozek et al. (1963). If a density of 1.100 had been assumed for all these women, the level of body fatness would have been overestimated for the obese and the athletic. Although the same densities of fat and fat-free tissue are regularly applied to women and men, more studies on women and other population groups are needed to validate tissue densities (Lohman, 1984).

Hydrostatic weighing also assumes that the density of fat and fat-free tissue is constant within a given population, when, in fact, considerable variability may exist. Lohman (1984) noted that variability is not well defined in many populations, including women. The reasons for variability in body density primarily focus on the FFM, with hydration being the largest single source of variation in density of the FFM. Grande and Keys (1980) examined data on cadavers from four studies and found water to make up 69.6 to 77.9% of the FFM. Siri (1956) proposed that water content of the FFM could vary by 1 to 3%, which would result in an error of +/- 2.7% in calculation of percentage fat.

Bone density also accounts for variation in density of the FFM (Bakker & Struikenkamp, 1977; Lohman, 1981). In normal adults, skeleton comprises 17 to 23% of the FFM, which would result in a range of FFM density from 1.089 to 1.101 g/ml (Bakker & Struikenkamp, 1977). Because bone has a relatively high density, an increase in the

mass of the skeleton would increase density of the FFM, and a decrease in the mass of the skeleton would decrease density of the FFM (Womersley et al., 1976).

A trained technician can obtain closely reproducible results from hydrostatic weighing (Behnke & Wilmore, 1974; Lukaski, 1987). However, there are potential sources of measurement error that could reduce the validity of body density detemined by hydrostatic weighing. The first and most significant of these is the residual lung volume (RV). It is essential to obtain an accurate measure of RV to account for air trapped in the lungs that will contribute to buoyancy during underwater weighing (Behnke & Wilmore, 1974; Lohman, 1984). Residual volume that is predicted rather than measured is a major source of error (Morrow et al., 1986).

A second source of measurement error is excessive gas in the gastrointestinal tract. This is not measurable and is not easily estimated (Garrow, 1982), and, therefore, must be controlled by instructing subjects to avoid gas producing foods for several days prior to underwater weighing (Behnke & Wilmore, 1974).

Error also occurs when the underwater weighing system is not calibrated carefully prior to each use and when the investigator fails to correct for water temperature that is higher or lower than the standard 37 degrees Centigrade (Lohman, 1984), although these sources of error are

minimized by a careful technician.

Finally, error can occur when uncooperative subjects are used. When a subject is not comfortable in or under water, considerable error can result due to failure to expel air maximally (Clark & Mayhew, 1980), excessive movement during measurement, and failure to remain submerged long enough (Lukaski, 1987).

The primary limitation of hydrostatic weighing as a valid and reliable measure of body composition is biological, not methodological. For young adult men, the method is considered accurate to within .002 g/ml, which is equivalent to +/- 1% error in body fat (Lohman, 1982). For women, underwater weighing may have a theoretical error rate of 2 to 4%, primarily due to hydration and skeleton differences which affect the density of the fat free body (Lohman, 1982). Nevertheless, hydrostatic weighing is widely considered to be the most practical and accurate method available for assessing body density (Lohman, 1982; Lohnamn, 1984).

Residual Lung Volume

Residual lung volume (RV) is the volume of air that remains in the lungs following a maximal expiration (Buskirk, 1961). With the expiratory reserve volume (ERV), it makes up the functional residual capacity (FRC).

ERV can be measured simply with a spirometer (Ruppel, 1986). As the individual exhales into the spirometer, the

spirometer bell moves up; on inhalation, the bell moves down. Up and down movements of the bell are recorded on a piece of paper attached to a drum. The principle is the same when ERV is measured on the MGC-1070, although the "tracings," seen on the cathode ray tube display (CRT) are in the opposite direction.

FRC cannot be measured by spirometry (Fox & Mathews, 1981; McArdle et al., 1981; Ruppel, 1986). The multiple-breath nitrogen washout method using open circuitry has been used as a method for assessing FRC for over 30 years (Kraemer et al., 1986). During a brief period of breathing 100% oxygen, nitrogen trapped in air spaces in the lungs is "washed out", permitting calculation, based on the volume of expired nitrogen, of the volume of the residual air spaces.

Determination of FRC by nitrogen washout is based on a concentration-dilution relationship. The classic equation for calculating FRC (Brugman et al., 1986) is:

$$FRC = \frac{(Nf \times Vs) - (Ni \times Vs)}{(80.0 - Nf)}$$

Where, Nf represents the percentage of nitrogen in the MGC-1070 system at the end of the procedure; Ni represents the percentage of nitrogen in the system at the start of the procedure; Vs is the total 1070 volume at the end of the test; and 80% is the assumed nitrogen content of alveolar gas.

Validity of the FRC procedure is predicated upon two assumptions (Jalowayski & Dawson, 1982). First, the initial concentration of nitrogen in the alveoli is assumed, since this cannot be precisely measured. Second, nitrogen can be absorbed into blood and tissues, such that tissue nitrogen might contribute to nitrogen collected during the washout. The procedure assumes that the contribution of tissue nitrogen is not significant. The two assumptions are widely regarded as correct. Sterk et al. (1980) validated the multiple-breath nitrogen method by a double tracer gas dilution technique which was based on mass balance equations for argon, an inert gas, washed into the lung simultaneously as nitrogen was washed out of the lung.

Low intrasubject variability has been found in studies of RV by nitrogen washout using open circuit spirometry, establishing the method as accurate and reliable (DeGroodt et al., 1984; Saniie et al., 1979; Sterk et al., 1980). Morrow et al. (1986) estimated accuracy to be within +/- 1%. When RV was measured on 14 males and 32 females enrolled in a fitness program and on a sample of 134 trained male athletes, the nitrogen washout method and oxygen dilution method gave similar results (Morrow et al., 1986). Available prediction equations for estimating RV were found to be inaccurate and would have resulted in major body density errors.

Small errors in measurement of ERV, FRC, or RV can have a major impact (greater than 2%) on calculation of percentage fat from body density. Marks and Katch (1986) calculated sources of error in RV measurement as 72% due to biovariability, 19% due to technical error, and 9% due to trend effect.

Sources of technical error have been well-documented. The primary cause of measurement error is leaks of nitrogen into the system, which can be detected and corrected before measurement when proper calibrations are performed (Jalowayski & Dawson, 1982; Miller et al., 1987). Other sources of error identified by Jalowayski and Dawson include insufficient equipment warm-up time, plugging of the needle valve, excessive moisture in the analyzer, and malfunction of the vacuum pump, all of which can be detected by periodic calibration of the system using the 3 liter syringe.

RV measured on land may not precisely reflect RV at the time of water immersion, such as during underwater weighing. It has been observed that hydrostatic pressure on the chest wall increases during immersion, as does thoracic blood volume (Arborelius et al., 1972; Begin et al., 1976). Although in theory, one would expect this to lower RV in water, Girandola et al. (1977) have found immersion to increase RV in some subjects and to decrease it in others. Most authors recommend that to minimize

error, RV be measured in the water at the time of underwater weighing (Behnke & Wilmore, 1974; Clark & Mayhew, 1980; Goldman & Buskirk, 1961), although these same authors note that the difference in body density using land-RV rather than water-RV is probably small. An exception to this is the data of Girandola et al. (1977), who found significant differences in RV measured by oxygen dilution on college-age males on land and in water ($p < .01$). This resulted, in one case, in 14% fat when calculated using land-RV versus 13.4% fat using water-RV.

Resting Metabolic Rate by Indirect Calorimetry

As cells utilize nutrients, energy in the form of heat is generated and released into the environment. Various techniques of calorimetry are used to measure this energy expenditure. Direct calorimetry measures actual heat loss. The technique requires subjects to remain in a chamber for a prolonged period of time, at least 24 hours, and is thus expensive and slow (Jequier, 1981). Indirect calorimetry, the measurement of gas exchange, is less expensive and more convenient and the preferred method of calorimetry today (Norton, 1980).

As cell mitochondria oxidize nutrients, oxygen is used and carbon dioxide is produced. Because the total cardiac output travels to the lungs through the pulmonary circulation, analysis of inspired and expired air provides a valid, although indirect, method of assessing cell

metabolism (Foss et al., 1982; Norton, 1980). When a nonrebreathing valve is used, inspired air can be separated from expired air for analysis. Oxygen consumed and carbon dioxide produced can then be converted to kilocalories using the formula of Weir (1949), where kcal/min is determined by:

3.9(O2 used in liters/min) + 1.1(CO2 produced in liters/min)

Both theoretically and in practice, indirect calorimetry and direct calorimetry are considered equivalent for assessing caloric expenditure (DuBois, 1936; Pittet et al., 1974).

As with the other measurements described in this section, reliability of resting metabolic rate by indirect calorimetry is dependent upon proper calibration and precision in use of the equipment (Blair & Buskirk, 1987; Norton, 1980). Because RMR is a determination of energy expenditure in the resting state, verification that the subject is at rest will yield a more accurate measure. This may be accomplished by having the subject sit at rest for at least 30 minutes before the measurement (Henson et al., 1987; Hoffmans et al., 1979; Zavala & Printen, 1984) or by measuring pulse rate immediately before and after the RMR measurement (Hoffmans et al., 1979). Avoiding unexpected sounds during the measurement, having subjects void before measurement, letting subjects find a

comfortable position, and checking the face mask for comfort and fit will also contribute to the resting state (Zavala & Printen, 1984). It has been recommended that RMR be measured while seated, since an 11% increase in RMR was observed when obese subjects were lying down (Paul et al., 1976). Continuing the measure for at least 10 minutes (Foss et al., 1982) or until at least five consecutive stable determinations of V02 and VC02 have been observed (Feurer et al., 1983) will yield reliable measures of energy expenditure in the resting state.

