MENOPAUSAL CHANGES IN BODY COMPOSITION AND ENERGY EXPENDITURE

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Abstract—Adult American women as a group tend to gain weight with age, and many women report that their weight gain started around the time of their menopause. Moreover, as women age, there are changes in body composition that include losses in bone mineral and body cell mass, and increases in total body fat, visceral fat, and extracellular fluid. It appears as if these body composition changes begin or accelerate during the menopausal years. The importance of weight gain and changes in body composition are their associations with an increased risk of developing some malignancies, cardiovascular disease, osteoporosis, and several other clinical conditions. This overview describes selected studies of menopause and aging-associated weight gain, changes in body composition, and alterations of energy expenditure in women. Gaps in the present understanding of these changes are highlighted, and an emphasis is placed on new research methodologies for investigating body composition and energy expenditure in vivo. A concluding section of the report summarizes areas in need of future investigation.

Key Words: menopause, body composition, energy expenditure

INTRODUCTION

ADULT AMERICAN women, on average, show an increase in body weight with age (Williamson et al., 1990). Many women indicate that their weight gain began at or near the time of their menopause. Moreover, body composition changes with age in women, independent of weight gain, and there is evidence that these changes begin around the time of menopause (Forbes, 1987; Aloia et al., 1991). Weight gain and changes in body
composition are associated with adverse health risks (Hirsch, 1985), thus underscoring the importance of these changes as they relate to menopause.

The aim of this review is to describe the changes in body composition that occur with age in women, with a focus on what is known about the relation of these changes to menopause. Our review is intended to highlight areas worthy of future investigation and is not intended to provide an exhaustive review of previous studies.

Two potential general mechanisms leading to body composition changes will be examined: reduced levels of physical activity and altered hormonal levels. Because weight gain, body composition, and energy expenditure are closely linked, an additional aim is to describe the changes in energy expenditure that occur with age in women. Because this review is intended to emphasize potential research directions, we describe the currently available body composition and energy expenditure methodology that might be employed in future studies.

WEIGHT GAIN AND MENOPAUSE

Several studies suggest that American women gain weight around the time of menopause. The main question, however, is whether the rate of this weight gain is more rapid in peri- and postmenopausal women than it is in premenopausal women. Several studies suggest that a distinct increase in the rate of weight gain in adult women does not occur at the time of menopause.

Wing and her colleagues (1991) carried out a prospective study of weight change and the effect of weight change on cardiovascular risk factors in a population-based sample of 485 middle-aged women. Subjects were evaluated prior to menopause when they were between the ages of 42 and 50 years, and then 3 years later. The average weight gain over the 3-year interval was (mean ± SD) 2.25 ± 4.19 kg. The women who remained premenopausal and those who had a natural menopause gained a similar amount of weight. The increment in body weight was significantly correlated with a rise in blood pressure and increased levels of total serum cholesterol, low-density lipoprotein cholesterol, triglycerides, and fasting insulin. Women are thus clearly at risk of weight gain during the menopausal years, and this weight increment is accompanied by an increase in cardiovascular risk factors. In this study, premenopausal and menopausal women gained weight at an equivalent rate.

Wing and colleagues (1991) also evaluated the weight change in 32 of the 485 women who were given hormone replacement therapy to treat menopause-associated symptoms. These subjects had a slightly greater increase in body weight and in skinfold thickness than their untreated counterparts.

The question of weight gain during the menopausal years was also examined by Williamson and colleagues using data from the First National Health and Nutrition Examination Survey Epidemiological Follow-up Study (Williamson et al., 1990). The investigators observed a body mass index (BMI) increase of 0.3 kg/m² between the ages of 45 to 55 years, which is considerably smaller than that observed by Wing and colleagues (1.16 kg/m² over 3 years). Thus, the rate of weight gain during the menopausal period is not consistent between studies.

In a related study on the same population, Williamson (1991) estimated the incidence of overweight as the proportion of women who were classified as overweight (BMI > 27.3) at the 10-year follow-up survey among those who were not overweight at the
baseline investigation. The peak incidence of becoming overweight (14%) was between the ages of 35 to 44 years and declined thereafter. This observation again suggests that for populations of women there is not a distinct increase in the rate of weight gain around the time of menopause, and that the greatest risk of developing obesity actually occurs during the early adult years.

