IMPACT OF SURGICAL MENOPAUSE WITH AND WITHOUT HORMONE REPLACEMENT ON WEIGHT CHANGES IN WOMEN

by

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Thesis submitted to the Faculty of the Virginia Polytechnic Institute and State University in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

in

Human Nutrition and Foods

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July, 1989

Blacksburg, Virginia
To determine the effect of estrogen on weight changes in women, eight adult females were followed for a period of six months subsequent to hysterectomy or ovariohysterectomy. Three groups comprised the study: 1) a hysterectomy or control group, 2) an ovariohysterectomy group with estrogen replacement therapy, and 3) an ovariohysterectomy without estrogen treatment group. Body weight, caloric intake, and activity level were recorded for the eight prospective subjects over the six month period. Weight data were gathered from past medical records on an additional 19 patients meeting the treatment criteria. Weight changes between groups were not statistically significant. A trend in weight changes among the groups was noted. The hysterectomy group lost five pounds, ovariohysterectomy treated group lost one pound and the untreated group, 0.2 pound. The same trend in weight changes was noted when data from prospective and retrospective subjects were combined. Caloric intake and activity levels did not explain all changes noted. Detailed information on subjects was presented as case studies. The results supported the concept that endogenous estrogen protects against weight gain; evidence did not support the comparable action of exogenous estrogen. Subjects having ovariohysterectomy stated that they
experienced appetite changes such as cravings for sweets, undesirable muscle tone and body contour changes, and difficulty in ability to control weight. Further research with a larger sample size is needed to determine direct relationships between female hormones and suppression of weight gain in women.
I wish to express my sincerest appreciation to the following people who have contributed toward bringing this project to fruition:

for giving of his time, patients, and advice so unselfishly. His dedication to research is a most admirable quality in today's practice of medicine;

Dr. Vera J. Wall, my advisor, for believing in my project. Her enthusiasm, guidance, and encouragement were enlightening and served to instill an appreciation of the trials and tribulations involved in becoming a disciplined researcher;

Mr. Russell A. Heare, deceased member of my committee, whose willingness to advise was never fully realized;

Dr. Ryland E. Webb and Dr. Robert B. Frary, members of the graduate committee, for their suggestions and moral support;

for her ability to meet typing deadlines with promptness and accuracy;

and

for teaching and assisting me with the nutrient software package and the computer system;

A special thanks to the dedicated subjects who are the backbone of this investigation;

To my loving husband and family for their patience; and most importantly of all, for their encouragement to allow me to broaden my horizons.
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CHAPTER I
INTRODUCTION

In the past two decades there has been an abundance of literature regarding the effects of ovariectomy (ovary removal) upon weight gain in animal subjects. Variations in activity level and food intake are considered responsible for the weight fluctuations. These factors in turn are influenced by the administration or withholding of estrogen or progestrone, or both. The interaction of factors which influence the overall energy balance in the ovariectomized animal is indeed complex and would suggest a similar situation in humans.

Recent and past research studies utilizing rodents and other animals demonstrate that estrogen exhibits a protective effect against weight gain. Estrogen and estrogenlike compounds appear to decrease food consumption in animals. Also, a cyclic pattern of food intake has been noted in female rats; specifically, when estrogen levels rise on the day of estrus there is a decrease in food intake and as estrogen levels decrease, food intake rises. This cyclic pattern of food intake can be abolished by ovary removal, resulting in an increase in body fat and weight gain (Krause and Mahan, 1984).

Although there is an abundance of literature regarding the effects of ovariectomy upon weight gain in animals, a paucity of knowledge exists on this topic regarding human subjects. Hysterectomy is the most common major operation performed in the United States; approximately 650,000 are performed annually. Each of these women represents not merely a statistic, but more significantly, a reservoir of individual
experiences and knowledge invaluable to research in the field of gynecology.

Animal laboratory results cannot be extrapolated directly to human subjects; research studies ideally should be performed upon humans in order to provide more beneficial information for society. Therefore, it is appropriate to study the effect of hysterectomy and ovariohysterectomy in women and to explore relationships between female sex hormones and weight status. Special emphasis should be placed on the effects of surgical menopause on weight gain in women in order to understand the interaction of any underlying factors. Therefore, the overall goal of this study was to investigate the effects of ovariohysterectomy with and without hormonal replacement therapy upon body weight, caloric intake, and activity level in women between the ages of 30 and 48 years of age.
DEFINITION OF TERMINOLOGY

The following are a list of terms (Miller, 1976) used throughout the text of this thesis. The definitions below will explain the context as they are used in this document.

Adrenal glands: a pair of endocrine glands located at the top of the kidneys that secrete a number of hormones which influence many bodily processes.

Corpus luteum: an ovarian structure which is actually a remnant cavity located at the site of a ruptured follicle.

Endocrine Gland: a gland that produces and releases a hormone directly into the bloodstream.

Hysterectomy: the surgical removal of the uterus or womb. Also known as a uterectomy or total or complete hysterectomy in the majority of cases whereby the cervix is also removed.

Ovariohysterectomy: the surgical removal of the uterus and one or both ovaries.

Pituitary Gland: a very important endocrine gland in the body; also called the hypophysis. The pituitary is a tiny mass of tissue attached by a thin stalk to the hypothalamus at the base of the brain.
CHAPTER II

REVIEW OF LITERATURE

Ovarian Functions

The ovaries are a pair of female sex glands that produce egg cells (ova) and secrete the sex hormones progesterone and the estrogens. These oval shaped glands measure about one and a half inches in length and are located in the lower abdomen on either side of the uterus. The ovaries contain thousands of tiny structures known as graafian follicles, where ova develop. Estradiol is secreted by the maturing graafian follicle. This form of estrogen represents the major estrogen secreted by the ovaries and is the most potent known endogenous estrogen. Estrone is also produced by the ovaries, but its principal source is from peripheral tissue through the conversion from androstenedione (an androgen). Secondary sexual development in women is estrogen-dependent. Estrogens enhance uterine growth, induce endometrial proliferation, thin cervical mucus, and contribute to the development of the breast's ductular systems. Other effects of estrogen include: decreased peripheral tissue sensitivity to insulin, increased plasma triglycerides, and increased hepatic synthesis of proteins which bind thyroxine (T-3), progesterone, and cortisol. Estrogens are secreted in insignificant amounts in men under normal conditions (McGilvery, 1983).

Progesterone is the major hormone produced by the corpus luteum. Additionally, synthesis occurs in the adrenal glands in minute amounts and the placenta. Progesterone induces glandular development of breast tissue, increases the core body temperature, initiates the proliferative
phase of the estrogen-primed endometrium, increases cervical mucus viscosity, and inhibits uterine contractions.

From the onset of puberty until menstruation ceases in middle age (menopause), the ovaries release one, or more, ova each month and secrete progesterone and estrogen in large quantities. A normal menstrual cycle is achieved by the coordinated operation of the central nervous system, the pituitary gland, the ovary, and the uterus. The central nervous system, through the hypothalamus, causes the release of gonadotropin-releasing hormone (GnRH). GnRH reaches the anterior pituitary gland and causes the release of the two gonadotropins, follicle-stimulating hormone (FSH) and luteinizing hormone (LH). During the first four days of a new menstrual cycle, the unfertilized egg and the lining of the uterus, produced in the previous cycle, are discarded. Simultaneously in one of the ovaries, follicles start to grow under the influence of FSH (Price and Wilson, 1982).

On day 12 the FSH accelerates the growth of one of the graafian follicles, while the others diminish in size. Estradiol is produced by the follicle and its secretion initiates the thickening of the uterus lining in preparation to receive a fertilized egg.

A further rise in estradiol at mid-cycle (day 14) triggers, through a positive feedback effect on the pituitary gland, a peak release of LH and FSH. This peak release of LH and FSH causes the rupture of the developing ovarian follicle and the ovum is released from the ovary. This stage is referred to as the period of ovulation. The egg will die within 48 hours if fertilization fails during the passage of the ovum along the Fallopian tube into the uterus (Miller, 1976).
Day 16 marks the formation of the corpus luteum. The cavity fills initially with blood and is replaced with yellowish granular cells called lutein cells. The corpus luteum produces estrogen and progesterone; but greater amounts of the latter. Progesterone, in conjunction with estrogen, causes the uterine lining to thicken even further.

Toward the completion of the menstrual cycle (day 24), the lining of the uterus reaches its maximum secretory capacity and begins to break down into the uterine cavity. The corpus luteum starts to degenerate in the ovary. At the completion of the cycle, estradiol and progesterone levels fall and menses occur. The unfertilized egg and the uterine lining are discarded in the menstrual flow on the 28th day of the menstrual cycle. If fertilization occurs, the menstrual cycle is disrupted and terminates until the end of pregnancy (Miller, 1976).

Menopause is the cessation of menstruation which occurs as the functioning of the ovary declines. In the majority of women, the menopause begins sometime between the ages of 45 and 55, and lasts for a period that may vary from six months to three years. The average age for onset of menopause in the United States is 47 (Price and Wilson, 1982). It is a period characterized by decreased levels of estradiol, and the ovary decreases in size and is virtually devoid of follicles. The decrease in estrogen levels is associated in most women with hot flashes, emotional lability, depression, and insomnia. At any age, surgical removal of the ovaries results in an artificial menopause with a marked reduction in estrogen production since the ovaries are the primary source of this hormone. Estrogen is normally prescribed for
women who experience a surgical menopause or for those women who experience a natural menopause with the troublesome symptoms previously mentioned. Use of oral estrogen, exclusive of oral contraceptives, is rising rapidly. Between 1984 and 1985, the conjugated equine estrogen (CEE) Premarin moved from 17th to 12th place in the list of the top 200 prescribed drugs in the United States. (Ross et al., 1988) This form of estrogen is actually derived from the testes of stallions and represents the richest tissue source of female hormones (estrogens). Gynecologists may elect to supplement estrogen replacement therapy with medroxyprogesterone acetate, a form of progesterone. This combination of hormone replacement therapy is currently widely prescribed due to recent studies (Ross et al., 1988) indicating that progesterone may act to reduce endometrial cancer risks.

Biosynthesis of Estrogen and Progesterone

Generally, the ovaries are thought to be the major source of estrogen; however, the adrenal cortex and peripheral body tissue metabolism of the body are major contributors to normal estrogen homeostasis. In recent years, with the ability to measure circulating levels of sex steroids by radio-immunoassay, it has become evident that many sex steroids including the estrogens are derived from both the gonads and the adrenals, in addition to peripheral conversion from other steroid precursors (Henley and Vaitukaitis, 1985).