It does not appear to matter whether the subject breathes into a mouthpiece or a facemask or uses a ventilated hood for the RMR measurement. No differences in RMR among the same subjects using a mouthpiece-noseclip or ventilated hood were observed (Owen et al., 1986), or among the same subjects using the ventilated hood, face mask, or mouthpiece-noseclip (Segal, 1987).

Data Analysis

Statistical analyses were performed to compare absolute resting metabolic rate per day (RMR/d), resting metabolic rate per kg body weight (RMR/BW), resting metabolic rate per kg fat-free mass (RMR/FFM), and resting metabolic rate per kg fat mass (RMR/FM) of nonobese, adult-onset obese, and child-onset obese females.

Prior to data analysis, data were examined for

normality and homogeneity of variance. The chi-square and Kolmogorov-Smirnov tests were used to determine goodness of fit of the data. The hypothesis of normality was upheld by these tests.

The assumption of homogeneity of variance was tested using Hartley's F test (Winer, 1971). Homogeneity of variance was upheld in all cases except one, in which case it was rejected because the observed F_{max} exceeded the table value for significance at the .05 level.

Under these conditions, hypotheses were tested using t tests. In addition, data were further analyzed using Pearson's coefficient of correlation and multiple regression analysis. All statistics were run on a Turbo Solution personal computer using Microstat statistical package (Ecosoft, Inc., Indianapolis, Indiana, c. 1984).

CHAPTER 4 RESULTS, DISCUSSION AND OBSERVATIONS

Results

The purpose of this study was to determine if obese females had a lower resting metabolic rate (RMR) than nonobese females. Further, the obese subjects were classified as adult-onset obese or child-onset obese, and the metabolic rates of these two groups were compared.

This section presents results of statistical data analysis to determine if differences existed between nonobese, adult-onset obese (AOO), and child-onset obese (COO) women in RMR/day, RMR/BW, RMR/FFM, and RMR/FM. Combined data from COO and AOO subjects were also analyzed to assess any differences between obese and nonobese women in measures of RMR. A discussion of the findings and subjective observations follow the analyses.

Demographic Data

To increase homogeneity in the population of interest, the study was limited to weight-stable, apparently healthy Caucasian nonobese and obese females having the following characteristics: a) ages 20 to 38 years, b) WHR less than 0.80, c) less than or equal to 26% fat (nonobese) or greater than 30% fat (obese), d) nonsmokers, and e) not taking any RMR-affecting medications.

Seventeen subjects meeting these criteria and one

very lean subject who was 3 years older than the age cut-off were retained for the study. Differences between groups in demographic characteristics were examined using *t* tests and, because of the small sample size, pooled estimates of variance. Level of significance was set at $p \leq .05$.

Obese females were characterized as child-onset based upon self reported obesity onset before puberty. Adult-onset were so classified if self reported obesity occurred after menstruation onset.

The AOO and COO groups did not significantly differ from each other in age, weight, height, percentage fat, fat-free mass (FFM), or WHR. Both AOO and COO subjects had significantly higher weight and percentage fat than the nonobese subjects, as would be expected. However, AOO and COO subjects did not differ significantly from nonobese subjects in age or height. AOO and nonobese subjects had very similar FFM, while FFM was significantly higher in COO than in the nonobese ($p < .05$). When the data of COO and AOO were combined, the difference in FFM between nonobese and obese subjects was not statistically significant. Characteristics of the 18 COO, AOO, and nonobese subjects may be found in Table 3.

To further characterize the 18 subjects, a screening questionnaire (see Appendix C) elicited information about educational level, occupation, frequency of exercise, and

Table 3

Subject Characteristics, Measured

	Age, yr	Wt, kg	Hgt, cm	FFM, kg	%Fat, Siri	WHR
Child-Onset Obese (COO)						
01	23	73.50	162.56	50.13	31.79	.75
05	26	136.50	171.45	68.60	50.25	.80
06	32	70.50	167.64	48.67	30.95	.73
07	34	72.50	158.75	47.65	34.27	.73
08	31	105.00	166.37	54.09	48.48	.78
09	33	111.50	175.01	55.40	50.31	.75
Mean	29.83	94.92	166.96	54.09	41.00	.76
+/-	+/-	+/-	+/-	+/-	+/-	+/-
S.D.	4.35	27.07	5.87	7.73	9.58	.035
Adult-Onset Obese (AOO)						
20	32	66.75	170.18	43.52	34.79	.76
21	21	82.50	167.99	53.69	34.93	.75
23	33	80.90	165.10	49.80	38.45	.73
24	30	68.20	157.99	41.69	38.86	.72
25	20	82.50	170.94	55.62	32.58	.74
29	33	93.25	168.91	49.22	47.22	.77
Mean	28.17	79.02	166.85	48.92	37.80	.745
+/-	+/-	+/-	+/-	+/-	+/-	+/-
S.D.	6.05	9.98	4.79	5.47	5.19	.019
Nonobese (NO)						
40	26	59.70	167.00	45.04	24.55	--
41	38	54.50	170.18	45.92	15.75	--
42	22	48.50	157.48	44.18	8.90	--
43	22	61.75	172.72	53.74	12.98	--
44	25	65.54	162.56	48.39	26.17	--
45	26	59.70	158.75	46.04	22.88	--
Mean	26.50	58.28[b,d]	164.78	47.22[a]	18.53[c,d]	--
+/-	+/-	+/-	+/-	+/-	+/-	
S.D.	5.92	5.97	6.19	3.49	6.99	

Level of Significance Key:
a - $p < .05$ between COO and NO
b - $p < .005$ between COO and NO
c - $p < .0005$ between COO and NO
d - $p < .005$ between AOO and NO

overall activity level. This information is briefly presented here and in Table 4.

All of the subjects except one in the COO group worked full-time outside the home, were full-time students, or had full-time responsibilities in the home with young children. Most of those who worked were in low-activity occupations. The exceptions: a homemaker with two small children in the AOO group and a flight attendant in the nonobese group. There were unequal numbers of students in each group.

Activity level and exercise frequency differed between the groups. Subjects who exercised more frequently tended to also be more active while those who exercised less frequently reported being less active. Pearson's coefficient of correlation between activity and exercise was statistically significant for AOO (r = .759), COO (r = .894), and nonobese subjects (r = .784; see Tables 7, 9, and 10). Thus, the women in the COO group who exercised less frequently also described their activity level as inactive or lightly active, compared with the more frequent exercisers in the AOO and nonobese groups.

There was very little variation in activity level within each group, but exercise frequency varied considerably. Based upon activity level categories selected by the subjects, the COO group could be

classified as having light activity, the AOO group as lightly to moderately active, and the nonobese group as moderately active.

Table 4

Subject Characteristics, Questionnaire

Item	Child-Onset Obese (n=6)	Adult-Onset Obese (n=6)	Nonobese (n=6)
Occupation			
Full-time	4	3	3
Part-time	1	0	
Student	1	2	3
Homemaker		1	
Education			
Yrs College	Range = 1-6 yr	Range = 0-4 yr	Range = 0-4 yr
	M = 3.6	M = 2.1	M = 3.16
Yrs Post-BA	M = 0.83	M = 0	M = 0.17
Activity Level	M = 2.17 +/- 0.40	M = 2.66 +/- 0.82	M = 3.10 +/- 0.98
1=sedentary 2=light 3=moderate 4=very active			
Exercise Freq.	M = 2.00 +/- 1.09	M = 3.16 +/- 0.75	M = 3.33 +/- 1.21
0=0/week 1=1/week 2=2/week 3=3/week 4=4/week 5=> 4/week			

Results of Hypothesis Testing

Three hypotheses were examined using t tests. In addition, Pearson's coefficient of correlation was used to examine the strength of the relationships between the variables.

Hypothesis 1: Obese females will have a lower RMR per unit of fat free mass (FFM), fat mass (FM), and body weight (BW) than nonobese females.

To test this hypothesis, data from COO and AOO subjects were combined. Table 5 illustrates RMR and other characteristics of the nonobese and obese subjects.

Mean absolute RMR of the obese subjects was significantly higher than the nonobese (1531 kcal/day versus 1332 kcal/day; $p < .05$). RMR adjusted for FFM (RMR/FFM) in the obese subjects was statistically indistinguishable from that of the nonobese subjects.

Despite higher absolute RMRs, the obese subjects had significantly lower mean RMR per kg BW and FM than the nonobese subjects. RMR/BW was 18.47 kcal/kg/day in the obese and 22.94 kcal/kg/day in the nonobese, a difference of 4.47 kcal/kg/day ($p < .05$). RMR/FM was 49.71 kcal/kg/day in the obese and 144.31 kcal/kg/day in the nonobese ($p < .0005$).

The hypothesis that obese subjects would have a lower RMR per unit of fat mass and body weight was upheld. RMR/FFM was not found to be different between the two

groups.