The findings of Wing et al. also differed from those of Hamman and colleagues (1975) with respect to weight gain at the time of menopause. Hamman et al. reported no weight gain at the time of menopause in Pima Indian women. Furthermore, cardiovascular risk factors showed no change. The Pima Indians are at high risk of developing obesity at an early age, and therefore they may differ from other populations with respect to physiological changes at the time of menopause. Nevertheless, the question of weight gain at the time of menopause in relation to ethnicity is an important one. In support of the idea that more information is needed for specific ethnic groups, the study of Williamson et al. (1990) found that black women tended to gain more weight between the ages of 45 and 55 years than did white women.

This brief overview highlights the need to longitudinally examine weight gain specifically during the menopausal period in women that vary in ethnicity and who do or do not use hormone replacement therapy.

BODY COMPOSITION

Body weight consists of many compartments and components, and thus weight change alone is an inadequate guide to the underlying changes in body composition that occur during menopause. Body composition can be considered at the five levels depicted in Fig. 1. The levels, in consecutive order, are atomic, molecular, cellular, tissue system, and whole body (Wang et al., 1992). Each level and its associated compart-

![Fig. 1. The five levels of human body composition [from Borkan and Norris (1977) with permission]. Abbreviations: ECF, extracellular fluid; and ECS, extracellular solids.](image-url)
ments are distinct, although connections exist between components at the different levels. For example, total body carbon, fat, fat cells, adipose tissue, and skinfold thickness at the five respective levels in consecutive order are all linked by their association with fatness.

**Measurement**

Methodologies exist that can be used by investigators to evaluate compartments and components at all five levels of body composition. In addition to the compartments shown in Fig. 1, methods are available for evaluating regional body composition. This is an important area, particularly for the study of changes in adipose tissue distribution at the time of menopause.

Other reviews provide an in-depth description of body composition methods. In reference to menopause, several important points are as follows:

1. Techniques are available for estimating total body fat, a molecular level compartment, that are independent of a subject's hydration (Heymsfield et al., 1990, 1991). Similarly, total body adipose tissue, a tissue-system level component, can be quantified reliably using imaging techniques (Baumgartner et al., in press).

2. Regional adipose tissue distribution can be evaluated using methods that include imaging techniques (e.g., magnetic resonance imaging), whole-body dual-energy x-ray absorptiometry, and anthropometry (Sjostrom, 1991).

3. Bone mineral mass and density can be quantified for either the whole body or for specific regions using several different techniques. These include delayed-gamma neutron activation analysis for total body calcium (Cohn et al., 1980), single and dual photon absorptiometry, dual-energy x-ray absorptiometry, and computerized axial tomography.

4. Fluid volumes can be estimated using radioisotopes and other dilution techniques. Initial studies also suggest that bioimpedence analysis can be used to evaluate extracellular and intracellular fluid volumes (Segal et al., 1991).

**Influence of menopause and aging**

There are substantial longitudinal and cross-sectional data that indicates that body composition changes in women with age (Forbes, 1987). Some general effects of aging on body composition in women are the following:

1. There is an increase in total body fat as a percentage of body weight (Cohn et al., 1985; Forbes, 1987). Adipose tissue increases also, mainly over the trunk and in the intra-abdominal or visceral compartment (Borkan and Norris, 1977).

2. Fat-free body and adipose tissue-free mass, similar compartments at the molecular and tissue-system levels of body composition (Wang et al., 1992), respectively, decline with increasing age (Cohn et al., 1985; Forbes, 1987; Aloia et al., 1991). All components of the adipose tissue-free compartment decrease in mass; these include brain, skeletal muscle, and skeleton (Grimby and Saltin, 1983; Aloia et al., 1991). The loss of skeleton is paralleled by a reduction in bone mineral mass and total body calcium (Cohn et al., 1985; Forbes, 1987).
3. Extracellular fluid is relatively increased in the elderly as a proportion of total body fluid, and intracellular fluid is relatively reduced (Borkan and Norris, 1977).