Approximately twenty percent of the total estrogen production by females with normal body weight occurs in other than ovarian tissues. The remaining eighty percent of estrogen is synthesized by specialized
cells called theca cells in the ovarian follicles. Even a normal adult man forms about forty-five micrograms of estrogen daily; this compares to the five hundred micrograms produced on the day of ovulation by a woman (McGilvery, 1983).

Actual isolation and characterization of estrogen from ovarian tissue was accomplished by MacCorquodale and co-workers (Grollman, 1974). Estrogen is classified as a steroid, as are all the sex hormones, and is specifically referred to as 17β-estradiol. Other estrogenic substances found in the various body fluids are actually derived from the metabolic degradation of the estrogen 17β-estradiol. Therefore, the various sex hormones including progesterone and testosterone are similar structurally.

Production of the female sex hormones is under the direct influence of the endocrine glands. Lauritzen and Klopper (1983) found that in the ovary, estrogen biosynthesis involves a cascade of enzyme-substrate events in which the product of an immediate reaction serves as the substrate of the succeeding reaction. Whitworth and Meeks (1985) summarize the process as follows:

"The first major step in the formation of estrogens by the ovary is the conversion of cholesterol to pregnenolone by hydroxylation. The process then proceeds along two alternative pathways: 1) conversion of pregnenolone to dehydroepiandrosterone or 2) conversion of pregnenolone to progesterone followed by hydroxylation of progesterone to 17-hydroxyprogesterone. Regardless of the route, the products of either of these two pathways provide the substrates for the next step, the formation of androstenedione, an androgen which can be further reduced to testosterone. Significant quantities of androstenedione are also secreted by the adrenal gland.

While androstenedione and testosterone may not be considered the primary end products of normal ovarian function, they are important in that they serve as immedi-
ate precursors for estrogen formation. The transformation of androgens to estrogens is referred to as aromatization; it is through this process that androstenedione is converted to estrone and testosterone is converted to estradiol. The importance of the aromatase reaction for the present discussion is that any nonglandular tissue possessing aromatase activity becomes a potential site of estrogen production through the uptake of circulating androstenedione or testosterone. It is for this reason that aromatization is thought to be the mechanism underlying extraglandular estrogen formation."

Estrogen and Its Relationship to Body Weight

Menarche occurs earlier in obese girls than in those who have less body fat. Although a minimal percentage of body fat (twenty-four percent) has been postulated as necessary for the onset of menarche, the exact mechanism that triggers puberty still has not been established (Henley and Vaitukaitis, 1985).

Obese women have elevated production rates of essentially all steroids, including estrogen. The altered metabolism has generally been attributed to excess adipose tissue. Results from several in vivo steroid kinetic studies (Longscope et al., 1969; MacDonald et al., 1967; and Grodin et al., 1973) showed a direct relationship between body weight and the efficiency of aromatization of androstenedione to estrone. This association was demonstrated on the basis of multiple body-weight-related parameters including total body weight, pounds of excess body weight, percent of ideal body weight, and the ratio of weight to height and body surface area (MacDonald et al., 1978; Edman and MacDonald, 1978; and Rizkallah et al., 1975). The percentage of intravenously infused radioisotopically labeled androstenedione converted to estrone in ovulatory women rose from 1.0% at 100-130 pounds of
body weight to 2.3% in subjects whose body weight was in excess of 200 pounds. In morbidly obese young women the extent of aromatization was two to five times greater than that of nonobese subjects. In postmenopausal women weighing 240-430 pounds, the fraction of circulating androstenedione converted to estrone was two to four times higher than that of postmenopausal women of normal weight (MacDonald et al., 1978). Because changes in body weight reflect, to a large extent, changes in adipose tissue mass, the investigators have concluded that adipose tissue is a major site of the aromatization of androgen to estrogen (Whitworth and Meeks, 1985).

Body fat may also influence steroid dynamics because of the lipid solubility of steroid hormones. Edman and MacDonald (1978) noted that during continuous intravenous infusion of radiolabeled androstenedione, women weighing more than 260 pounds required five to six times longer to reach steady-state equilibrium conditions between the rate of androstenedione infusion and the plasma concentration of labeled estrone. He also observed that the rate of entry of estrone into the plasma from aromatizing sites is inversely related to body weight. These findings were interpreted to indicate that adipose tissue may act to sequester the estrogen product of androgen aromatization.

"These findings suggest that the rise in nonglandular estrogen production associated with increasing body weight is probably due to the increasing amounts of adipose tissue mass and aromatase activity. Also, because of the lipid solubility of steroid hormones, the adipocyte may be a site of androgen sequestration, thus providing a reservoir of substrate for subsequent aromatization to estrogen." (Cleland et al., 1983)
In both women with anorexia nervosa and those with simple weight loss, amenorrhea occurs most frequently in those individuals with severe and rapid weight loss. Because of inadequate gonadotropin stimulation, ovarian secretion of estradiol is reduced in most women with anorexia nervosa (Henley and Vaitukaitis, 1985). Reduced stores of body fat also may contribute to the low estradiol levels because of the decreased peripheral aromatization of androgens to estradiol (Schwahe et al., 1981).

Hypothalamic-Pituitary-Gonadal Axis Relationships

The hypothalamus produces a single releasing hormone that stimulates the synthesis and secretion of the two pituitary hormones, luteinizing hormone and follicle-stimulating hormone. Luteinizing hormone promotes the secretion of progesterone by cells of the corpus luteum in the ovary and the follicle-stimulating hormone promotes the secretion of estradiol by granulosa cells in the developing ovarian follicles.

The hypothalamus has traditionally been considered to be the neural center for the control of food intake. It composes less than one percent of the total brain volume. Two areas of the hypothalamus have been regarded as important in the control of food intake; the ventromedial hypothalamus and the lateral hypothalamus (Krause and Mahan, 1984).

The ventromedial hypothalamus has become known as the "satiety center" for several reasons. Electrical stimulation of the ventromedial
The ventromedial hypothalamus has led to cessation of eating. Even if an animal was starved, it ceased eating (as if satiated) when the ventromedial hypothalamus was stimulated. Destruction of the ventromedial hypothalamus caused the animal to become hyperphagic, eventually leading to obesity. The animal overconsumed by increasing the size of individual meals as if it could not detect when it was satisfied (Krause and Mahan, 1984).

The lateral hypothalamus has been referred to as the "feeding center" for similar reasons. Electrical stimulation of the lateral hypothalamus caused animals to begin eating. A lesion in the lateral hypothalamus area caused the animals to under-eat by decreasing the size of individual meals, as if they were satiated earlier or could not detect hunger. These animals became aphagic, lost a considerable amount of weight and might die if not force-fed (Krause and Mahan, 1984).

Animal studies such as these have led to the practice of dividing the brain simplistically into a "satiety center" and a "feeding center". However, this subdivision of the hypothalamus is questionable since the brain is not organized into discrete centers that control specific functions. Kupfermann (1982) suggested that the results observed in the ventromedial hypothalamus and the lateral hypothalamus lesion studies were due to a multitude of factors.

The mechanism by which estrogen exerts its negative effect upon food intake in rats has been postulated by Wade (1976) to include a set-point, hypothalamus regulator involvement. In female rats, estradiol was the principal ovarian steroid influencing behavioral regulation of energy balance.
"It was likely that estradiol acts directly on the brain to lower the set-point of a neural lipostatic mechanism. Lowering the body weight set-point reduces food intake, which in turn, lowers body weight (or the proportion of the total body mass devoted to fat stores). The changes in eating behavior following hormonal manipulations are seen as attempts to align body weight with the new set-point. A very likely site of action of estradiol on eating and body weight is the ventromedial hypothalamus, and estradiol may simply cause a "fine tuning" of the lipostatic control mechanisms in this part of the brain." (Wade, 1976)

The thyroid gland is another endocrine gland involved in the cascade sequence mechanisms which influence the release of hormones and feedback controls. Thyroid function is regulated by the hypothalamic pituitary axis. Thyrotropin (thyroid stimulating hormone, TSH) secreted by the adenohypophysis stimulates the thyroid gland to release thyroxine (T-4) and triiodothyronine (T-3). The thyrotropin-forming cells of the anterior pituitary gland are in turn stimulated by another hormone, the thyrotropin releasing hormone, which is formed in the hypothalamus and is transported to the anterior pituitary gland through a portal circulation in the pituitary stalk (McGilvery, 1983).

Bauer (1982) discovered moderate increases in T-4 levels in pregnancy and following the administration of estrogens or oral contraceptives. These latter increases were mainly caused by increases in the thyroxine binding globulin content of the serum proteins. Miyamoto (1978) determined that the elevations of plasma thyroxine-binding globulin and T-4 levels in women taking combined estrogen-progesterone oral contraceptive agents are generally attributed to the estrogen component. In pregnancy there was an increase in T-3 uptake (decreased level of thyroid activity) resulting from an increase in thyroxine-binding globulins caused by increased estrogen secretion (Bauer, 1982).
The regulation of hormone production and of neural center control on food intake was more complex than previously thought. It has become increasingly apparent that food intake is controlled by neural and neuroendocrine influences that still remain to be defined (Krause and Mahan, 1984).

Animal Studies

The effects of ovarian steroid hormones upon body weight in animals have long been known. Estrogen holds a reputation as an anorexic hormone associated with decreased food intake, body weight, and adiposity in female rats. Progesterone has been appropriately nicknamed the "hungry hormone" and produces the opposite effects of estrogen (Wade, 1972; Gentry et al., 1976; and Hervey and Hervey, 1965).