Table 5

Resting Metabolic Rates of Nonobese and Combined Obese Subjects

	Obese (n = 12)	Nonobese (n = 6)	Difference
Age, yr	29.00 +/- 5.09	26.50 +/- 5.92	n.s.
Wt, kg	86.97 +/- 21.15	58.28 +/- 5.97	$p < .005$
FFM, kg	51.51 +/- 6.93	47.22 +/-3.49	n.s.
FM, kg	35.46 +/- 15.38	11.06 +/- 4.85	$p < .005$
Hgt, cm	166.91 +/- 5.11	164.78 +/- 6.19	n.s.
% Fat	39.41 +/- 7.54	18.53 +/- 6.99	$p < .00005$
RMR/d, kcal	1531.17 +/- 164.61	1332.00 +/- 129.57	$p < .05$
RMR/BW, kcal/kg	18.47 +/- 4.47	22.94 +/- 1.95	$p < .05$
RMR/FFM, kcal/kg	30.26 +/- 5.40	28.31 +/- 3.27	n.s.
RMR/FM, kcal/kg	49.71 +/- 17.94	144.31 +/- 70.38	$p < .0005$

All values are mean +/- s.d.

Pearson's coefficient of correlation was used to suggest reasons why RMR/FM and RMR/BW differed between obese and nonobese women while RMR/FFM did not. Coefficient correlations of the combined obese and the nonobese subjects may be found in Tables 6 and 7.

Table 6

Resting Metabolic Rate and Body Composition: Correlation Coefficients of Combined Obese Subjects

	BW (1)	FFM (2)	FM (3)	%F (4)	RMR/D (5)	RMR/BW (6)	RMR/FFM (7)	RMR/FM (8)	ACTIV (9)	EXER (10)
(1)	1.000	.870	.977	.848	.003	-.858	-.594	-.885	-.240	-.372
(2)		1.000	.745	.482	-.040	-.758	-.733	-.633	.134	-.167
(3)			1.000	.939	.022	-.834	-.486	-.924	-.383	-.431
(4)				1.000	.029	-.737	-.294	-.920	-.524	-.410
(5)					1.000	.471	.685	.278	.097	-.026
(6)						1.000	.860	.932	.207	.214
(7)							1.000	.623	-.091	.023
(8)								1.000	.386	.287
(9)									1.000	.765
(10)										1.000

Critical Value (.05) = +/- .524

In the obese subjects, RMR/BW correlated significantly ($p < .05$) with BW ($r = -.858$), FFM ($r = -.758$), FM ($r = -.834$), percentage fat ($r = -.737$), RMR/FFM ($r = .860$), and RMR/FM ($r = .932$). The direction of the correlations was the same in nonobese subjects, but

Table 7

Resting Metabolic Rate and Body Composition: Correlation Coefficients of Nonobese Subjects

	BW (1)	FFM (2)	FM (3)	%F (4)	RMR/D (5)	RMR/BW (6)	RMR/FFM (7)	RMR/FM (8)	ACTIV (9)	EXER (10)
(1)	1.000	.584	.812	.744	.605	-.509	.169	-.839	-.440	-.157
(2)		1.000	.001	-.103	.092	-.590	-.509	-.145	.323	.365
(3)			1.000	.991	.679	-.203	.574	-.929	-.774	-.455
(4)				1.000	.697	-.108	.652	-.929	-.824	-.528
(5)					1.000	.375	.809	-.647	-.879	-.600
(6)						1.000	.683	.292	-.445	-.457
(7)							1.000	-.464	-.949	-.747
(8)								1.000	.656	.408
(9)									1.000	.784
(10)										1.000

Critical Value (.05) = + /- .740

correlations were weaker. In fact, RMR/BW did not correlate well with any variable in the nonobese.

There was a positive relationship between RMR/BW and RMR/FFM in both obese (r = .86) and nonobese (r = .683) women, indicating that changes in RMR adjusted for BW would be accompanied by similar changes in RMR adjusted for FFM; however, the correlation was only significant in the obese. There was even a stronger correlation between RMR/BW and RMR/FM in the obese (r = .932).

The factor accounting most for the difference between RMR/BW in the obese and nonobese was found in the body fat of the obese women studied. There was a strong negative relationship between RMR/BW and FM (r= -.834) and percentage fat (r= -.737) in the obese but only a weak negative relationship in the nonobese (r= -.203; r= -.108). Thus, above a certain percentage fat, but not below it, degree of fatness affected RMR/BW. As fatness increased, RMR/BW decreased.

Degree of obesity apparently did not affect RMR/FFM in the combined obese subjects in this study, since no strong correlation was found between RMR/FFM and either percentage fat (r= -.294) or FM (r= -.486). In both obese and nonobese subjects, FFM was negatively correlated with RMR/FFM (r= -.733 in the obese and r= -.509 in the nonobese); the correlation was significant only for the obese group.

Nevertheless, there was a relationship between BW and RMR/FFM in the obese, but not the nonobese, subjects. In the obese, an increase in BW was accompanied by a decrease in RMR/FFM ($r = -.594$; $p < .05$).

Hypothesis 2: COO females will have a higher RMR per unit of fat free mass (FFM), fat mass (FM), and body weight (BW) than AOO females.

To test this hypothesis, data from AOO and COO subjects were analyzed using t tests; significance was set at the .05 level. Table 8 presents mean values and differences between groups.

Results indicated that mean absolute RMR was lower in COO than AOO females and that RMR per unit of BW, FFM, and FM was lower in COO than AOO subjects. However, differences were not statistically significant.

Lack of statistical significance could be the result of great variance within each group in the variables being measured. The range of RMR per unit of body composition within each group (AOO and COO) was considerable. In an effort to statistically pull some meaning from this variance, the data were probed further by using Pearson's coefficient of correlation and multiple regression analysis. Correlations may be found in Tables 9 and 10.

Table 8

Resting Metabolic Rates of COO, AOO, and Nonobese Subjects

	RMR, kcal/day	RMR/BW, kcal/kg	RMR/FFM, kcal/kg	RMR/FM, kcal/kg
Child-Onset Obese (COO)				
01	1580.00	21.49	31.50	67.60
05	1489.00	10.91	21.93	21.70
06	1452.00	20.59	29.83	66.51
07	1437.00	19.82	30.15	57.85
08	1392.00	13.26	25.74	27.35
09	1778.00	15.94	32.09	31.69
Mean	1521.33	17.00	28.54	45.45
+/-	+/-	+/-	+/-	+/-
S.D.	140.72	4.32	3.93	20.83
Adult-Onset Obese (AOO)				
20	1677.00	25.13	38.54	72.24
21	1240.00	15.03	23.09	43.04
23	1665.00	20.58	33.43	53.51
24	1649.00	24.18	39.55	62.23
25	1680.00	20.36	30.20	62.50
29	1335.00	14.32	27.13	30.32
Mean	1541.00	19.93	31.99	53.97
+/-	+/-	+/-	+/-	+/-
S.D.	198.94	4.49	6.45	15.19
Nonobese (NO)				
40	1426.00	23.89	31.66	97.34
41	1207.00	22.15	26.29	140.70
42	1178.00	24.29	26.66	272.68
43	1334.00	21.60	24.83	166.47
44	1326.00	20.22	27.39	77.29
45	1521.00	25.48	33.04	111.36
Mean	1332.00[a,c]	22.94[b]	28.31	144.31[b,d]
+/-	+/-	+/-	+/-	+/-
S.D.	129.57	1.95	3.27	70.38

Level of Significance Key:
a - $p < .05$ between COO and NO
b - $p < .005$ between COO and NO
c - $p < .05$ between AOO and NO
d - $p < .005$ between AOO and NO

In the COO group BW was highly correlated with FM (r = .992), FFM (r = .943), and percentage fat (r = .931). In AOO subjects BW only correlated significantly with FM (r = .844). This suggests that increased weight had different meanings in the two groups. In both groups BW

Table 9

Resting Metabolic Rate and Body Composition: Correlation Coefficients of Child-Onset Obese Subjects (n = 6)

	BW (1)	FFM (2)	FM (3)	%F (4)	RMR/D (5)	RMR/BW (6)	RMR/FFM (7)	RMR/FM (8)	ACTIV (9)	EXER (10)
(1)	1.000	.943	.992	.931	.207	-.951	-.706	-.945	-.388	-.405
(2)		1.000	.892	.758	.102	-.869	-.793	-.800	-.251	-.402
(3)			1.000	.970	.241	-.953	-.651	-.973	-.429	-.394
(4)				1.000	.274	-.921	-.532	-.984	-.471	-.336
(5)					1.000	.061	.519	-.111	.204	.284
(6)						1.000	.819	.972	.509	.485
(7)							1.000	.664	.369	.522
(8)								1.000	.521	.412
(9)									1.000	.894
(10)										1.000

Critical Value (.05) = +/- .740

was highly negatively correlated with RMR/BW, implying that as BW increased, RMR/kg BW decreased. Only in the AOO group was there a significant correlation between BW and RMR/FFM (r = -.826). So, only in AOO subjects did RMR/FFM decrease as BW increased.