4. Total body protein decreases with age, although the relative loss of intracellular proteins appears to exceed the loss of extracellular proteins such as collagen (Tominlinson et al., 1969; Fujisawa, 1974). Total body protein in the elderly may therefore consist of a greater proportion of extracellular proteins compared to intracellular proteins.

The changes in body composition that occur with aging in women appear to begin at or near the time of menopause and progress linearly with time (Forbes, 1987; J.A. Gasperino, M. Russell, J. Wang, et al., unpublished). There is a suggestion for some compartments, such as bone mineral and total body potassium, that a rapid loss occurs in the menopausal period followed by a slower decline thereafter (Forbes, 1987).

Aloia and colleagues (1991) studied the rate of change in several different compartments in 304 pre- and postmenopausal Caucasian women. The investigation included both cross-sectional and longitudinal cohorts. Body composition was relatively stable in the premenopausal women, whereas a linear decline in bone mineral and total body potassium was observed in the postmenopausal women. The loss in total body potassium was most rapid in the first 3 years following menopause. The loss of total body potassium suggests a decrease in both skeletal muscle and body cell mass. A linear increase in total body fat was observed in the postmenopausal women, although body mass index also increased in the group with age.

Thus, it is unclear if the increase in body weight accounted for the increasing fat mass with age, or if there was also a relative increase in fat independent of the change in body weight.

Gasperino and colleagues (unpublished) also studied body composition in pre- and postmenopausal women. The women were divided into two ethnic groups, black (n = 34) and white (n = 34). The groups were further matched on age, weight, height, and menstrual status. There was no correlation between body mass index and age in either group and the women were all of normal body weight (i.e., body mass index 18–25 kg/m²). As in the study of Aloia et. al. (1991), women in both groups had a linear decline in total body potassium, fat-free body mass, and bone mineral mass with age. Both groups had a similar amount of total body fat, although the black women had a significantly increased waist to hip circumference ratio, suggesting an upper body distribution of adipose tissue. The waist to hip ratio is usually used as a measure of adipose tissue distribution, although the validity of this ratio across ethnic groups is unknown.

Total body fat increased with age in both groups. The rates of change, calculated as the slope of the compartmental weight versus age, for all of the compartments were similar between both ethnic groups. However, at all ages the black women had a greater total body bone mineral mass than did the white women. Total body potassium was significantly greater in the young black women, although the difference in potassium between the two groups tended to diminish with age.

There is some evidence that there is seasonal variation in body composition. Dual-energy x-ray absorptiometry was used by Dawson-Hughes and colleagues to examine regional changes in fat, lean, and bone tissue for over 1 year in 125 postmenopausal women (Dawson-Hughes and Harris, 1992). The investigators found no overall changes
in body weight over the study interval, although there was a net (mean ± SE) 1.08 ± 0.39% loss of lean tissue in the legs and a net 3.43 ± 1.12% increase in trunk fat tissue. Moreover, there appeared to be seasonal variation in body composition with significant changes in regional fat, lean, and bone tissues related to time of year.

Poehlman et al. (1993) showed pronounced changes in body composition coincident with the onset of menopause. That is, no significant change in fat-free mass (from underwater weighing) in healthy menstruating women up to age 50 years, whereas after age 50 years, a dramatic decline in fat-free mass and increase in fat mass was noted. The suggestion is that the estrogen-deficient state may contribute to alterations in body composition. Kohrt et al. (1992) examined the association of age and physical activity on body composition and fat distribution in endurance-trained and sedentary, younger and older women. These investigators showed that the average difference in fat mass between younger and older sedentary women was 12.2 kg, but only 5.5 kg in the trained women. These findings suggest that chronic participation in endurance exercise during menopause may reduce the accumulation of body fat, especially in the upper truncal regions, thus lowering the risk of developing cardiovascular and metabolic disorders. Gardner and Poehlman (1993) showed a significant decline in leisure-time physical activity (measured by activity questionnaire) in postmenopausal relative to premenopausal women that was greater than that attributed to the aging process, per se. Furthermore, the accelerated decline in physical activity was associated with a greater increase in body fat. The implication from this study is that physical activity may play an important role, particularly in postmenopausal women, in offsetting the gain in body fat and in preserving fat-free mass.