Most of the studies concerning the interactions between feeding and ovarian hormones have been conducted with the laboratory rat. A summary of the most important findings include: a) estradiol appears to be the principal ovarian hormone for regulating body weight; b) at proestrus (when estradiol is at its peak) food intake and body weight decrease; c) during diestrus (when progesterone is high and estrogen is low) food intake and weight increase; d) meal size increases after ovariectomy but treatment with estradiol causes a return to control levels; and e) in intact female rats, treatment with progesterone causes an increase in feeding and body weight, and no change is evident in feeding following progesterone administration to ovariectomized rats (Gentry et al., 1976 and Hervey and Hervey, 1967).
The combination of estrogen plus progesterone has a negative effect upon weight gain. Lumb and coworkers (1985) treated groups of rats with a progesterone—estrogen combination for 50 weeks and noted a significant body weight gain suppression and reduction in food consumption which reversed after withdrawal. Thomas and colleagues (1986) reported similar findings; the influence of ovarian hormone removal in female rats was observed to cause weight gain after ovariectomy. The weight gain was mainly attributed to reduced activity. Others (Czaja and Goy, 1975) observed that in immature rats, ovariectomy had no effect on body weight and estrogen treatment did not decrease food intake as it did in adults. These investigators suggested that an unknown mechanism not active until sexual maturity was responsible for this occurrence.

Czaja (1975) noted that female primates also display a cyclic pattern of food intake that is associated with ovarian changes throughout the menstrual cycle. Gilbert and Gillman (cited in the previous reference) observed a decreased food intake at midcycle, an interval characterized by a preovulatory surge of estrogen. When primates that had been ovariectomized were injected with estradiol, a similar depression of food consumption occurred. Food consumption was significantly higher during the luteal phase of the menstrual cycle than during the rest of the cycle. This finding led Gilbert and Gillman to hypothesize that progesterone, which is increased during the luteal phase, acts as an appetite stimulant. They administered progesterone to baboons with ovaries intact during the midcycle of the menstrual period and found that there was an increase in food intake.
Other studies do not support the notion that progesterone acts as an appetite stimulant. Czaja (1975) discovered that administration of progesterone to ovariectomized female monkeys did not influence their food intake. In addition, Hess and Resko (1973) showed that raising progesterone levels during the periovular and follicular stages of the menstrual cycle had the effect of lowering the estradiol level and preventing its normal surge before ovulation; the observed increase in feeding was evidently secondary to the decreased level of estradiol. The question was raised by these researchers as to whether progesterone acts as an antagonist to estradiol. Ovarian hormones obviously affected food intake in the primates, but it was not clear exactly how they did so.

There were similarities between studies of the rat and the primate, but the results with the rat cannot be generalized to other mammalian species without certain qualifications. Rats had an estrous cycle; primates had a menstrual cycle (Czaja, 1975 and 1978). The rat had a four to five day estrous cycle in which estrogen dominated except when progesterone showed a brief surge on the night of proestrus. The primate menstrual cycle averaged 29 days, and differed primarily in that it had a prolonged spontaneous luteal phase after ovulation which was dominated by progesterone (Hotchkiss et al., 1971 and Karsch et al., 1973).

The levels of serum estrogen, progesterone and LH in the rhesus monkey during the menstrual cycle resembled those of the human female except for two differences (Wade, 1972 and Moghissi et al., 1972). First serum estradiol and LH concentrations reached their peak simulta-
neously in the monkey while in the human female, the estradiol peak preceded the LH peak. Second, human females had a sustained luteal phase serum estrogen peak whereas this had been noted by Hotchkiss et al. (1971) in only one rhesus monkey.

Pfaff and McEwen (1983), in their review of studies, cited investigators who found that ovarian hormones acted directly on nerve cells, particularly in the hypothalamus, to either directly alter electrical activity or modify responsiveness to other stimuli. Experiments showing that the discharge rates of hypothalamic neurons were altered during the estrous cycle of the female rat provided the first clue to the possibility that sex steroids would alter nerve cell electrical activity. Terasawa and Sawyer (Pfaff and McEwen, 1983) recorded elevations in electrical activity of nucleus neurons in the hypothalamus, correlated with ovulation, while Kawakami et al. (Pfaff and McEwen, 1983) noted elevated discharge rates on the afternoon of the day of proestrus, a time considered critical for triggering of ovulatory discharge of luteinizing hormone. Microelectrode recording of single unit activity (Pfaff and McEwen, 1983) showed high firing rates on the day of proestrus for nerve cells specifically in the ventral portion of the medial anterior hypothalamus. Cross and Dyer (Pfaff and McEwen, 1983) stated that in these experiments, circulating hormones were probably acting directly on hypothalamic tissue, since similar microelectrode recording in animals with surgically prepared hypothalamic islands revealed similar variations of anterior hypothalamic neuronal activity across the estrous cycle.
Because several steroid and protein hormones fluctuated during the periods covered by the microelectrode recording experiments, a simpler means to analyze the specific electrical effects of estradiol was to compare ovariectomized animals with or without estrogen treatment. Under these conditions, estrogen treatment led to increased resting discharge rates in the medial anterior hypothalamus and in basomedial hypothalamic neurons (Pfaff and McEwen, 1983). One report (Pfaff and McEwen, 1983) indicated that in spayed female cats electrical activity in the ventromedial nucleus and medial anterior hypothalamus was more responsive to peripheral stimulation after estrogen administration.

Another inductive effect of estradiol, that of increasing the number of receptors for progesterone has been shown to occur in the ventromedial nuclei (Warembourg, 1978). It was postulated that this regulatory event could underlie synergisms between estradiol and progesterone which affect several endocrine and behavioral phenomena (Young, 1961).

The voluntary exercise level of rats, as measured via running wheel activity, correlated positively with estrogen status (Thomas et al., 1986 and Wade, 1976). Wade (1976) found that ovariectomy of adult female rats not only increased food intake, but also decreased voluntary exercise and consequently markedly accelerated weight gain. Withdrawal of ovarian estradiol was the likely reason given for these behavioral changes following spaying because daily treatment with physiological doses of estradiol benzoate was sufficient to restore preovariectomy levels of eating, voluntary exercise, and body weight.
Clearly, a myriad of factors is involved in ovarian hormone metabolism and the mediation of the effect of estrogen and progesterone upon body weight. Variations in ovarian hormones, both over the estrus/ menstrual cycle and following ovariectomy, with and without exogenous replacement, are associated with major disturbances in energy balance in the rodent and the primate. As previously mentioned, body weight, food intake, and activity level have been reported to change significantly with ovarian hormone fluctuations.
Human Studies

Ovarian hormones and the roles they play in mammals have been extensively studied for their effects on reproductive behavior, activity, body weight-regulating behaviors, and pattern of food intake (Wade, 1972). Yet, most research in human studies has centered on ovarian hormones as a factor in premenstrual tension and depression (Morton et al., 1953, and Smith and Sauder, 1969). A definite relationship in several mammals has been observed to exist between sex steroids and pattern of food intake (Czaja, 1975; Gentry et al., 1976; and Blaustein and Wade, 1976). There was a depressed intake at ovulation when estrogen levels were at their peak (Czaja, 1975). Dalvit (1981) stated it was logical that a similar pattern existed in human females.

The void in human research studies prompted Dalvit to conduct an investigation to determine the effect of the menstrual cycle upon patterns of food intake in female human subjects. In his investigation, Dalvit (1981) observed food intakes of eight females experiencing menstruation and found systematic fluctuations in caloric intake during the menstrual cycle, with the intake being about 500 kcal/day higher during the ten days preceeding the onset of the menstrual period (post-ovulatory phase characterized by low estrogen levels) than during the ten days following (characterized by estrogen level surge). The fluctuations correlated with changing ovarian conditions and may have resulted from or were influenced by steroid levels. In particular, estrogen levels began to fall after ovulation and began to rise at menstruation. It was postulated that estrogen may be an appetite-suppressing hormone,
and the change in its concentration may account for the observed changes in food intake.

Dalvit (1981) suggested that the pattern of food intake shown by his subjects may provide useful background information for future research studies of the factors affecting human food behavior. In addition, he stated the findings may benefit women who have difficulty controlling their weight.

The earliest study in which mention was made of a varied food pattern or particular cravings associated with the menstrual cycle was done by Morton et al. (1953). In this study, prison inmates were questioned to determine the incidence and severity of premenstrual symptoms. A craving for sweets was reported by 37%, and increased appetites by 23%. Sugar tolerance tests showed a hypoglycemic curve in the premenstrual period, indicating an alteration in carbohydrate metabolism to account for an increased sugar tolerance. Hypoglycemia is characterized by an increased appetite, craving for sweets, and depression.

These results were confirmed and extended in a more recent study by Smith and Sauder (1969), who reported associations between a) cravings for food or sweets and premenstrual tension, b) the occurrence of fluid retention and a craving during a specific time such as during menstrual periods or depression, and c) compulsive eating and a tendency to more frequent depression. The results indicated there might be a physiological basis for the cravings and suggested the hypoglycemic phenomenon. However, following a literature search, no studies were found that tested this hypothesis.
The above studies with humans were based on subjects' qualitative impressions of their food intakes or cravings obtained via questionnaire. Dalvit's (1981) investigation was undertaken to obtain food intake records in order to extract from them more quantitative information on the relationship between food intake and the menstrual cycle.

Three preliminary reports with 24-hour data have indicated an energy expenditure increase during the post-ovulatory half (luteal phase) of the cycle. Aschoff and Pohl (1970) published oxygen uptake for one woman, showing higher levels before menstruation than following it. Bisdee and James (1983) found that nine women had a six percent increase in sleep metabolism in their post-ovulatory phases, and Webb (1981) reported that four young women showed increases ranging from seven to fifteen percent in 24-hour expenditure following ovulation.

Webb (1986) recently studied ten healthy women ranging from 20 to 48 years of age who had normal menstrual cycles, utilizing both direct and indirect calorimetry. Continuous direct calorimetry was performed during 46-hour periods by means of a water cooled suit; indirect calorimetry by respiratory exchange was performed simultaneously. Two 46-hour measurements were performed before and two after ovulation. Phases of the menstrual cycle were determined retrospectively by taking the onset of the menstrual flow as the signal that ovulation had occurred 14 days earlier. Excretion of urinary pregnandiol was also measured before and during the estimated date of ovulation. The variability of the energy expenditure measurements was three to four percent.
Results of Webb's study revealed that the mean 24-hour energy expenditure increased 11.5 ± 2.6% (standard deviation) during the postovulatory phase of the menstrual cycle (p<0.001) in eight of the ten women studied; two subjects showed no significant change. Based upon the mean values of all ten cases, the rise in energy expenditure amounted to about 150 kcal/day during the second half of the cycle.