Table 10

Resting Metabolic Rate and Body Composition: Correlation Coefficients of Adult-Onset Obese Subjects (n = 6)

	BW (1)	FFM (2)	FM (3)	%F (4)	RMR/D (5)	RMR/BW (6)	RMR/FFM (7)	RMR/FM (8)	ACTIV (9)	EXER (10)
(1)	1.000	.697	.844	.512	-.614	-.909	-.826	-.870	-.045	.473
(2)		1.000	.202	-.258	-.362	-.653	-.819	-.367	.571	.907
(3)			1.000	.892	-.567	-.752	-.514	-.897	-.488	-.033
(4)				1.000	-.390	-.443	-.129	-.716	-.771	-.468
(5)					1.000	.880	.828	.838	.139	-.361
(6)						1.000	.946	.936	.062	-.515
(7)							1.000	.772	-.225	-.751
(8)								1.000	.393	-.186
(9)									1.000	.759
(10)										1.000

Critical Value (.05) = +/- .740

Correlations between RMR/d and RMR/unit of body composition are suggestive of some differences between AOO and COO females. In AOO, RMR/d correlated positively and significantly with RMR/FFM ($\underline{r}$ = .828), RMR/BW ($\underline{r}$ = .880), and RMR/FM ($\underline{r}$ = .838). Thus, as RMR/d varied in AOO subjects, RMR/unit of body composition similarly varied. None of these significant correlations were seen in COO females studied.

Although there were only 6 subjects in each group, the investigator used multiple regression analysis to explore the data more fully. Accordingly, FFM and FM were used as independent variables and RMR/d as the dependent variable in multiple regression analysis of data from COO and AOO subjects. Subsequently, the independent variables, activity level and exercise frequency, were added to the multiple regression analysis.

As Tables 11 and 12 illustrate, the R^2 increased in both COO and AOO women when activity and exercise were used in addition to the independent variables FM and FFM. In the AOO subjects, exercise frequency accounted for 44% of the variance in RMR/d; activity and exercise accounted for less of the variance in RMR among COO women, but R^2 was strengthened by their addition to the analysis.

Table 11

Variation in Absolute Resting Metabolic Rate in Child-Onset Obese Subjects: Multiple Regression Analysis

1. Independent Variable	Std. Error	Partial r^2
FFM	21.8338	.0667
FM	40.8233	.1116

Std. Error of Estimate = 170.3450

R^2 = .1208

2. Independent Variable	Std. Error	Partial r^2
FFM	71.0215	.1702
FM	26.9172	.2308
Activity	1371.2384	.1258
Exercise	478.9032	.0614

Std. Error of Estimate = 251.5977

R^2 = .3607

Table 12

Variation in Absolute Resting Metabolic Rate in Adult-Onset Obese Subjects: Multiple Regression Analysis

1. Independent Variable	Std. Error	Partial r^2
FFM	16.7855	.0940
FM	12.5696	.2931

Std. Error of Estimate = 201.2861

R^2 = .3858

2. Independent Variable	Std. Error	Partial r^2
FFM	60.5952	.2140
FM	24.5689	.1927
Activity	312.3976	.2473
Exercise	513.1023	.4404

Std. Error of Estimate = 259.9289

R^2 = .6586

Hypothesis 3: COO and AOO females will have a lower RMR per unit of fat free mass (FFM), fat mass (FM), and body weight (BW) than nonobese females.

T tests were performed to study differences between COO, AOO, and nonobese women in RMR per unit of body

composition. Significance was set at the .05 level. Results are summarized in Table 8.

Absolute RMR per day was higher in COO (M = 1521.33 kcal/day) than nonobese subjects (M = 1332 kcal/day), and the difference was statistically significant ($p < .02$). However, RMR/BW was significantly lower ($p < .005$) in COO (M = 17.00 kcal/kg) than nonobese (M = 22.94 kcal/kg) subjects. RMR/BW was lower in AOO subjects (M = 19.93 kcal/kg) than nonobese subjects, but the difference was not significant ($p < .08$). RMR/FFM of COO and nonobese subjects was virtually indistinguishable (M = 28.54 and 28.31 kcal/kg, respectively). RMR/FFM was actually higher in AOO (M = 31.99 kcal/kg) than nonobese subjects, although the difference was not statistically significant. In both AOO and COO females, RMR/FM was significantly lower than in nonobese females (M = 45.45, 53.97, and 144.31, kcal/kg, respectively).

The hypothesis that COO and AOO females would have lower RMR/FM than nonobese females was upheld. The hypothesis that COO females would have lower RMR/BW than nonobese females was upheld. No other statistically significant differences between COO, AOO, and nonobese females were found.

The relationship between RMR, adjusted RMR, and various components of body composition was examined using Pearson's coefficient of correlation. As reported

previously in this section, BW was strongly correlated with FM in AOO (r = .844) and COO (r = .992) subjects. BW also correlated strongly with FM in the nonobese (r = .812). Thus, in all three groups of women, an increase in BW would be associated with an increase in FM. AOO and nonobese subjects were alike in that BW only correlated significantly with fat, whereas in the COO group, significant correlations were also found between BW and FFM. So, in the COO subjects, who were heavier and fatter, both lean and fat tissue made a contribution to weight gain.

Self-reported activity le and exercise frequency were similarly correlated in nonobese, COO, and AOO subjects. There was a significant positive relationship between activity and exercise in all three groups. Only in AOO subjects was there a strong positive relationship between FFM and exercise, a higher frequency of exercise being associated with a larger FFM. There were no significant correlations between activity or exercise and any other variables in COO subjects.

As previously reported for AOO and COO subjects, multiple regression analysis was performed on data from nonobese women using FFM and FM as independent variables and RMR/d as the dependent variable. Subsequently, the independent variables activity level and exercise frequency were added to the multiple regression analysis.

Table 13 illustrates a much higher R^2 (.4698) for nonobese women than that found for COO (Table 11) or AOO (Table 12), when only FFM and FM were the variables.

Table 13

Variation in Absolute Resting Metabolic Rate in Nonobese Subjects: Multiple Regression Analysis

1.

Independent Variable	Std. Error	Partial r^2
FFM	15.6005	.0156
FM	11.2308	.4652

Std. Error of Estimate = 121.7994

R^2 = .4698

2.

Independent Variable	Std. Error	Partial r^2
FFM	5.2114	.9282
FM	5.9732	.7738
Activity	41.4777	.9607
Exercise	22.5520	.5786

Std. Error of Estimate = 34.9532

R^2 = .9854

Interestingly, in nonobese subjects FM explained 46% of

the variance in RMR/d, compared with 29% in the AOO and 11% in COO. When the independent variables, activity and exercise, were added to the multiple regression analysis, R^2 increased to .9854 in the nonobese, .6586 in the AOO, and .3607 in the COO. In both AOO and nonobese women, activity and exercise accounted for much of the variation in RMR/d. In the COO, activity and exercise did not have a similar effect.

Additional Data Analysis

Although subjects were not matched with respect to FFM, group means for FFM were similar, as shown in Table 3. No significant differences in FFM were found between COO (M = 54.09 +/- 7.73 kg) and AOO (M = 48.92 +/- 5.47 kg) subjects, or between AOO and nonobese (M = 47.22 +/- 3.49 kg) subjects. However, a significant difference did exist between COO and nonobese subjects in FFM ($p < .05$).

To determine if this difference might be confounding the interpretation of RMR/FFM, the 18 subjects were divided into two groups, one group having a mean FFM below the mean FFM for all 18 subjects, and the other group having a mean FFM above the mean FFM for all 18 subjects. Group 1 consisted of 11 subjects having "low" FFM (M = 46.37 kg). Group 2 consisted of 7 subjects having "high" FFM (M = 55.89 kg). A dependent t test was performed using the pooled estimate of variance to assess the difference between the two groups in RMR/FFM. The low-FFM

group had a higher RMR/FFM (M = 31.24 +/- 4.59 kcal/day) than the high-FFM group (M = 27.05 +/- 4.16 kcal/kg/day). This difference was statistically significant (p = .03).

Because one subject had a FFM that was 12.98 kg greater than the next highest FFM, the t test was repeated omitting this subject's data. Mean FFM for the low-FFM group then became 45.30 kg (n = 8), and mean FFM for the high-FFM group became 52.26 kg (n = 9). Results of this analysis indicated that the low-FFM group still had a higher RMR/FFM than the high-FFM group (31.46 +/- 4.86 kcal/kg/day versus 28.50 +/- 3.80 kcal/kg/day), but the difference was no longer statistically significant (p = .09).

Discussion

This study examined the resting metabolic rate (RMR) of 6 nonobese and 12 obese women. Six obese women reported obesity onset before puberty and were classified child-onset obese (COO); six reported obesity onset after puberty and were classified adult-onset obese (AOO).

Absolute RMR was elevated in the obese subjects in this study, as others have also found (Felig et al., 1983; Ljunggren et al., 1961; Prentice et al., 1986). Mean RMR for combined COO and AOO subjects in the present study was 1531.17 kcal/day, approximately 15% higher than the mean RMR of lean subjects ($p < .05$). This difference is

similar to differences found by Blair and Buskirk (1987), Hoffmans et al. (1979), and Prentice et al. (1986). There were no significant differences in absolute RMR/day between AOO and COO subjects.

One would expect the larger cell mass of the obese, whether AOO or COO, to generate more energy than the nonobese each day. Of greater interest than absolute RMR, therefore, is the expression of RMR by unit of body mass or body composition, permitting a more informative comparison of RMR of people who have different body weights and body compositions. Lower RMR/BW, RMR/FM, or RMR/FFM would suggest a degree of metabolic efficiency in the obese, which might partly account for maintenance of the obese state.