Mechanisms

At least two explanations have been proposed in an attempt to explain senescence-related changes in body composition. First, physical inactivity reduces the biomechanical forces on bone and skeletal muscle. Force or tension are trophic stimuli for both bone and skeletal muscle growth (Doyle et al., 1970; Ellis and Cohn, 1975). There is good evidence that physical exercise, particularly strength training, in previously sedentary subjects can partially reverse the characteristic decline in skeletal muscle strength and muscle mass observed with aging (Evans, 1992). Additionally, it appears that postmenopausal women can achieve similar levels of cardiovascular fitness to premenopausal women. Wells et al. found no differences in cardiorespiratory fitness in relation to age, training, and menopausal status in trained masters women endurance athletes, ages 35 to 70 years (Wells et al., 1992). The authors concluded that a decline in cardiorespiratory fitness in and around the menopausal years is most likely the combined result of aging and a reduction in physical activity. Notelovitz et al. (1986) reported no differences in cardiorespiratory fitness between age-matched pre- and postmenopausal women. Cowan and Gregory (1985) reported no differences in the ability of previously sedentary pre- and postmenopausal women to respond to cardiorespiratory training.

The second proposed mechanism of senescence-related changes in body composition involve hormonal changes that occur with both menopause and with aging in general. Some of these changes may be directly related to weight gain and body composition change with menopause. The following are some relevant body composition–hormone interrelations.
**Estrogens.** Estrogens may influence food intake, physical activity level, and adipose tissue distribution (Wade and Zucker, 1970; Wade, 1975; Roy and Wade, 1977). An increase in body weight coupled with hyperphagia accompanies ovariectomy in adult female rats (Roy and Wade, 1977). Such effects can be reversed with the administration of estradiol. Similarly, there is a suppression of running-wheel activity with ovariectomy (Wade and Zucker, 1970; Wade, 1975; Roy and Wade, 1977). This too can be reversed with estradiol treatment. Although body weight increases and running-wheel activity decreases with ovariectomy, it is not surprising that carcass fat content was found to double in these female rats, a condition that can be reversed with estradiol treatment.

Ovarian hormones also influence the food intake and feeding of other animal species. Bielert and Busse found a significant difference in food intake between preovulatory and luteal phases of the menstrual cycle in female baboons (Bielert and Busse, 1983). Exogenously administered estradiol to ovariectomized females demonstrated an inhibitory effect of estradiol on food intake. There were no effects of exogenously administered progesterone on food intake. Rosenblatt and colleagues (1980) investigated the relation between food intake and the menstrual cycle in rhesus monkeys. The investigators observed a significant decrease in the quantity of food consumed with midcycle estrogen and gonadotropin surges. The amount of food consumed by the female monkeys was also greater during the luteal phase than in the earlier follicular phase. A low food intake was also observed around the time of ovulation in guinea pigs and rhesus monkeys in the study of Czaja and Goy (1975). Food intake was lowered in ovariectomized animals of both species with administration of estradiol. No effects of progesterone on food intake were observed.

Estrogen combined with progesterone administration to postmenopausal women appears to attenuate the increase in abdominal fat that is characteristic of the postmenopausal period. Haarbo and colleagues (1991) investigated postmenopausal women who were followed up for 2 years in a prospective, randomized, placebo-controlled trial. They found that combined estrogen–progesterone treatment prevented the increase in abdominal fat, evaluated by dual-energy x-ray absorptiometry, after menopause. The hormonal treatment also reduced postmenopausal bone loss.

Sex steroids may also influence the regional characteristics of adipose tissue in pre- and postmenopausal women. Rebuffe-Scevone and colleagues (1986) observed different patterns of lipoprotein lipase activity and lipolytic responsiveness to norepinephrine in pre- and postmenopausal women. The investigators hypothesized that the secondary sex characteristics of adipose tissue distribution in women might be mediated by region-specific effects of sex steroid hormones on the metabolism of adipose tissue.

**Progesterone.** Food intake and running-wheel activity are not influenced by progesterone treatment of ovariectomized rats (Wade and Zucker, 1970; Wade, 1975; Roy and Wade, 1977). However, concurrent progesterone treatment of ovariectomized rats attenuates the effects of estradiol on food intake and body weight in rats. This attenuation of the hypophagic actions of estradiol by progesterone may explain why food intake and body weight increase during pregnancy when serum progesterone levels are elevated.