Body composition measured by underwater weighing exhibited a wide range of fat mass, varying from 12 to 46% of body weight. The postovulatory increase in energy expenditure was not correlated to percent of body fat nor to age. The increased level of progesterone secreted by the corpus luteum phase in each of the ten subjects, confirmed by the higher levels of its metabolic product, urinary pregnanediol, was the likely cause of the elevated 24-hour expenditure reported since natural progesterone acts as a general metabolic stimulant (Landau, 1974), especially the elevated levels evidenced in pregnancy (Webb, 1986).

The nine percent higher energy expenditure that followed ovulation which was noted by Webb (1986) may be related to the observation by Dalvit (1981) that women consume 500 kcal/day more in the days following than in the days before ovulation. Webb also observed carbohydrate craving during the postovulatory phase of the menstrual cycle.

Webb concluded that the measurements indicated that there is a nine percent elevation in 24-hour energy expenditure in the postovulatory (luteal) phase of the menstrual cycle presumably caused by the increased secretion of progesterone.
It has been well documented that there is a marked decline in plasma estrogen levels following ovariectomy in premenopausal women. Less frequently acknowledged is the significant decrease in plasma testosterone levels that occurred subsequent to the removal of both ovaries in this same population (Sherwin and Gelfand, 1985). A decrease in plasma testosterone levels negatively affected extraglandular estrogen formation because the aromatization of testosterone to estrogen became significantly inhibited. The overall effect of ovariectomy, therefore, was a significant decrease in the biosynthesis of estrogen.

With the removal of the uterus (hysterectomy) there was no accompanying loss of estrogen since the ovaries were retained. A study by Coppen and Bishop (1981) assessed 60 hysterectomy patients before and after surgery and concluded there was no significant change in body weight during the three year time period of the study. They suggested that this finding was not surprising in view of the fact that estrogen levels were maintained at pre-surgery levels following hysterectomy (under normal conditions). Standeven et al. (1986) observed that postmenopausal women who discontinued estrogen usage were heavier than their postmenopausal counterparts who continued estrogen usage. The researchers suggested that extragonadal estrogen production by fat cells reduced the frequency of menopausal symptoms.

The only study (Sherwin and Gelfand, 1985) found which was appropriate to the understanding of hormonal influences following ovariectomy was disappointing because symptom assessments including weight gain were grouped collectively. Measurements of menopausal somatic symptoms (inclusive of weight gain among other indices) within Sherwin and
Gelfand's study groups (estrogen, androgen, and estrogen-androgen treated) showed that all steroid-treated groups experienced a significant increase in scores during the placebo month compared to the treatment phase scores. This finding could be interpreted to mean that estrogen treatment acts to reduce menopausal symptoms such as weight gain. The authors of the study stated "further research in this area ought to focus on the response of individual symptoms to the administration of each of the sex steroids."

It appears that many of the human studies indicate a similar cyclic pattern of food intake as found in animal studies and that the hormones estrogen and progesterone and their characteristic secretory cycle may dictate patterns of eating behavior and energy expenditure. A disturbance in the normal secretory cycle, as found in ovariohysterectomy, would likely disturb natural patterns of energy balance and eating behavior. Thus, the purpose of this study is to determine if weight changes occur in women as a result of surgical menopause and if exercise and food intake behavior impacts upon those changes.
CHAPTER III
METHODOLOGY
Research Design

The basic experimental research model utilized for this study was a three (groups) by three (time periods) repeated measures design (Joseph and Joseph, 1979) depicted below.

<table>
<thead>
<tr>
<th>Treatment Groups</th>
<th>Weight Measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 Months Pre-surgery</td>
</tr>
<tr>
<td>A. Hysterectomy</td>
<td></td>
</tr>
<tr>
<td>B. Ovariohysterectomy without hormonal treatment</td>
<td></td>
</tr>
<tr>
<td>C. Ovariohysterectomy with estrogen alone</td>
<td></td>
</tr>
</tbody>
</table>

Weight, the dependent variable, was measured approximately two weeks prior to surgery (zero months), at three months post surgery, and six months post-surgery. Activity level and caloric intake, the independent variables, were also measured at these time intervals. The duration of the study was six months in an effort to allow adequate time for observations of dietary intake as well as weight and activity level changes.

In an effort to provide some baseline data with larger numbers of subjects, retrospective data were extracted from the medical records of subjects having had similar treatment. The retrospective data were limited to weight measurements at zero, three and six months due to the

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unavailability of caloric intake and activity level data from past medical records.

Population Sample and Subjects

Patients of participating gynecologists were recruited over a six month period; those agreeing to participate were assigned to one of the three treatment groups according to their scheduled type of surgery and were followed for six months.

Subjects receiving a hysterectomy served as the control group. Subjects having an ovariohysterectomy were assigned to one of the two experimental treatment groups according to prescribed hormone treatment: one receiving estrogen and the other group receiving no hormone therapy. The hysterectomy group with ovaries intact provided a control for weight changes that might have been due to the surgical procedure itself. The ovariohysterectomy group without estrogen treatment additionally acted as a control by controlling for the effects of an altered hormonal status consequent to ovariohysterectomy. Comparisons between the three treatment groups could be drawn with an increased reliability with the inclusion of the aforementioned controls. Every attempt was made to eliminate confounding variables from this investigation; however, certain variables such as activity level and food intake were more difficult to control due to the reliance on subject activities, comments, and records.
Recruitment of Subjects

Recruitment of subjects was initiated following the research study's approval by The Investigative Review Board of Fairfax Hospital located in Falls Church, Virginia. Subjects were recruited primarily through a screening process performed by a gynecologist affiliated with The Fairfax Hospital who agreed to assist with the research project. One additional subject was recruited by the researcher who became aware of a potential subject meeting the necessary criteria and who expressed a desire to participate. Approximately 35 other physicians associated with The Fairfax Hospital were invited to participate but elected not to recruit subjects for the study. Additionally, letters of invitation were mailed to approximately ten gynecologists in Northern Virginia and Hagerstown, Maryland with no positive responses.

The criteria for selection of subjects included each of the following:

1. Age: 30-48. This age group was sought because a pre-menopausal population was desired. The average age of menopausal onset is 47 in the United States.
2. No definite plans to move outside of the greater Washington D.C. area within the year.
3. Ability to read and write at an eighth grade level or above, thus enabling participants to properly complete dietary and other necessary forms.
4. Surgery scheduled for reasons other than malignant disease since a healthy population was needed.
5. The exclusion of menopausal or post-menopausal women. This criteria was screened based on the incidence of menopausal symptoms as recorded on the personal data questionnaire (Appendix A). The hormone levels of women experiencing the menopause could bias the data since pre- and post-surgery differences would not differ appreciably.

6. Surgery had to be completed at least two weeks following recruitment in order to allow sufficient time for subjects to complete records for information needed.

The gynecologists' subjects who met the above criteria for selection (as judged by the physician and the investigator) and who expressed a desire to participate in the study were recruited. Problems or questions which arose concerning the selection of subjects were clarified by the doctor with the investigator by phone. The doctor mentioned the study to his patients who met the criteria for selection and if the patient appeared willing to participate, a post card (Appendix B) was completed and mailed promptly to the investigator. The potential subject was contacted by phone, the nature of the study and its requirements were explained, and the subject's verbal consent for participation was requested. Additionally, the confidentiality of all data and anonymity was discussed with each individual. Following the phone call, a packet of information was mailed to each consenting subject to complete previous to her scheduled surgery date. The contents of the information packet included: the patient consent form (Appendix C), a personal data questionnaire (Appendix A), a food frequency checklist (Appendix D), instructions for recording food intake (Appendix E), a
sample dietary intake form which served as a guide (Appendix F), and a set of three day dietary intake forms (Appendix G). Appendix D was patterned after forms commonly used by health departments. Appendixes E and G were adapted from similar forms developed by McLeroy (1971). When completed, the packet was mailed by the participant in a self-addressed, stamped envelope provided by the investigator.

After six months of recruitment efforts for subjects, with no cooperation from physicians or subjects except one clinic, the decision was made to continue with subjects from the one cooperating clinic, as they came available. Retrospective data on subjects, selected by utilizing past medical records of patients meeting the applicable criteria of the prospective group, were drawn from gynecological patients. Three of the six criteria were required for retrospective eligibility; other criteria such as geographic requirements, educational requirements, and surgery deadline were inappropriate. Weight data recorded at zero, three and six months, were obtained from patient medical charts of two doctors. The data were recorded by office personnel on a form supplied for this purpose. Dietary and activity level data were unavailable. Since the selection of retrospective subjects was made without the consent or knowledge of the subjects, code numbers were utilized to identify subjects. In some of the cases, three month weight measurements were unavailable. However, this did not affect the overall weight change since only the zero and six month weight measurements were used in the calculation.
Data Collection

Demographic and subjective data from the subjects were obtained by the use of personal data questionnaires (Appendixes A and H). The personal data were supplemented with those obtained from the three research study variables: body weight, caloric intake, and activity level. Information was sought on any variable that potentially impacted upon weight of the subject. Each subject in the study, both perspective and retrospective, was assigned a code number to maintain anonymity during data collection.

Body Weight Measurements

The first body weight measurement for each prospective subject was taken approximately two weeks prior to surgery at the gynecologist's office; each subject was weighed without shoes and in indoor clothing. It was imperative that the initial weight measurement occur prior to surgery to allow pre- and post-surgery weight comparisons to be made. A routinely calibrated physician's scale was utilized and a registered nurse performed the weighing and recording. The measurement was entered into the patient's medical chart and then onto a post card which was mailed to the investigator. Patients were notified at three and six months to make their post-surgery office visits in order to be weighed. The mailing of each set of the subjects dietary records coincided with the scheduled office visits. Office visits at the specified time intervals posed no major inconvenience to the patients or staff since pre- and post-surgery visits were normally scheduled by the gynecologist.
at these time intervals for his surgical patients. Near the completion of the study, weight measurements were obtained from subjects' medical records for the three and six month post-surgery time periods.

In order to obtain the pre-surgery, three month and six month post-surgery weight measurements on retrospective subjects, the patients must have had surgery at least six months previous to the day of data collection. Medical staff from two doctors' offices supplied this data (Appendix I) since the investigator was not granted access to past medical records.

Each subject's ideal body weight as well as their percentage of ideal body weight were determined by utilizing formulas from the nutrition division of Winchester Medical Center, Winchester, Virginia. Ideal body weight for the female subjects was calculated by using 119 pounds and sixty inches in height as baseline figures and adding three pounds for each additional inch over sixty inches. The percentage of ideal body weight was obtained by dividing the individual's actual weight by their ideal body weight and multiplying this quotient by 100.