Metabolic Efficiency in Obesity

It was hypothesized that RMR per unit of body weight (BW), fat mass (FM), and fat free mass (FFM) would be lower in obese than nonobese subjects. It was further hypothesized that RMR/BW, RMR/FM, and RMR/FFM would be lower in AOO than COO subjects. Although some authors have found evidence which is suggestive of energy sparing in the COO (Bessard et al., 1983; Kaplan & Leveille, 1976), others have theorized that the greater number of adipocytes seen in COO would result in a higher metabolic activity (Miller & Parsonage, 1975).

Indeed, the hypothesis that RMR/BW would be lower in

the combined obese than nonobese was upheld, with combined obese subjects expending 18.47 kcal/kg BW/day and lean 22.94 kcal/kg BW/day ($p < .05$). Similar results were found in a study using subjects comparable to those in the present study in terms of age, percentage fat, and stage of menstrual cycle when measurements were taken. Hoffmans et al. (1979) found obese women to have significantly lower RMR/BW than lean women, 21.8 kcal/kg/d versus 24.4 kcal/kg/d for the lean.

When data from the obese subjects were analyzed separately, COO women were found to expend fewer kcal/kg BW than AOO women (17.00 kcal/kg BW/day versus 19.93 kcal/kg BW/day), although the difference was not statistically significant. The AOO group was not statistically different from the nonobese in RMR/BW, but RMR/BW in the COO was significantly lower than RMR/BW in the nonobese ($p < .005$). This suggests that there are some small differences between women obese since childhood and women having obesity onset after puberty, with the COO showing slightly greater metabolic efficiency per kg BW. The difference between COO and nonobese was particularly pronounced. A 70.5 kg COO woman whose RMR was 17.00 kcal/kg BW/day would expend approximately 1200 kcal/day through the RMR. If she had the RMR/BW of a nonobese woman (22.94 kcal/kg BW/day), her RMR would be approximately 1617 kcal/day, a difference of over 400

kcal/day. This caloric savings could make weight loss extremely difficult for the COO woman.

The metabolic efficiency of the obese is also quite evident when RMR/FM is calculated. Nonobese women had a mean RMR/FM of 144.31 +/- 70.38 kcal/kg/day, significantly higher than RMR/FM of the combined obese ($\underline{M}$ = 49.71 +/- 17.94 kcal/kg/day; $\underline{p} < .0005$). The large difference in percentage fat between nonobese and obese women probably accentuated this difference. A strong negative correlation was found between FM and RMR/FM in the combined obese ($\underline{r}$ = -.924), nonobese ($\underline{r}$ = -.929), AOO ($\underline{r}$ = -.897), and COO ($\underline{r}$ = -.973). This suggests that as as FM increased, RMR adjusted for FM decreased. Since the obese subjects were fatter than the nonobese, their lower RMR/FM is consistent.

However, even when data only from the obese subjects were compared, differences in RMR/FM were apparent. The lowest RMR/FM were seen in COO subjects ($\underline{M}$ = 45.45 +/- 20.83 kcal/kg/day). Although not significantly different from RMR/FM of AOO ($\underline{M}$ = 53.97 +/- 15.19), nor close to significance, there was a difference and considerable variability in RMR/FM within the obese sample. This variability, especially in COO subjects, probably prevented the difference between AOO and COO women from being statistically significant.

Table 8 indicates that three COO subjects (numbers 5,

8, and 9) had extremely low RMR/FM: 21.70, 27.35, and 31.69 kcal/kg, respectively. The mean RMR/FM of these three subjects was 26.91 kcal/kg, compared with a mean RMR/FM of 63.96 kcal/kg for the other COO subjects. Only one AOO subject (number 29) had a RMR/FM below 32 kcal/kg, and the other AOO subjects had a mean RMR/FM of 58.70 kcal/kg.

The relative efficiency of fat tissue in the obese could account for the reduced RMR/BW. The coefficient of correlation between RMR/BW and FM was significant for the combined obese (r = -.834), AOO (r = -.752), and COO (r = -.953), but not for the nonobese. This suggests that in fatter individuals, and particularly in those who have been obese since childhood, an increase in body fat is associated with a decrease in RMR/BW.

The three COO women having the lowest RMR/FM also had low RMR/BW. Interestingly, these three subjects were the heaviest and fattest subjects in the study.

Studies of very large and very small mammals have indicated that RMR/BW declines as animal size increases, because organs having high metabolic rate (such as the liver) occupy proportionately less body weight in the larger animal (Grande, 1980). The decrease in RMR/BW may result from a decrease in the metabolic rate of certain tissues, including muscle and fat, as the body weight increases (Holliday et al., 1967). It is also possible

that a decreased RMR/BW might precede weight gain, in some cases, thereby becoming the cause, rather than the consequence, of obesity. To increase RMR/BW, then, metabolic activity of either muscle or fat tissue would have to change, a phenomenon that might be impossible for some individuals.

Metabolic activity of lean tissue was not found to be different between nonobese and obese subjects in the present study, even when subjects were grouped as low-FFM or high-FFM. These findings are similar to those of Bessard et al. (1983), Prentice et al. (1986), and Schutz et al. (1984), which were summarized in Table 2. Felig et al. (1983) found no differences in RMR/FFM between 10 COO and 10 lean women, even though obese subjects were an average of 12 years older than the lean. And in another study, even when subjects were matched to FFM, no significant differences in RMR/FFM were seen between 8 lean and 8 obese men (Segal et al., 1987).

Segal et al. (1987) did, however, find a lower RMR/BW in obese men when compared to lean men of similar age, height, and LBM. This occurred despite the fact that absolute RMR did not differ significantly between the two groups. In the present study, mean absolute RMR was not significantly different between low-FFM subjects ($\underline{M}$ = 1427.4 +/- 173.68 kcal/day) and high-FFM subjects ($\underline{M}$ = 1495.11 +/- 176.21 kcal/day).

Studies of total daily energy expenditure have suggested a degree of metabolic efficiency in the obese. Blair and Buskirk (1987) found 8 COO women to expend significantly fewer kcal/kg FFM/day than 8 AOO women, when total daily energy expenditure rather than RMR was measured. Even when RMR/FFM was found to be the same between 20 obese and 8 nonobese subjects, Schutz et al. (1984) found total-daily-energy-expenditure-at-zero-activity/FFM to be significantly lower in the obese.

The active components of FFM consist of muscle, organs, glands, and intracellular water (Bakker & Struikenkamp, 1977). Skeletal muscle, which makes up 40% of BW only accounts for 16-30% of RMR (Grande, 1980). Naeye and Roode (1970) studied autopsy records and tissue from 41 nonobese and 26 obese young adults who had died suddenly from accidents or trauma. Some of the obese had significantly larger organs, including the heart, kidney, pancreas, and liver, than nonobese subjects matched for body length, age, and sex. Cleary et al.'s study of the genetically obese Zucker rat also found greater liver and kidney weight in obese versus lean littermates at age 15 weeks (cited in Colt et al., 1981). Thus, an increase in FFM in obesity need not be due solely to an increase in skeletal muscle. If caloric expenditure/kg FFM is lower when people are up and about (i.e., total daily energy expenditure), muscle may be accounting for less of the

caloric expenditure in the obese than in the lean, especially given evidence than organs may increase in size in obesity.

FFM is considered to approximate metabolically active tissue (Ravussin et al., 1986), and FFM usually correlates highly and positively with RMR (Bernstein et al., 1983; Cunningham, 1980; Felig et al., 1983; Halliday et al., 1979; James et al., 1978; Owen et al., 1986; Schutz et al., 1984). Unlike many other studies, however, the present study did not find FFM to correlate with RMR, in the nonobese (r = .092), the combined obese (r = -.040), AOO (r = -.362), or COO (r = .102). The relationship between RMR and FFM did not improve when subjects were divided into low-FFM (M FFM = 45.30 kg; r = -.15) and high-FFM groups (M FFM = 52.26 kg; r = .18). In the subjects in the present study, an increase in FFM would not necessarily be associated with an increase in RMR.

When Miller & Parsonage (1975) found a weak and insignificant relationship between BMR and LBM (r = .33) in 29 obese women, the lack of significance was attributed to caloric restriction. In the present study, all subjects were weight stable, and none of the subjects reported recent dieting behavior. Nevertheless, past dieting could have had a long-term effect. Although subject diet history was not examined, most of the subjects (including the nonobese) described in

conversations with the investigator some past caloric restriction. It is also likely that the lack of relationship between RMR and FFM in the present study was due to variability in both RMR and FFM in the 18 subjects.

The heaviest subject in the present study was a 26 year old COO woman who weighed 136.5 kg and was 50.25% fat. This individual had the largest FFM of all 18 subjects, 68.60 kg. The subject reported always being the tallest, heaviest person in her class and even provided photographs to illustrate this. Given her size, her absolute RMR was extraordinarily low (1489 kcal/day), lower even than subject 45, who weighed 59.7 kg, 46 kg of which was FFM. Subject 5 had very low RMR/BW, RMR/FFM, and RMR/FM, which had an impact on variability within the COO group.

In contrast, subject 9, who weighed 105 kg and was similar to subject 5 in percentage fat, had an absolute RMR of 1778 kcal/day, highest in the study. Subject 8, who weighed 105 kg, had an RMR of under 1400 kcal/day, more like the RMR of the nonobese, lighter subjects. Because one trained investigator performed all measurements, it is unlikely that this great variability was due to measurement error.