**Sex Hormone Binding Globulin (SHBG).** The presence of upper body obesity emerges as a risk factor for morbidity and mortality in many investigations. For example, Lapidus and colleagues (1984) found that the waist to hip circumference ratio was...
positively correlated with the 12-year incidence of myocardial infarction, angina pectoris, stroke, and sudden death in women from Gothenburg, Sweden.

Total body and upper body adiposity are both associated with increases in free serum testosterone and a reduction in SHBG. The serum level of SHBG is an important determinant of the free to bound plasma testosterone ratio. Haffner and colleagues (1991) observed in postmenopausal women that SHBG is inversely correlated with total adiposity and upper body obesity.

Serum cortisol and ACTH. The association between high serum cortisol levels and central deposition of adipose tissue in patients with Cushing's Syndrome is well known. Kaye and Folsom (41) examined the associations of body fat distribution, as evaluated by the waist to hip circumference ratio, with serum cortisol and ACTH in healthy postmenopausal women. Their results suggested that neither serum cortisol levels nor ACTH were associated with adipose tissue distribution in postmenopausal women.

Other hormones may play important roles in determining body composition changes with aging, although they are not reviewed here in the specific context of menopause.

ENERGY EXPENDITURE

For body weight to increase over the long term, there must be positive energy balance. Intake of energy from foods must therefore exceed total energy expenditure. In this section, we give a brief overview of methodology available for evaluating energy expenditure and then examine some of the changes in energy expenditure in postmenopausal women.

Methods

Energy expenditure can be divided into three main components: resting, thermic effect of food, and physical activity (Ravissin and Bogardus, 1989) (Fig. 2).

Resting energy expenditure reflects the postabsorptive metabolic rate. Basal meta-
bolic rate, which is slightly lower than resting energy expenditure, is usually defined as the minimum rate of resting postabsorptive thermogenesis. The thermic effect of food represents the energy expended for the 3–6-h period following meals. Energy expended in physical activity constitutes the remainder of total calories expended over 24 h (Ravussin and Swinburn, 1992).

There are two approaches to estimating energy expenditure in vivo: direct and indirect calorimetry. Direct calorimetry is not widely used today, and most investigators apply indirect techniques.

1. Resting energy expenditure and the thermic effect of food are readily measured by conventional and widely available indirect calorimetry systems (Ravussin and Bogardus, 1989; Ravussin and Swinburn, 1992). Protocols are also available for evaluating the thermic response to specific physical activities.

2. Large respiration indirect calorimeters are now available within which subjects can remain for periods of up to 1 week (Ravussin et al., 1986). These systems allow extended measurements of sleeping, resting, and basal metabolic rates. They also allow measurement of total energy expenditure and the energy expended in physical activities.

3. The restrictions imposed by conventional indirect calorimetry and respiration chambers limit evaluation of subjects in their natural setting. Two indirect calorimetry procedures are now available for measuring total energy produced in free-living adults. These are doubly labeled water (Prentice, 1990) and labeled bicarbonate elimination (Elia et al., 1992). The doubly labeled water technique allows measurement of total energy expenditure for periods of up to about 14 days in outpatients. The labeled bicarbonate method can be applied over shorter time periods, usually 24–48 h. Both methods are accurate to within ± 5%.

This brief overview indicates that all major components of energy expenditure can now be measured in humans. These methods can be applied either alone or in combination with body composition techniques to examine thermogenesis during menopause.

Influence of menstrual cycle, menopause, and aging

There is a clear association between resting energy expenditure and changes in the menstrual cycle. This association is important in two respects. First, when studying both pre- and postmenopausal women, it is important to clearly define phase of menstrual cycle in which metabolic measurements are made. Second, a small rise in energy expenditure is associated with the menstrual cycle that is no longer present in postmenopausal women. This may be one factor that reduces total energy requirements in postmenopausal women.