Dietary Measures

The subjects were responsible for maintaining and completing three day dietary records on three different occasions at approximately two weeks prior to surgery (Set I), three months post-surgery (Set II), and six months post-surgery (Set III). Participants utilized the instructions for recording food intake (Appendix E) to properly record the necessary information onto the dietary intake form (Appendix G). The diet record included pertinent information such as time of day when food
or beverage was consumed, the name of that food or beverage, its method of preparation, description, size, and amount eaten or drunk. At the study's completion, a series of nine days of dietary records representing three time periods was obtained from each subject with the exception of one set of dietary records that were lost in the mail.

After receiving verbal consent of participation, the first set of dietary intake forms was mailed before surgery with instructions for recording food intake as well as a sample dietary intake form. In addition, a food frequency checklist was also completed. A self-addressed, stamped envelope was provided for the return of the completed three day dietary intake forms. The second and third sets of dietary forms were mailed and returned in the same manner as the first. Patients were encouraged to phone the investigator concerning any questions relevant to the study. Also, the subjects were contacted throughout the study to encourage their continuous participation, to answer any questions, provide moral support, and to resolve any questionable information sent to or received from them.

All foods and beverages recorded by each subject on the three sets of dietary intake forms were coded manually by the investigator. The computer nutrient software package RECALL (Virginia Cooperative Extension Service) was used to calculate the percentage of RDA for nine nutrients and kilocalories with caloric value being of main interest to this study. An average caloric value as well as average nutrient percentage values were calculated for each of the three sets of dietary records via computer. Data regarding the percentage distribution of total calories from fat, carbohydrate, and protein were also calculated.
These nutrient percentages were provided for the benefit of the subject and it was not the intention of this study to determine their impact upon the subject's nutritional status.

A computerized print-out depicting the nutritional summary of the three sets of food records was sent to each participant free of charge upon completion of the study. The offering of a free dietary analysis served a multiple purpose. Firstly, it was valuable as an enticement to participate and to complete the study. Secondly, the dietary analysis was useful because it offered the subjects some nutritional feedback information and thirdly, suggestions were made for improvement of diet at the subject's request.

**Activity Level**

Data pertaining to activity level during the six-month duration of the study were collected utilizing subject responses to questions about physical activity (Appendixes A, G, and H). Questions regarding activity level were included on the personal data questionnaire administered at zero months and on Set II (three-months post surgery), and Set III (six-months post surgery) of the dietary intake forms. The initial activity level (just prior to surgery) served as a reference point to compare with the activity levels at three- and six-months post-surgery. Consequently, each participant served as their own control. Each subject was assigned an activity level code of (0) for the pre-surgery activity level irregardless of her degree of activity.

Activity level codes were assigned for each subject at three-months and six-months post-surgery. The codes were designated as (+1) to
indicate the subject was more active during the three or six month post-surgery period than prior to surgery, (-1) to indicate less active, and (0) to indicate no change. The determination of the code number was based on both qualitative and quantitative information submitted by the participant about activity level.

The major criteria for assigning a code involved a series of steps. First, the responses submitted by the subjects were used to determine if the subject remained the same or was more or less active than prior to surgery. This was a subjective judgment by the participant. Secondly, the minutes of exercise per week as recorded by the subject at three months and six months post-surgery were compared with the minutes of exercise per week pre-surgery to insure the subjective judgement concerning overall activity level was substantiated. Thirdly, if a discrepancy existed, the subject was called for an explanation of the qualitative and quantitative information. Therefore, activity level codes were clarified and determined jointly. A code level difference was determined to be greater than sixty minutes difference between pre-surgery and post-surgery exercise levels as measured in minutes per week.

Pilot Study

A pilot study was conducted with five subjects who met the identical criteria of the subjects comprising the six month prospective research study. The purpose of the pilot study was to test and refine the methodology and procedure protocol for the subsequent study.
The pilot subjects were patients from the same doctor's office; he referred the subjects upon their qualification and willingness to participate in the pilot project. Each subject was visited personally, the general scope of the study and its requirements were explained, and a data packet which included a consent form with accompanying letter, a personal data questionnaire, a food frequency checklist, dietary intake instruction sheets, and one set of dietary intake forms were distributed. This packet of information was completed by each participant, returned by mail, and reviewed for inaccuracies resulting from ambiguous or inappropriate questions. Additionally, the three day food records were analyzed for caloric value and nutrient content utilizing the Practocare computer software package at The Fairfax Hospital. Dietary record information was limited to one three-day period for the pilot study.

Weight measurements were taken at the gynecologist's office of each participant approximately two weeks prior to surgery, recorded into the patient's medical chart, and phoned to the investigator. The caloric values obtained from the computer analysis of the subjects' dietary food records were recorded on a data collection form along with the weight measurements. The dietary analysis and computer print-out were discussed and presented to each subject at the conclusion of the pilot study.

There were two main differences between the pilot study and the research study. Firstly, the investigator did not visit each subject personally in the research study due to scheduling difficulties.
Secondly, since Practocare and RECALL are comparable computer programs, RECALL was selected for the research study due to convenience of access.

Results of the pilot study indicated a need to rephrase specific items on the personal data questionnaire for further clarification and to write the subject's name on each dietary form to facilitate identification in the event of separation of materials from subject's main folder. Furthermore, it was ascertained to print two copies of the computer dietary analysis instead of one to enable both the investigator and subject to maintain a copy.

Data Analyses

A two-way factorial analysis of variance was performed on the weight changes from zero to six months. One independent variable was treatment category which consisted of three levels: hysterectomy, ovariohysterectomy without estrogen treatment, and ovariohysterectomy with estrogen treatment. The other independent variable was type of study group which consisted of two levels: prospective and retrospective. The dependent variable was weight change. The 0.05 level of significance was adopted a priori.

The purpose of this analysis was to evaluate mean weight change differences across the treatment categories between the prospective and retrospective groups. A significant interaction between independent variables would mean that the prospective and retrospective groups differed within some treatment category but not with one another.

The mean weight changes among the study groups were obtained by subtracting the pre-surgery weight measurement from the six month
post-surgery weight measurement to obtain the overall weight change. The overall weight change values for each group were summed and this figure divided by the number of subjects in each group to arrive at a mean weight change for each group. The mean weight changes were calculated for the three weight measurement periods and plotted graphically for each combined group.

The three day dietary intakes for each recording period were averaged by the computer software package RECALL to provide a single caloric value for each time interval. The percentage of the RDA for nine nutrients was calculated for each of the three day dietary intake periods and the three sets of nutrient values were averaged together to arrive at an overall percentage of each RDA nutrient for each subject. The percentage breakdown of caloric intake into fat, protein, and carbohydrate was also calculated and the values were averaged in the same manner as the RDA percentages.

The zero month activity level and caloric intake values represent the pre-surgery data and the average of the three and six month activity levels and caloric intake values represent the post-surgery data. The pre-post surgery activity level and caloric level change for each subject was calculated by subtracting the average of the three and six month activity and caloric levels from the subject's pre-surgery values. The pre-post surgery activity level and caloric level change values for each prospective group were summed and this figure divided by the number of subjects in each group to arrive at a mean caloric and mean activity level change for each group. The zero, three, and six month values for
weight, activity level, and caloric level were used in analyzing differences at each of the time intervals for the prospective subjects.

Limitations

The most limiting factor of the study was the small sample size, particularly in the ovariohysterectomy group without estrogen treatment. Patients undergoing this type of surgery are seldom not prescribed hormone treatment, thus making recruitment efforts for this group very difficult. The unavailability of ovariohysterectomy patients receiving the hormonal treatment combination of progestesterone and estrogen prohibited the inclusion of this treatment group. The assisting gynecologist in this investigation did not prescribe this hormonal treatment; typically it is a treatment favored on the west coast of the United States (Ross et al., 1988).

Initially, criteria for selection of subjects in this study were to include women between the ages of 30 and 45 with both ovaries to be removed if undergoing a ovariohysterectomy. However, because the investigator accepted the limited number of patients as they became available for surgery, it was decided to broaden these criteria. One subject had only one ovary removed and almost a fourth of the participants were over 45 years of age.
CHAPTER IV

RESULTS AND DISCUSSION

The purpose of this investigation was to determine if estrogen (endogenous and/or exogenous) protects against weight gain in women as has been demonstrated in female animals. Endogenous estrogen levels are normally maintained in women undergoing hysterectomy (uterus removal) since the ovaries continue to secrete the hormone. However, the major source of estrogen ceases upon ovary removal, ovariohysterectomy, thereby often requiring an exogenous source in the typical form of estrogen replacement treatment.

Description of Subjects

A total of eight subjects participated in the prospective study. Two subjects comprised the hysterectomy group, one subject comprised the ovariohysterectomy group without hormone treatment, and five subjects comprised the ovariohysterectomy with estrogen treatment group. All data were received from the subjects except for the loss of one set of dietary intake forms in the mail. One subject verbally consented to participate in the study but was excluded when she failed to complete her consent form and dietary forms prior to surgery.

The eight Caucasian subjects ranged in age from 31 to 48 years with the mean age being 42. All participants were actively employed throughout the study; seven resided in a metropolitan area while one lived in a rural setting. This sample represented an upper middle class group with a mean annual income of $58,000. The majority of the subjects were
college graduates; the mean years of education was 15. During the course of the investigation, three fourths of the participants practiced some form of diet limitation, although they were requested to refrain from dieting. Upon entry into the study, five of the eight subjects were above 100% of their ideal body weight. Mean parity was two with a range of zero to four children per subject. Personal characteristics of subjects are depicted in Table 1.

Table 1. Personal characteristics of prospective subjects

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.0</td>
<td>31-48</td>
</tr>
<tr>
<td>Weight (pounds)</td>
<td>152.9</td>
<td>130-194.5</td>
</tr>
<tr>
<td>Parity</td>
<td>2.0</td>
<td>0-4</td>
</tr>
<tr>
<td>Yearly income (dollars)</td>
<td>58,000</td>
<td>40,000-70,000</td>
</tr>
<tr>
<td>Years of education</td>
<td>15.1</td>
<td>12-18+</td>
</tr>
</tbody>
</table>

In addition to the eight prospective participants, information was retrieved from medical records on 19 subjects in an effort to complement and determine verification of the limited data gathered from the prospective study. Twelve hysterectomy subjects, two ovariohysterectomy subjects without hormone treatment, and five ovariohysterectomy subjects with estrogen treatment comprised the retrospective study group. The individuals ranged in age from 33 to 48 years with the mean age being 41 years. Body weight measures only were provided since activity level and caloric level data were unavailable.