In summary, when RMR was expressed per unit of BW (RMR/BW), combined obese subjects had lower metabolic activity than nonobese subjects, and COO subjects, in

particular, showed an efficiency of metabolic rate. Unexpectedly, COO subjects had lower RMR/BW than AOO, but the difference was not statistically significant. RMR/FFM was not significantly different between nonobese, AOO, COO, and combined obese. This does not preclude reduced metabolic activity of certain fat-free tissues, including muscle tissue, in the obese.

Influence of Activity and Exercise on RMR

Self-reported activity level and exercise frequency differed between the subjects in this study, with COO tending to report light activity level, AOO reporting light to moderate activity, and nonobese reporting moderate activity; see Table 4. The coefficient of correlation between activity level and exercise frequency was positive and significant for all groups, indicating that those who reported being more active were also more frequent exercisers and those who reported being less active were less frequent exercisers. COO subjects exercised an average of two times per week, AOO an average of 3.16 times per week, and nonobese an average of 3.33 times per week.

Results of multiple regression analysis indicated that in all groups -- nonobese, AOO, COO, and combined obese -- more of the variance in RMR was explained when the variables activity and exercise were used in addition to the variables FM and FFM. When only FM and FFM were

used in multiple regression analysis in the nonobese group, 46% of the variance in RMR was explained. The addition of activity and exercise to the analysis increased the explained variance to 98%. Activity and exercise also increased explained variance in the AOO subjects.

Activity and exercise apparently had a much smaller effect on COO subjects, the group in which self-reported activity level and exercise frequency was lowest. The addition of activity and exercise to multiple regression analysis increased the explained variance due to FM and FFM from 12% to 36%, but activity and exercise did not, themselves, explain much of the variance in RMR in COO women.

Curtis and Bradfield (1971) found 6 obese housewives (39%-49% fat) to report 5% less time in moderate activities and 5% more time in sitting and light activities than normal housewives. Blair and Buskirk (1987) found total daily energy expenditure per kg FFM to be significantly less in 8 COO than 8 AOO women. These results suggest that COO women, or more obese women, not only expend less energy in activity but are less able to get metabolic benefit from the activity that they do engage in.

A recent study of energy expenditure in 18 infants found that infants who later became overweight had

significantly lower total daily energy expenditure per kg BW at age 3 months than normal weight infants (Roberts et al., 1988). Low energy expenditure was apparently due to reduced energy expenditure through physical activity, rather than due to any differences in metabolic rate. The authors hypothesized that the infants who became overweight might have been subconsciously conserving energy to attain a genetically determined weight or percentage fat. This may be the case in the present study, as well.

Influence of Age of Obesity Onset on RMR

Because the obese are a heterogenous group, subjects in the present study were classified as AOO or COO based on age of obesity onset. Table 3 indicates that COO and AOO subjects were not significantly different in age, weight, height, FFM, percentage fat, or waist-hip girth ratio (WHR), although the COO tended to be fatter and heavier. In fact, the three heaviest and most obese subjects were from the OO group.

AOO and COO women were not significantly different from each other in absolute RMR/day, RMR/BW, RMR/FM, or RMR/FFM. Miller and Parsonage (1975) and Bernstein et al. (1983) found high correlations between fat cell number and BMR, such that as fat cell number increased, BMR increased as well. Assuming that COO subjects had greater fat cell number than AOO subjects, the data in the present study

suggests the opposite trend: COO had slightly lower absolute RMRs and slightly lower RMRs per kg BW, FM, and FFM than the AOO.

One way of examining and evaluating the data from COO and AOO subjects is to look at what is lost by combining data from the obese subjects. The combined obese subjects had significantly lower RMR/BW than the nonobese. However, when age of obesity onset was taken into consideration, the difference disappeared in some cases. The AOO were not statistically different from the nonobese in RMR/BW and the COO were very different from the nonobese in RMR/BW.

The reason for the apparent metabolic difference between COO and AOO women may be found in the difference in the composition of weight gained. Coefficients of correlation between BW and FM and FFM indicated that a gain in BW in COO women was associated with both a gain in FM (r = .992) and a gain in FFM (r = .943). The correlation between BW and FM was high and significant for the AOO (r = .844), but the relationship between BW and FFM was not significant (r = .697). As with the nonobese, weight gain in AOO women was associated with gain in FM but not necessarily with a gain in FFM.

Similarly, FM and FFM did not correlate well in the AOO (r = .202) or the nonobese (r = .001). The correlation between FM and FFM was high in the COO (r =

.892), suggesting that a gain in one tissue was associated with a gain in the other.

The similarities between AOO and nonobese women were lost, however, when data from all the obese were combined. FM correlated strongly with FFM in the combined obese (r = .745), and correlations between BW and FFM (r = .870) and between BW and FM (r = .977) were both significant (p < .05).

Forbes (1964) observed a larger LBM and FM in individuals obese since infancy, whereas individuals having obesity with a later onset showed only enlarged adipose tissue. Naeye and Roode (1970) speculated that age of obesity onset might explain why some obese subjects in their autopsy study had larger organs, whereas others had normal-sized organs. The same might be hypothesized about subjects in the present study.

Perhaps greater differences between the COO and AOO would have been noted if the variability in RMR within these groups were not so great. Even when site of fat deposition and recent dieting behavior were controlled, the obese had slightly more variability in absolute RMR than the nonobese, particularly the AOO.

Subjective Observations

This study suggested that the obese have a degree of metabolic efficiency which may account, in part, for maintenance of the obese state. Age of obesity onset and

the associated differences in adipose cellularity may serve as intervening variables in this metabolic efficiency.

Considerable variation exists in RMR within the population, and absolute RMR is typically elevated in obesity as a consequence of the greater tissue mass (Ravussin et al., 1988). However, even when RMR is adjusted for BW, FM, or FFM, it is estimated that there may be up to 30% variation in RMR among individuals (Horton & Danforth, 1982), and this variability is larger than methodological error or intraindividual biological variation would explain (Bogardus et al., 1986; Ravussin et al., 1986). A number of factors have been theorized to account for the often considerable variation in adjusted RMR. Those that may relate to the present study will be briefly discussed here.

Composition of the Diet

Several authors have suggested that when carbohydrates make up the majority of excess calories consumed, more energy is lost as heat and less excess energy is stored than when excess calories are in the form of fat (Danforth, 1985; Horton & Danforth, 1982). Rats fed a high-fat diet in infancy gained 26% more BW than control-diet rats (Corbett et al., 1986), resulting in both an increase in fat cell size and number.

The average American consumes 42% of his/her calories

in the form of fat, substantially higher than the recommended 30% (U.S. Department of Agriculture, 1985b). Even American children consume approximately 34% of their total daily calories in the form of fat (U.S. Department of Agriculture, 1985a). Perhaps COO women in the present study habitually consumed more fat calories than the nonobese or AOO. Although composition of the diet was not assessed in this study, it should not be overlooked as a factor that might account for energy expenditure differences between nonobese and obese women and between AOO and COO women.

Sodium-potassium Pump

The sodium-potassium pump maintains sodium and potassium concentration in the cells and facilitates transport of materials across cell membranes, thereby accounting for 20-50% of the energy used at the basal level in humans (De Luise et al., 1980; Horton & Danforth, 1982). De Luise et al. (1980) found 23 obese men and women (147-277% of ideal body weight) to have 22% fewer sodium-potassium pump units in red blood cells than 28 nonobese men and women (84-123% of ideal body weight). There was a negative correlation between percentage of ideal body weight and reduction in sodium-potassium pump units, suggesting that the more overweight would have greater metabolic efficiency.

In the present study, the slightly more obese COO

subjects had significantly lower RMR/BW than the nonobese, whereas there was no significant difference in RMR/BW between AOO and nonobese women. Reduced number of sodium-potassium pump units in the COO could be a factor involved in this difference.

Substrate Cycling

Various metabolic cycles operate in the human body to produce and dissipate energy without subsequent synthesis or breakdown of materials (Horton & Danforth, 1982). These cycles are, thus, often termed "futile cycles."

The cycle between fructose 6-phosphate and fructose bisphosphate in skeletal muscle, which helps regulate anaerobic glycolysis, is an example of a futile cycle. Newsholme (1980) estimated that at its maximum rate over 24 hours, this cycle could produce approximately 1,500 calories/day in a 70 kg man, an unlikely event, but illustrative of its potential. Stress, exercise, and eating may stimulate this (and other) cycles.

Of interest in the context of exercise is the observation that the fructose 6-phosphate-fructose bisphosphate cycle is not only stimulated during exercise but for 7 to 8 hours after exercise (Newsholme, 1980). Exercise has also been shown to increase the thermic effect of food in the lean (Segal & Gutin, 1983; Segal et al., 1984; Segal et al., 1985) and, by at least one investigator, in obese women (Bradfield et al., 1968).

Thus, via diet-induced thermogenesis or substrate cycles, exercise may have long-term benefit and be useful in weight control.

Results of the present study, however, suggested that exercise and activity were of questionable benefit to RMR in COO women. Perhaps this was due to some failure of substrate cycles, such as the fructose 6-phosphate-fructose bisphosphate cycle. Or, perhaps it was due to reduced activity of the sympathetic nervous system, which also has a role in diet-induced thermogenesis and substrate cycling (Horton & Danforth, 1982). Whatever the hypothesis, it apparently was not as problematic for AOO women.