The main finding is that core temperature and energy expenditure increase during the luteal phase of the menstrual cycle. For example, Webb (1986) observed an 8–16% increase in total energy expenditure measured by direct and indirect calorimetry during the 14-day luteal phase following ovulation. Solomon and colleagues (1982) observed a cyclic variation in basal energy expenditure in women studied on a metabolic ward. The lowest basal energy expenditure occurred 1 week before ovulation and then continued to rise until the beginning of the menstrual cycle. The difference in basal metabolic rate from its zenith before menses to its nadir after ovulation was 359 kcal/day. Bisdee and
colleagues (1989a,b) studied energy expenditure in women under metabolic ward conditions throughout a single menstrual cycle. Total energy expenditure and its components were evaluated in a respiratory chamber indirect calorimeter. Sleeping metabolic rate was lowest in the late follicular phase and highest in the late luteal phase (difference, mean ± SD, 6.1 ± 2.7%). Total energy expenditure was also increased during the luteal phase, although the difference from the follicular phase was not statistically significant. Exercise efficiency did not change throughout the menstrual cycle.

In addition to cyclic changes in thermogenesis with the menstrual cycle, women experience a gradual fall in resting energy expenditure with age (Ravussin and Bogardus, 1989; Poehlman et al., 1993). There appear to be at least three components that contribute to this change. First, the loss of ovarian function and luteal phase of the menstrual cycle theoretically reduces energy expenditure by about 15 000 to 20 000 kcal per year (Ferraro et al., in press). Second, loss of fat-free body mass with aging in women is associated with a lowering of resting metabolic rate (Ravussin and Bogardus, 1989; Poehlman et al., 1993). Arciero et al. (in press) has shown that the lower RMR in postmenopausal women relative to premenopausal women was primarily related to the loss of fat-free mass and a decline in physical activity. Furthermore, in this study, menopausal status was a significant and independent factor contributing to the lower RMR in older women that was independent of the aging process itself. Work from Poehlman et al. (1993) showed no age-related changes in RMR in healthy women up to age 50 years, whereas after this period, a dramatic decline in RMR was noted. Third, there appears to be a small lowering of resting energy expenditure with age in women in excess of that explained by loss of fat-free body mass (Ravussin and Bogardus, 1989; Poehlman et al., 1993; Allison et al. in press).

Mechanisms

The most likely cause of the increased postovulatory elevation in energy expenditure is elevated levels of progesterone. Progesterone administration to normal and ovariectomized women is hyperthermic, and progesterone levels are increased during the luteal phase of the menstrual cycle (Bisdee et al., 1989a,b). Further studies are needed to define the specific role of progesterone and other possible factors in regulating energy balance and core temperature during the postovulatory phase of the menstrual cycle. Estrogens do not appear to play a role in the cyclic variation of energy expenditure with the menstrual cycle.

The cause of excess lowering of resting metabolic rate beyond that explained by a reduction of fat-free body mass with age in women is unknown (Poehlman et al., 1993). Taken collectively, the loss of ovarian function, the progressive decline in fat-free body mass, and the additional as-yet unexplained small reduction in resting energy expenditure not accounted for by fat-free body mass loss all contribute to the lowering of resting energy expenditure in postmenopausal women. If physical activity also declines (Gardner and Poehlman, 1993), there could be substantial reductions in total energy expenditure and energy requirements for weight maintenance in postmenopausal women.

Future studies are needed to fully quantify the changes in energy expenditure with menopause and aging in women. Improved understanding of the mechanisms of these changes is also needed.
Our overview of body composition and energy expenditure changes with menopause was designed to highlight the many possible future areas worthy of investigation. Specifically, our committee at the March 1993 NIH Workshop on Menopause identified six potential research questions:

1. What are the longitudinal changes in body composition during menopause?
2. Is there a relationship between body composition changes and menopausal symptoms, psychological changes, risk factors for disease, morbidity/mortality, or quality of life?
3. What mechanisms, such as neuroendocrine function, energy balance, life-style factors, genetic determinants, and psychological factors, contribute to changes in body composition?
4. Are there ethnic/racial differences in menopausal changes and, ultimately, in morbidity/mortality?
5. What interventions, such as physical activity, hormone replacement therapy, caloric restriction, smoking, and other life-style factors, affect body composition changes during menopause?
6. What is the cost:benefit ratio of interventions for the individual as well as for the population?

Providing answers to these questions would give new insight into the mechanisms, adverse health consequences, and treatments for the changes in metabolism and body composition that begin around the time of menopause.

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