A comprehensive data summation chart including pertinent information gathered on each subject in this study is presented in Appendix I.
Group mean values for overall body weight, activity level, and caloric level changes are presented in Table 2.
### TABLE 2. Group mean values for body weight, activity level and caloric level changes

<table>
<thead>
<tr>
<th>Subject Groups</th>
<th>Mean Pre-Post Surgery Caloric Change (kcal)</th>
<th>Mean Pre-Post Surgery Activity Level Change (hr.)&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Mean Pre-Post Surgery Body Weight Change (lbs.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>-296.5</td>
<td>+0.75</td>
<td>-5.0</td>
</tr>
<tr>
<td>Group B</td>
<td>-307.0</td>
<td>+1.0</td>
<td>-1.0</td>
</tr>
<tr>
<td>Group C</td>
<td>-417.2</td>
<td>+0.1</td>
<td>-0.2</td>
</tr>
<tr>
<td>Group AA</td>
<td>-</td>
<td>-</td>
<td>-1.65</td>
</tr>
<tr>
<td>Group BB</td>
<td>-</td>
<td>-</td>
<td>+3.63</td>
</tr>
<tr>
<td>Group CC</td>
<td>-</td>
<td>-</td>
<td>+4.10</td>
</tr>
<tr>
<td>Group A + AA</td>
<td>-</td>
<td>-</td>
<td>-2.13</td>
</tr>
<tr>
<td>Group B + BB</td>
<td>-</td>
<td>-</td>
<td>+1.95</td>
</tr>
<tr>
<td>Group C + CC</td>
<td>-</td>
<td>-</td>
<td>+2.08</td>
</tr>
</tbody>
</table>

<sup>1</sup> Unit of 1.0 for activity level = approximately one hour

Propective Study Groups

- **A** = Hysterectomy
- **B** = Ovariohysterectomy without hormone treatment
- **C** = Ovariohysterectomy with estrogen treatment

Retrospective Study Groups

- **AA** = Hysterectomy
- **BB** = Ovariohysterectomy without hormone treatment
- **CC** = Ovariohysterectomy with estrogen treatment
Results

Table 2 indicates there were mean body weight losses of 5.0, 1.0, and 0.2 pounds for Groups A, B, and C respectively. Although Group A (the hysterectomy group) exhibited the greatest depression of weight of the prospective study groups, it experienced the least reduction in caloric intake with a decrease of 296.5 kcal pre- to post-surgery. The mean activity level was increased pre- to post-surgery by a factor of +0.75 or approximately 45 minutes per week.

Group B (ovariohysterectomy without estrogen) reduced the pre- to post-surgery mean caloric intake by 307.0 kcal which was approximately 10 fewer kilocalories than Group A, yet Group B lost one pound as opposed to the five pounds lost by Group A. Also activity level of the subject in Group B was increased by a factor of +1.0 or about a total of an hour per week over pre-surgery levels; this change represented an increase of about 15 minutes more per week than Group A.

Group C (ovariohysterectomy with estrogen treatment) had the smallest mean body weight change, -0.2 pound, but had the largest mean caloric decrease, -417.2 kcal, and the smallest mean activity level change, +0.1, which represented about 6 minutes per week increase over pre-surgery levels. When mean pre- to post-surgery values between groups were compared, Group C had a mean weight change of 0.8 pound less than Group B which corresponded to 110 fewer kilocalories and a decreased activity level of 0.9. There were no significant differences among or between the groups for weight, caloric, or activity level changes.

A graphic illustration of the group mean weight changes of the retrospective and prospective groups combined is presented in Figure 1.
Group A  N = 14  _____ Hysterectomy
Group B  N = 3  ----- Ovariohysterectomy without estrogen
Group C  N = 10  ..... Ovariohysterectomy with estrogen

Figure 1. Time series graph of group mean weight changes of prospective and retrospective subjects combined
The graph shows Group B experienced a greater weight loss at three months post-surgery than displayed by either Group A or Group C. Thereafter, weight gain was observed in Group B until at six months post-surgery, the level of weight gain was slightly below Group C. Overall, Group A displayed a steady weight loss; Group C showed a steady weight gain.

The depiction of mean weight changes of groups of subjects in Figure 2 shows a progression of weights whereby the hysterectomy groups (A, AA, and A+AA) lost the greatest amount of weight of the three treatment groups, with Groups B, BB, and B+BB losing somewhat less weight, (gaining in some instances) and Groups C, CC, and C+CC losing the least amount of weight (gaining in some instances). The analysis of variance yielded no significant F ratios (p 0.05) for mean weight changes between the treatment and study groups. The F ratio for the interaction between treatment category and prospective versus retrospective was only 0.01, indicating extreme parallelism across the treatment category cells for the prospective and retrospective groups.

Discussion

The greater activity level and lesser caloric reduction exhibited by Group B (Table 2) may have offset the lesser activity level and greater caloric reduction of Group C; this observation could explain the similar overall weight changes experienced by these two groups. Similarities between Group B and C appear to negate any effect of estrogen treatment in maintaining stable weight loss or providing protection against weight gain.
Mean body weight changes in pounds of prospective groups

A
(-5.0)
N=2

B
(-1.0)
N=1

C
(-0.2)
N=5

Mean body weight changes in pounds of retrospective groups

AA
(-1.65)
N=12

BB
(+3.63)
N=2

CC
(+4.1)
N=5

Mean body weight changes in pounds of prospective and retrospective groups combined

N=14

A
+AA
(-2.13)

N=3

B + BB
(+1.95)

N=10

C + CC
(+2.08)

Study Groups

A = Hysterectomy
B = Ovariohysterectomy without estrogen
C = Ovariohysterectomy with estrogen

Figure 2. Pyramidal depiction of mean weight changes of groups of subjects
Several suggestions could be proposed for the phenomenon observed in Figure 1, whereby Group B displayed a sharp decline in weight three months post-surgery. First, having only one subject could skew the mean weight of the group. Secondly, the shock of ovary removal without estrogen replacement possibly could signal a message to the satiety center of the brain and cause temporary anorexia. Thirdly, residual estrogen in the body could temporarily protect against weight gain.

The overall findings indicated by the graph whereby the hysterectomy group displayed the greatest degree of weight loss were expected and are in keeping with the theory of endogenous estrogen protecting against weight gain. This finding supports those of Wade (1972), Gentry et al. (1976), and Hervey and Hervey (1967), who observed that the action of estradiol produced by the body appears to stabilize body weight in rodents. The steady weight gain of the ovariohysterectomy group with estrogen was not expected. Subjects receiving an exogenous source of estrogen were expected to respond similarly to those with an endogenous source of estrogen. The weight gain may have been caused by a disruption in estrogen equilibrium or have been due to increased retention of fluid. Of course, in all of the cases, food intake and activity level may have played a role.

A trend was observed when examining each of the pyramids whereby the hysterectomy groups lost the greatest amount of weight of the three treatment groups. This suggests that the endogenous form of estrogen, present from the maintained ovaries, protected against weight gain. The exogenous form of estrogen, as received by the ovariohysterectomy groups with estrogen treatment, did not appear to protect the subjects against
weight gain to the same degree as the endogenous source as found in the hysterectomy groups.

It was interesting to note that the prospective group pyramidal progression of weight change was identical to the larger retrospective group. This may indicate that the small sample size was representative of a larger population. The difference between Group AA (hysterectomy) and Group CC (ovariohysterectomy with estrogen treatment) was more pronounced than the difference between Groups A and C. Since the retrospective group had no knowledge of being "scrutinized", their weight measures are probably more indicative of a normal population.

The exogenous source of estrogen in the form of estrogen treatment did not appear to have any influence upon weight gain suppression; especially since the overall weight changes experienced by the two ovariohysterectomy groups (with and without estrogen) were very similar. The endogenous source of estrogen (as found in the hysterectomy group with ovaries intact) seemed to protect against weight gain. The two-way analysis of variance failed to indicate any significant differences in mean weight changes between the groups. These results are similar to those of Thomas and colleagues (1986) who found no significant differences in weight gain between rodents with ovaries intact and estrogen replaced animals, or between these animals and ovariectomized animals not receiving estrogen treatment.

Perhaps a larger number of subjects followed for a longer period of time would have revealed significant differences between the study groups. Preliminary evidence presented herein emphasizes a need for further investigation in this area.
Introduction to Case Studies

Since individuals differ biologically as well as in their dietary and activity practices, it was decided that the group data would have further meaning if case study data were also presented. In this manner, individual changes occurring in the subjects could be emphasized. Appendix I may be consulted when data are mentioned in the presentation of the case studies.

CASE #1

Medical History

This subject was a 31 year old Caucasian female with a medical history of a right ovarian cyst, endometriosis, and spastic colon. Previous surgery was limited to a laparoscopy to explore the condition of the female sex organs. A hysterectomy was performed during the course of this study and qualified the patient for inclusion in the study. Previous to hysterectomy surgery, the patient was treated with Deproprovera to temporarily block the functioning of the ovaries. The medication brought on menopausal symptoms temporarily. No hormonal treatment was administered subsequent to surgery. The subject had two children aged four and six years.

Descriptive Information

Medical records indicated the subject's body weight was 135 pounds two weeks prior to surgery, which was 94% of her ideal body weight of 143 pounds; she measured five feet eight inches in height. At the conclusion of the six month study, the subject weighed 133 pounds,
resulting in a net loss of two pounds during the study. The patient noted that she had further reduced her weight by eight pounds in the three months subsequent to her completion of the study with a particular loss noted in the abdomen region. She stated that in years previous to hysterectomy surgery, her normal weight was $135 \pm 2$ pounds.

Dietary Assessment

Average daily caloric intake was increased by 401 kcal three months post-surgery and decreased by about 90 kcal six months post-surgery as compared to the pre-surgery caloric value. Although the subject stated that recording her dietary intake improved her food choices nutritionally, several nutrient inadequacies were observed. Nutrient levels determined to be less than 75% of the RDA's included: 63% of caloric intake, 61% of calcium, 53% of iron, and 34% of potassium. Nutrient values for protein, vitamin A, riboflavin, niacin, and vitamin C were determined to be adequate. The distribution of total kilocalories was 17% from protein, 41% from fat, and 42% from carbohydrate. The subject commented that post-surgery she became very depressed and that this triggered a total loss of appetite whereby she cut out food for as much as three days at a time until she slowly regained the ability to eat.