Differences in FFM

Forbes (1964) has suggested that early onset obesity is associated with a larger FM and FFM, whereas obesity with a later onset is associated only with an enlarged FM. The enlarged FFM of COO obesity may be due to the enlargement of certain organs, including the heart, liver, pancreas, and kidney (Naeye & Roode, 1970).

The present study found no differences in RMR/FFM between nonobese, AOO, or COO women. It might be speculated that components of the FFM making a contribution to RMR were different in COO than in AOO or nonobese. If COO women did have enlarged hearts, livers, kidneys, and other organs, these nonfat tissues might have

been making a greater contribution to RMR than muscle tissue. In fact, the contribution of muscle to RMR might actually have been reduced in the COO. This might further clarify why activity and exercise, in which working muscle metabolism should increase, explained less of the variance in RMR in the COO than in the AOO or nonobese.

Genetic Factors

Faulty substrate cycling, less active sodium-potassium pump, suppressed sympathetic nervous system activity, and early onset of obesity could all be inherited factors that would predispose an individual to energy conservation. Corbett et al. (1986) found that obese rats fed a high-fat diet in infancy were less active during a period of food restriction than control-diet nonobese rats. This is similar to the findings of Roberts et al. (1988), in which human infants, who subsequently became overweight, had a significantly lower total daily energy expenditure as early as 3 months old.

Indeed, Bogardus et al. (1986) found 11% of the variance in RMR among 130 nondiabetic southwestern American Indians to be accounted for by family membership. Although not included in the present study, genetic factors could have and probably did contribute to the variability in RMR observed within and between the groups and possibly contributed to some of the differences seen between AOO and COO subjects.

CHAPTER 5 SUMMARY AND CONCLUSIONS

Summary

The purpose of this study was to determine if obese females expended fewer kcal through the resting metabolic rate (RMR) than nonobese females and, if so, to determine what component of body composition might account for this energy efficiency. Further, obese women in the study were categorized as child-onset obese (COO) or adult-onset obese (AOO), and RMR of obese subjects in the two groups were compared.

The study had three hypotheses:

1. Obese females will have a lower resting metabolic rate per unit of fat free mass (FFM), fat mass (FM), and body weight (BW) than nonobese females.

2. Child-onset obese females will have a higher RMR per unit of FFM, FM, and BW than adult-onset obese females.

3. Child-onset obese and adult-onset obese females will have a lower RMR per unit of FFM, FM, and BW than nonobese females.

To minimize variability in the population of interest, only Caucasians between ages 20-38 years who were apparently healthy nonsmokers were included in the study. Obese subjects were weight-stable, not following calorie-restricted diets, and had predominantly lower-body

fat deposition.

One measure of resting metabolic rate was taken on each subject in the morning following a 12-14 hour fast. No exercise was allowed for the previous 24 hours. Body composition was determined by hydrostatic weighing. Eighteen subjects were retained for the study.

Hypotheses were tested using *t* tests. Pearson's correlation coefficient and multiple regression analysis were used for additional data analysis. Significance was set at the .05 level.

Combined obese (AOO and COO) subjects (n = 12) were found to have lower mean RMR/BW and RMR/FM than nonobese subjects (n = 6), despite having significantly higher absolute RMR/day. RMR/FFM did not differ statistically between obese and nonobese women.

When data were analyzed separately for the COO (n = 6) and AOO (n = 6) subjects, no significant differences were found in absolute RMR/day, RMR/BW, RMR/FFM, or RMR/FM. Values for COO women were slightly lower than AOO on every measure. Both COO and AOO subjects had significantly lower RMR/FM than nonobese subjects. Only COO subjects had significantly lower RMR/BW than the nonobese.

Pearson's coefficient of correlation suggested that combined obese subjects experienced a drop in RMR/BW when they gained weight, whether the weight was FFM or FM. The

negative correlation between FM and RMR/BW was particularly strong for the combined obese. When COO and AOO subjects were looked at separately, differences in the meaning of BW became more apparent. There were high positive correlations between BW and both FM and FFM in COO women, suggesting that both components of weight increased as weight increased. However, BW only correlated well with FM in the AOO.

Multiple regression analysis indicated that in all groups -- nonobese, AOO, COO, and combined obese -- more of the variance in RMR was explained when the variables, activity and exercise, were used in addition to the variables, FM and FFM. However, the effect of activity and exercise on explained variance in RMR was much smaller in COO women.

Conclusions

Results of this study suggest that obese women, especially those having childhood-onset obesity, may be more metabolically efficient than nonobese women. This metabolic efficiency could translate into a caloric savings of 300-500 kcal/day, which would very effectively maintain the obese state. The greatest difference in RMR/BW was seen between COO and nonobese women. This suggests that obesity having its onset before puberty might predispose an individual to greater metabolic

efficiency than obesity having its onset later in life.

Various theories were proposed for this caloric savings, including the composition of the diet, reduced activity of the sodium-potassium pump, faulty substrate cycling, and the composition of FFM. Self-reported activity level and exercise frequency were lowest in COO women, and the results of multiple regression analysis suggested that even if the COO increased exercise and activity, RMR might be unaffected. This suggested a further mechanism for caloric savings: unintentional reduction in energy expenditure by the COO to defend body weight or fatness.

Implications for Future Research

This study leaves many questions about RMR unanswered and suggests several directions for future research. Certainly, additional study is needed to ascertain other characteristics of the obese, in addition to the age of obesity onset, which might affect the RMR. The effect of age of obesity onset on RMR itself needs to be explored more fully. For example, are COO individuals having obesity with very early onset more metabolically efficient than COO having obesity with onset later in childhood?

In addition, it will be useful to study the effect of the level of fatness on metabolic rate. The morbidly obese COO woman may be more metabolically efficient than

the 30-40% fat COO women, although research available to date does not suggest at what level of fatness metabolic efficiency commences. Pairing subjects by body weight or percent fat may help answer some of the questions about metabolic efficiency.

More longitudinal studies with children would be extremely helpful in pinpointing the cause of metabolic efficiency in the obese. If low-calorie intake is one cause of reduced RMR/BW, for example, research will have to look beyond immediate past dieting behavior to correlate diet history with metabolism. However, the difficulties of metabolic studies, in particular, and longitudinal studies, in general, may make this impossible.

The possible lack of effect of exercise on RMR of COO women is alarming, given that obese individuals are best advised to increase activity rather than reduce caloric intake as a weight loss strategy. Future research must look at substrate cycling in muscles of AOO and COO women and at the composition of the FFM in the obese population. Specific forms of exercise must be evaluated to determine the relative effectiveness of each in stimulating total daily energy expenditure and RMR. If, for example, the COO woman has more metabolically efficient muscle tissue but a normal overall RMR/FFM due to enlargement of various organs, perhaps weight training would be stimulatory in

some way. In addition, more detailed questions about exercise and activity level may help clarify apparent energy expenditure differences among the AOO and COO.

Implications for Health Education

Obese individuals having the highest RMR have been found to be the most successful in losing weight, whereas the obese who have the lowest RMR have shown the greatest incidence of weight gain and the most difficulty in losing weight (Ravussin et al., 1988; Zavala & Printen, 1984). Thus, RMR can be used in certain situations by health counselors to predict success in weight loss programs.

When actual RMR is not available, this study suggests that health counselors may anticipate the least success in weight loss programs among women who have been obese since before puberty. Further, exercise may not be as effective in stimulating RMR in this group, although activity and exercise would still contribute to weight loss by increasing caloric expenditure. Weight loss goals may therefore have to be more conservative with the COO group. Self-image counseling and preparation for reaching weight-loss plateaus may be more critical.

Early intervention to prevent child-onset obesity is clearly of great importance to avoid metabolic efficiency and energy conservation. If metabolic efficiency is a consequence of fasting and low-calorie

diets, health education efforts must center on promotion of proper nutrition. This has implications not only for elementary health education programs, but particularly for prenatal and parenting education programs.

APPENDIX A PROPOSAL COMMITTEE APPROVAL

COMMITTEE APPROVAL SHEET

Following student consideration of committee recommendations for ammendments to the research project outlined in the following proposal, the signatures of all members of the thesis/dissertation examining collection, pending approval by the University Committee for Experimentation on Human Subjects.

Student Researcher: Liane M. Summerfield

Project Title : Resting Metabolic Rates in Adult-Onset and Child-Onset Obese Females

Project Approval

Name	Signature	Date
Patricia A. Reason (Advisor)		10/16/87
[illegible]		10/16/87
Catherine M. Miller		10/16/87
Margaret H. Ryder		10/16/87
Robert W Stumpf		10/28/87

Following full committee approval, this sheet is to be forwarded to and signed by the Director of Research and Graduate Studies.

Signature Date

rm 2-82

APPENDIX B INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL

UNIVERSITY OF MARYLAND
College Park, MD 20742

INSTITUTIONAL REVIEW BOARD

PRINCIPAL INVESTIGATOR:
(or Faculty Advisor) PATRICIA MANN

Full Committee Review X
Expedited Review ____

STUDENT INVESTIGATOR: LIANE SUMMERFIELD

PROJECT TITLE: RESTING METABOLIC RATES IN ADULT-ONSET AND CHILD-ONSET OBESE FEMALES

The University IRB reviewed the above-mentioned project on 2-2-88 in accordance with Public Health Service grant policy as defined in "The Institutional Guide to DHHS Policy on Protection of Human Subjects," 12-1-71, and in Title 45, Code of Federal Regulations, Part 46.