Activity Level

Activity level was increased from zero minutes pre-surgery to 60 minutes per week three month post-surgery, and was maintained at 60 minutes per week six months post-surgery. A Nordic Track exercise apparatus was utilized as the exclusive means of exercise. Subject specified prior to surgery that her health problems had prevented her
from exercising, however, her energy level was restored following her recovery period.

Discussion

The patient attributes her weight loss to decreased food consumption, more prudent selection of healthful foods, and an increased activity level. In view of the subject's data profile, this appears to be an accurate assessment regarding weight loss concomitant with increased activity. The caloric consumption indices indicate that weight loss would be expected since the subject consumed an average of only 63% of the recommended kilocalories during the course of the study. However, the post-surgery caloric intakes averaged 155 kcal above the presurgery caloric intake. The increased activity level may have negated the effect of increased kilocalories.
CASE #2

Medical History

The subject was a 48 year old Caucasian female with a past medical history of pneumonia, surgical ligation of varicose veins in her right leg, and tubal ligation. A hysterectomy was performed. The patient was using aspirin and Actofed as needed for allergies. A regimen of multivitamins was ingested daily. No hormone treatment was prescribed previous to or subsequent to hysterectomy surgery. The subject had three children aged 17, 20, and 22.

Descriptive Information

Medical records revealed the subject's body weight was 194.5 pounds two weeks prior to surgery; height was five feet four inches. Her ideal body weight and percentage of ideal body weight were calculated to be 131 pounds and 147% respectively. At the conclusion of the six month study, the subject weighed 186.5 pounds. Therefore, a net loss of eight pounds was realized following surgery. The subject stated that she was making a conscious effort to lose weight following surgery and that 194.5 pounds was her usual weight in recent years.

Dietary Assessment

Daily caloric intake decreased by 287 kcal at three months post-surgery and was reduced by 588 kcal at six months post-surgery as compared to the pre-surgery caloric value. The subject commented that by maintaining food records she actually consumed less junk food than normal. She successfully followed a self-imposed diet pre-surgery as well as post-surgery. Her nutrient intake analysis revealed no deficits
below 75% of the RDA. The distribution of total kilocalories was 13% from protein, 37% from fat, and 50% from carbohydrate.

**Activity Level**

Activity level was increased from 170 minutes per week pre-surgery to 390 minutes per week three months post-surgery and decreased to 160 minutes per week six months post-surgery. Walking was the primary mode of exercise. The subject stated inadequate time was the limiting factor accounting for the reduction in exercise time experienced at the six month post-surgery time period.

**Discussion**

The subject attributes her weight loss to two factors: increased activity level and decreased food consumption. The data substantiates these claims. Her dieting efforts proved successful since she decreased her pre- to post-surgery daily average caloric intake by 437 kcal and increased her pre- to post-surgery activity level by a factor of +0.5; ultimately leading to an overall body weight change of eight pounds at the conclusion of the study.
CASE #3

Medical History

This subject was a 31 year old Caucasian female with a medical history of severe endometriosis. The patient had undergone surgery to remove endometriosis on six occasions. An ovariohysterectomy was performed during the course of this study with the removal of both ovaries. Hormonal treatment was not prescribed. The subject had no children.

Descriptive Information

Medical records indicated the subject's body weight was 132 pounds two weeks prior to surgery and her height was five feet ten inches. Ideal body weight and percentage of ideal body weight were calculated to be 149 pounds and 88.6% respectively. Six months post-surgery, the subject weighed 131 pounds, resulting in a net loss of one pound. The subject stated that her normal body weight was 132 ± 2 pounds. The subject noted smaller breast size and decreased muscle tone in her abdomen region after surgery.

Dietary Assessment

Average daily caloric intake decreased by 219 kcal three months post-surgery and decreased by 395 kcal six months post-surgery as compared to the pre-surgery caloric level. The subject observed that she required more frequent, smaller meals during the six months following surgery than previous to this time period. She also commented that she could no longer skip a meal without feeling sick.
The nutrient intake analysis indicated that the subject's average calcium intake was 67% of the RDA and her average potassium intake was 65% of the RDA. The breakdown of kilocalories showed that the subject consumed 42% of her kilocalories in the form of fat, 17% in the form of protein, and 41% in the form of carbohydrate.

Activity Level

Activity level was increased from a baseline level of 105 minutes weekly to 180 minutes at both three months and six months post surgery. A variety of sports and activities were engaged in including walking, swimming, tennis, aerobics, water skiing and snow skiing. The subject stated she had previously been a very active person and despite lower energy levels following the ovariohysterectomy, she forced herself to maintain a high level of activity.

Discussion

The subject's individual profile indicates a pre- to post-surgery caloric decrease of 307 kcal and a pre- to post-surgery activity level increase of one. A depression of caloric intake to this degree with an increased activity level of at least 60 minutes weekly led to a reduction in weight of only one pound. Clearly another variable must account for this result. The loss of the patient's chief endogenous source of estrogen (manufactured by the ovaries) coupled with no hormone replacement may have had an impact, thereby causing weight maintenance to become a challenge.
Medical History

The subject was a 45 year old Caucasian female with a medical history of kidney stones. In 1987, lithrotripsy surgery was performed to remove the stones and later an ovariohysterectomy was performed. The patient received estrogen treatment (dosage level 0.625 mg) in the form of Premarin three months previous to surgery and during the six month period following surgery. Estrogen administered previous to surgery was intended to allow for an adjustment period to the medication. Subsequent to surgery, the patient took the diet pill Fasten as prescribed by her gynecologist. The subject has four children ages 20 to 26 years.

Descriptive Information

Medical records showed that the subject weighed 193 pounds prior to surgery and her height was five feet five inches. Her ideal body weight was determined to be 134 pounds. The subject was 144% of her ideal body weight; she stated that her normal weight was 193 ± 10 pounds. At the study's conclusion, the subject weighed 196 pounds. Thus, a net gain of three pounds was realized during the pre- to post-surgery period. No localized areas of fat accumulation were reported by the patient.

Dietary Assessment

Average daily caloric intake decreased by 149 kcal during the three months post-surgery and decreased by 633 kcal during the six months post-surgery as compared to the pre-surgery caloric level. The subject's overall nutrient analysis based on the RDA's indicated the following inadequacies: 63% of caloric intake, 61% of calcium, 53% of
iron, and 34% of potassium. The distribution of total kilocalories was 18% from protein, 40% from fat, and 42% from carbohydrate.

The subject noted that she craved sweets more frequently following surgery and she reported recurrent hunger pangs. Despite a regimen of diet pills and dieting throughout the duration of her participation in the study, the subject failed to achieve weight loss. Furthermore, the patient stated that she was rapidly gaining weight after the study's conclusion.

**Activity Level**

Prior to surgery, the patient did not engage in any form of exercise. At three and six months post-surgery, she increased her activity level by walking one and a half hours weekly. The subject felt noticeably more energetic during the six months following surgery than prior to this time period.

**Discussion**

The patient's efforts to reduce her weight were not realized for unknown reasons. Perhaps she did not follow the diet conscientiously, although the subject did not mention this as a reason for her lack of success with weight loss. The pre- to post-surgery caloric intake decreased 391 kcal and her pre- to post-surgery activity level increased by one; these data appear to contradict the weight increase of three pounds. The patient stated that if she had not been taking diet pills, consuming less food, and exerting herself physically, she would have gained considerably more weight.
A possible explanation for the weight gain could be that the prescribed exogenous source of estrogen (Premarin in this case) failed to exert the same physiological effect as the natural endogenous source (as found in hysterectomy subjects with ovaries intact). As previously mentioned, this subject had undergone an ovariohysterectomy with hormonal treatment.
Medical History

This subject was a 44 year old Caucasian female with a medical history of mitral valve prolapse. Prior surgeries included two caesarean sections. Before ovariohysterectomy with the removal of only one ovary, the patient was displaying some pre-menopausal symptoms. Premarin was prescribed for two years prior to surgery to relieve these symptoms. She continued to take Premarin (1.25 mg. daily dosage) and Motrin following surgery. The subject had two children aged 20 and 23 years.

Descriptive Information

The subject weighed 168 pounds two weeks prior to surgery and measured five feet seven inches in height. Her ideal body weight and percentage of ideal body weight were calculated to be 140 pounds and 120% respectively. At the conclusion of the six month study, the subject weighed 174 pounds. Thus, a net gain of six pounds was realized during the pre- to post-surgery period. The patient stated that her usual weight was 169 ± 5 pounds.

The patient followed the Weight Watcher's Diet during the final month of the study and lost eight and a half pounds. She observed that her body looked older and her waist was thicker pre- to post-surgery despite the weight loss. This indicated shifts in body deposits.
Dietary Assessment

The subject's average daily caloric intake increased by 60 kcal three months post-surgery and decreased by 336 kcal six months post-surgery as compared to the pre-surgery caloric value. Nutrient levels determined to be less than 75% of the RDA's were: 73% of kilocalories, 44% of iron, and 53% of potassium. The distribution of total kilocalories among the energy sources was 18% protein, 40% fat, and 42% carbohydrate.

The subject noted an increased appetite with a craving for sweets and snack items post-surgery. A desire to eat additional food for more energy was also expressed by the patient.

Activity Level

The subject commented that it was definitely harder to lose weight following surgery. She learned that she had to increase her activity level in conjunction with dieting in order to produce weight loss.

The activity level was maintained at 60 minutes per week at three months post-surgery and was increased to 120 minutes per week six months post-surgery. Walking was the subject's only form of exercise.

Discussion

The subject's profile for body weight, activity level, and caloric change during the pre- to post-surgery period is somewhat confusing. By reducing her average daily kilocalories by 138 and increasing activity level by one-half post-surgery, this individual actually displayed a weight gain of six pounds at the conclusion of the study; this final weight reflected an eight and a half pound weight loss during the last
30 days of the study. As with several other subjects in the ovariohysterectomy group, the caloric and activity level data usually did not correspond with the pre- to post-weight change.