The University IRB is:

Willard D. Larkin, Assoc. Professor, Psychology - CHAIRMAN
Margaret Bridwell, M.D., Director, Health Center
EMC. Evelyn M. Cox, Ph.D., Non-University Member
Patrick J. DiRocco, Ph.D., Asst. Professor, Physical Education
Andrew Egel, Ph.D., Assoc. Professor, Special Education
Conrad Johnson, Ph.D., Assoc. Professor, Philosophy
RWK Richard W. Kelley, B.D., Non-University Member
ESP Elizabeth Prather, Ph.D., Professor, Food, Nutrition & Inst. Admin.
AS Anne Slater, M.S., Contract Administrator, Office of Sponsored Programs

____ The IRB has determined that the research is exempt. However, any change in research subjects or protocol will require review by the IRB to maintain the exempt status. Exemption No. ____

X The IRB effected an independent determination of: (1) the rights and welfare of the individual or individuals involved, (2) the appropriateness of the methods used to secure informed consent, and (3) the risks and potential benefits of the investigation. The IRB has concluded that proper safeguards have been taken by the principal investigator as stated in the research proposal. The IRB approves this project as conforming to University and Public Health Service Policy in protecting the rights of the subjects.

Willard D. Larkin
Chairman of the Institutional Review Board

The Principal Investigator and Program Director, in signing this report, agree to follow the recommendations of the IRB, to notify the Office of the Dean for Graduate Studies and Research of any additions to or changes in procedure subsequent to this review, to provide information on the progress of the research on an annual basis, and to report any instances of injuries to subjects and unanticipated problems involving risks to subjects or others. Any consent forms used in connection with this project must be retained by the Principal Investigator for three years after completion of the research.

Principal Investigator (or Faculty Advisor) Student Investigator

THE NEXT REVIEW OF THIS PROJECT IS SCHEDULED FOR 2-89

PLEASE RETURN ONE SIGNED COPY TO GRADUATE SCHOOL, 2133 SOUTH ADMINISTRATION BUILDING.

AGW:bcr
2-85

IRB-3

APPENDIX C QUESTIONNAIRE

_____
number

1. Date of Birth: _____/_____/_____
month day year

2. Height: _____ft. _____ ins.

3. Weight: _____lbs.

4. Have you ever smoked cigarettes? Yes No

5. If YES, how many cigarettes per week did you smoke?

6. When did you quit smoking?_____

7. Are you presently following a calorie-restricted diet to lose weight? Yes No

8. If YES, briefly describe your diet:

9. Have you ever been told by a physician that you have:

	NO	YES	If yes, briefly describe
a. thyroid problem			
b. diabetes			
c. high blood pressure			
d. heart disease			
e. chronic lung disease			

10. List any nonprescription or prescription medications that you regularly use:

11. Are you comfortable holding your breath underwater for brief periods of time? Yes No

12. Is there any medical reason why you cannot put your head underwater for brief periods of time?
Yes No

13. Have you lost or gained more than 5 pounds in the past three months?

No _____ Yes _____

Unsure_____ Lost _____ pounds

Gained _____ pounds

14. What is your occupation?

15. Years of education since high school:

College: _____ years

Post-bachelors degree: _____ years

16. Check one of the following that best describes your activity level:

_____ a. Inactive (sedentary)
_____ b. Lightly active (describes most professionals, many students, office workers).
_____ c. Moderately active (describes active students, most people in light industry, building workers, department store workers).
_____ d. Very active (full-time athletes, dancers, construction workers and others in heavy occupations).

17. Are you involved in competitive athletics? Yes No

18. If YES, briefly describe:

19. How many times per week do you engage in moderate exercise lasting at least 20 minutes:

Briefly describe exercise:

_____ a. 0 - 1
_____ b. 2
_____ c. 3-4
_____ d. more than 4

20. At what age did you begin to menstruate: _____ years

21. Do you menstruate approximately every 28 days?

22. If NO, briefly elaborate:

Weight History

23. Birth weight _____lbs _____ ounces

24. Birth length _____ inches

25. How would you classify your weight during childhood (before puberty):

_____ a. underweight

_____ b. normal weight

_____c. moderately overweight

_____d. extremely overweight

26. If you were overweight in childhood, at what age can you recall feeling overweight or having others call you overweight, fat, or chubby? _____

27. How would you classify your weight at the age at which you began to menstruate?

_____ a. underweight
_____ b. normal weight
_____ c. moderately overweight
_____ d. extremely overweight

28. How would you compare your weight today with your weight at the age at which you began to menstruate?

_____ a. underweight then and now
_____ b. normal weight then and now
_____ c. overweight then and now
_____ d. normal weight then, overweight now
_____ e. overweight then, normal weight now

APPENDIX D INFORMED CONSENT

Project Title: Resting Metabolic Rates in Obese and Nonobese Females

I state that I am over eighteen years of age, in good physical health, and wish to participate in a program of research being conducted by Liane Summerfield at the Graduate School, University of Maryland at College Park, Department of Health Education.

The purpose of this research is to determine if any differences exist in resting metabolic rate between nonobese and obese females and between females obese since childhood and females obese since adulthood.

The procedures involve three measures, all of which may be conducted on the same day, and requiring approximately three hours: resting metabolic rate, residual lung volume, and underwater weighing.

I understand that there are no known risks associated with the measures taken in this study.

All information collected in the study is confidential, and my name will not be identified at any time.

I understand that I am free to ask questions or to withdraw from participation at any time.

Principal Investigator: Liane M. Summerfield
5437 N. 22nd Rd.
Arlington, VA 22205
237-0004 (h) 284-1627 (w)

Signature of Subject _____

Date _____

APPENDIX E DESCRIPTION FOR SUBJECTS

Basal Metabolism Study: Description

This is a study of basal metabolic rates of women who have been overweight since childhood, overweight since adulthood, or who are normal weight. The study is being conducted by a faculty member at Marymount University to fulfill requirements for the PhD from the University of Maryland. All study procedures will be carried out at the University of Maryland's Exercise Physiology Laboratory; only the principal investigator, Mrs. Liane Summerfield, will be present and strict confidentiality will be observed. Transportation can be arranged.

Individuals who meet criteria for the study will undergo three measurements:

1. Basal Metabolic Rate. This procedure involves measurement of oxygen consumption for 15-30 minutes following a rest period of about 30 minutes. BMR must be measured in the morning following an overnight fast. An oxygen mask which fits snugly around the nose and mouth will be worn while breathing normal air. During that time, the investigator will monitor oxygen consumption and carbon dioxide production using a computerized system. Calories of energy expended during the measurement period will be calculated from amount of oxygen consumed.

2. Residual Lung Volume. This measurement is taken before underwater weighing to account for gases trapped in

the lungs which would make the research subject more buoyant in water. Following BMR measurement and a 5-10 minute rest period, the subject will be fitted for a mouthpiece and a noseclip. The mouthpiece will be attached to a breathing apparatus. Residual lung volume will be measured using a method called "nitrogen washout," whereby the subject takes a few normal breaths, exhales maximally, and then breathes 100% oxygen for about 1 minute while nitrogen is washed out of the lungs. Breathing oxygen for such a brief period has not been found hazardous to healthy individuals. At least three measures of residual volume will be taken with a 5 minute rest period between each. No adverse effects are to be expected from this procedure.

3. Underwater Weighing. This procedure can be done immediately after lung volume has been determined. While wearing a close-fitting bathing suit, the research subject will sit on a chair attached to a scale and suspended in a tank of warm water. When ready, the subject will exhale as much air as possible and duck her head under the water, continuing to blow out air. A noseclip can be worn. The researcher will take a rapid, computerized measure of weight. This procedure will be repeated 3 to 5 times. Weight underwater is used to compartmentalize body weight into fat and muscle and is essential for accurate determination of body composition.

Procedures for Metabolism Study Subjects

Please observe the following procedures for the day before and day of your scheduled measurements. Scheduled date: _____.

Basal Metabolic Rate

1. Do not participate in exercise during the day or evening before your BMR is measured.
2. The night before your measurement:
   * Eat a normal dinner by 7:00 PM
   * Avoid alcohol and caffeine (tea, coffee, chocolate, colas)
   * Eat no food and drink no liquids (except water) after 8:00 PM
   * Take no medications, except prescriptions already discussed with Liane
   * Do not participate in physical activity
3. The morning of your measurement:
   * Do not eat breakfast or drink anything except water
   * Be at the Human Exercise Research Lab, Room 2127 of the PERH Building, University of Maryland, by 9:15 AM
   * Wear or bring with you a lightweight shirt, lightweight shorts, and socks
   * Use the bathroom before the rest period in the Lab begins

Underwater Weighing

1. The night before your measurement:
   * Eat a normal dinner by 7:00 PM
   * Avoid alcohol and caffeine (tea, coffee, chocolate, colas)
   * Eat no food and drink no liquids (except water) after 8:00 PM
   * Take no medications, except prescriptions already discussed with Liane
   * Drink plenty of water (so you won't be dehydrated)
2. The morning of your measurement:
   * Do not eat breakfast or drink anything except water
   * Drink plenty of water
   * Bring a snug-fitting bething suit and a towel
   * You can shower afterwards if you wish

Residual Lung Volume - No special instructions.

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