The fact that this patient had only one ovary removed complicates the picture. The loss of one ovary may diminish the weight protective factor, especially to a greater extent in some individuals than others. Also her dietary records may not have been representative of her true eating habits while she was recording food intake. Another explanation may have been retention of water with a sudden decrease in weight that some individuals experience.
CASE #6

Medical History

A 48 year old Caucasian female with an unremarkable medical history, with the exception of having hypertension, experienced pre-menopausal symptoms prior to surgery. The patient had undergone ovariohysterectomy surgery with the removal of both ovaries. She received hormonal treatment in the form of Premarin and Amen (progesterone based formulation) eight years prior to surgery. The gynecologist prescribed this medication after the patient discontinued using oral contraceptives at age 40. Subsequent to the ovariohysterectomy, the physician doubled the dosage level of Premarin to 1.25 mg daily. Additional supplements and medications used by the patient included Dyazide, to alleviate fluid retention; Tenormin, to control blood pressure; and calcium tablets to protect against osteoporosis. The subject had one child aged 18 years.

Descriptive Information.

The subject weighed 130 pounds two weeks prior to surgery and was five feet four inches in height. Her ideal body weight and percentage of ideal body weight were calculated as 131 pounds and 99.2 respectively. At the conclusion of the study, the subject weighed 128.5 pounds. Thus, a net weight loss of one and a half pounds was realized during the period of the study. The subject generally maintained a weight of 130 ± 2 pounds. She observed no changes in skin elasticity or body shape following surgery.
**Dietary Assessment**

The average daily caloric intake decreased by 314 kcal three months post-surgery and decreased by 470 kcal six months post-surgery as compared to the pre-surgery caloric level. Compared to the recommended allowances, the subject's overall nutrient analysis indicated the following inadequacies: 69% of calcium, 61% of iron, and 64% of potassium. The distribution of total kilocalories was 13% from protein, 46% from fat, and 41% from carbohydrate.

The subject was allergic to eggs, milk, chicken, and corn products. She noticed that her food consumption decreased and was more nutritious since she began to record her intake.

**Activity Level**

The subject stated that she felt very energetic throughout the period following surgery and continued to swim a half mile six days per week. She reported no overall change in activity level from pre- to post-surgery. Swimming was reported as her only form of exercise.

**Discussion**

Considering that the subject reduced her pre- to post-surgery caloric intake by 392 kcal daily and maintained the same level of exercise post-surgery as prior to surgery, her net loss of one and a half pounds appeared low. A net reduction of 392 kcal daily with an unchanged activity level theoretically could lead to a loss of one pound every nine days based on nutrition findings that an energy deficit of 3500 kcal is necessary to induce a one pound weight loss (Krause and Mahan, 1984). Yet this patient reduced her daily average food intake by
392 kcal from six weeks to six months post-surgery and only lost a total of one and a half pounds. Clearly, other factors must be responsible. The subject's dietary records may have been inaccurate or not representative of her true intake, although she states her appetite was normal. She stated that she had to watch weight gain very closely. The possibility exists that the exogenous (Premarin) and the natural endogenous sources of estrogen differ in their functions related to weight.
CASE #7

Medical History

This subject was a 45 year old Caucasian female with a medical history of appendicitis. An appendectomy was performed in 1974. During the course of the study the patient underwent an ovariohysterectomy with the removal of both ovaries. No medications were routinely used with the exception of Estrace (dosage level of 2.0 mg daily) subsequent to surgery. The subject had four children ages 15, 17, 20, and 21 years.

Descriptive Information

The subject weighed 132 pounds two weeks prior to surgery and her height was five feet one inch. Her ideal body weight and percentage of ideal body weight were calculated to be 122 pounds and 108% respectively. At the six month conclusion of the study, the subject weighed 135 pounds. Therefore, she had a net gain of three pounds. The weight gain resulted although the subject lost four pounds during the course of the study by following a self-directed diet. She was compelled to diet during the study because she noted weight gain. The subject's weight normally fluctuates as much as 10 pounds annually. The patient observed a change in body shape in the post-surgery period with a rounder hip region specifically mentioned. The subject was the only individual in the study who smoked; she smoked an average of seven cigarettes daily.

Dietary Assessment

The average daily caloric intake was decreased by 492 kcal six months post-surgery as compared to the pre-surgery value. Unfortunately, the three month value was unavailable since the record was lost in
the mail. The subject's overall nutrient analysis based on the RDA's indicated the following inadequacies: 73% of calcium, 55% of iron, and 58% of potassium. The breakdown of caloric intake into fat, protein, and carbohydrate sources showed 20% of the diet was derived from protein, 53% from fat, and 27% from carbohydrate. The patient stated that although she sometimes felt as if she lacked her usual appetite, she still gained weight.

Activity Level

The subject stated qualitatively that her activity level was decreased at six months post-surgery as compared to pre-surgery. She reported a lower energy level subsequent to surgery. Prior to surgery she did not exercise regularly. Vague information was obtained as to the actual amount of time involved in exercise prior or subsequent to surgery. The three month activity level was unavailable because it was lost in the mail. A decrease by a factor of one during the pre- to post-surgery time period was confirmed with the patient as her overall activity level change during this period.

Discussion

The three pound weight gain from pre- to post-surgery was attributed to being less active. The degree of less activity was not obtainable due to conflicting information received from the patient. She stated that her appetite was below normal during certain periods post-surgically and that weight gain had always been a constant battle for her. The influence of cigarette smoking on the subject's metabolism is difficult
to assess; it should be noted that the fact that she did smoke cigarettes did not protect her from gaining weight.

To ascertain if the subject's overall status regarding caloric intake and activity level corresponds to her weight change is worthy of comment although analysis is particularly complex in this case. An average daily decrease in caloric intake of 492 kcal with a decreased level of exercise could conceivably result in weight gain after six months if the exercise level was markedly decreased, although it seems unlikely. The suppression of caloric intake did not represent the three month time period since that data was not available. It is possible that information supplied by this subject may not have been reliable. Therefore, influence of ovary removal may have been negligible, if any, in this case since the subject's activity level was reduced and her weight normally fluctuated ten pounds annually.
CASE #8

Medical History

The subject was a 46 year old Caucasian female with a medical history of migraine headaches. An ovariohysterectomy with the removal of both ovaries was performed and the gynecologist prescribed Premarin (dosage of 1.25 mg daily) prior to and subsequent to surgery. Other medications taken by the patient included Valium and Meprobamate for nerves and Amen. Progesterone use was discontinued after surgery. The subject had no children.

Descriptive Information

The subject weighed 138.5 pounds prior to surgery and measured five feet four inches in height. Her ideal body weight was determined to be 131 pounds and her percentage of ideal body weight was calculated as 105.7%.

At the conclusion of the six month study, the subject weighed 127 pounds; thus, an overall net loss of 11.5 pounds was attained. The subject stated that her weight normally fluctuated ten pounds annually. Under the doctor's supervision, she dieted and lost 13 pounds.

She started a diet of 1,000 kcal a day five weeks after surgery and seven weeks later she had reduced her weight to 125 pounds and maintained this weight plus or minus two pounds throughout the duration of the study. The subject noted that it was much easier to diet and to keep weight off post-surgery than pre-surgery.

Dietary Assessment

The average daily caloric intake was reduced by 704 kcal three months post-surgery and 642 kcal six months post-surgery as compared to
the pre-surgery caloric value. The subject's nutrient analysis showed
the following deficits below 75% of the RDA: 65% of kilocalories, 66%
of calcium, 57% of vitamin A, and 53% of potassium. The distribution of
total kilocalories was 17% from protein, 40% from fat, and 43% from
carbohydrate.

Activity Level

No overall activity level change was noted by the subject because
she continued her typical pre-surgery routine of walking two miles at
least five times a week for the duration of the study.

Discussion

The subject attributes her overall weight loss of 11.5 pounds to
reduced consumption of food. Her average daily caloric intake was
reduced by 673 kcal post-surgery and her activity level remained un-
changed. Irregardless of surgery, she could conceivably have lost one
pound every five to six days with her stable activity level. For the
five month duration of the study, the subject consumed 1,000 kcal daily,
which indicated that a potential loss of approximately 20 pounds could
have been attained during this time period. The patient did not attain
this degree of weight loss, although the patient stated it was actually
easier to lose weight in the period following surgery than previous to
it.
Results and Discussion of Case Studies

Both of the subjects in the hysterectomy group experienced weight loss and each followed a diet plan during the study. One subject lost two pounds pre- to post-surgery; the other decreased her weight by eight pounds. General comments reported by these group members included the following (number in parenthesis designates the tally of subjects in the group expressing the particular comments): lots of energy (1), loss of appetite (1), lost weight in stomach (1), body seems less fat overall (1), and recording of food intake made her eat more nutritiously (2). The comments pertain to the post-surgery time period.

Only one subject comprised the ovariohysterectomy without estrogen group. She did not diet during the study and lost one pound by increasing her activity level and decreasing her caloric intake. This participant observed that subsequent to surgery, she could no longer skip a meal without feeling ill (i.e., dizziness, headaches). She mentioned that she did not feel as energetic as prior to surgery; however, she stated that she forced herself to be active. The subject noted that her breasts were much smaller and her abdomen was rounder following surgery.

Four of the five members of the ovariohysterectomy with estrogen group followed a diet plan during the study. Three of the subjects gained weight and two lost weight during the study. An overview of the comments expressed by these participants concerning the pre- to post-surgery period included: craving for sweets (2), more energy (3), easier to lose weight (1), more difficult to lose weight (2), loss of appetite (1), thicker waist (1), and decreased abdominal muscle tone (1).
Overall, the three groups of participants were similar with respect to personal characteristics and medical history. Distinctions arose based upon the type of surgery the subjects received and by their individual comments.

The hysterectomy group of subjects appeared to be successful with their dieting efforts, felt more energetic, and noted less body fat overall and in the abdomen following surgery. These comments are not surprising because hysterectomy (uterus removal only) does not induce surgical menopause since the ovaries are retained. As expected, the endogenous source of estrogen appeared to have protected against weight gain in this group of subjects.

The ovariohysterectomy group exhibited symptoms indicative of the hypoglycemic reaction discussed by Morton et al., (1953) which may occur when estrogen levels are low. The subject's observation of being less energetic and noting smaller breast size with a rounder abdomen are signs of the surgical menopause, which would be expected in this subject since she lost her endogenous source of estrogen and did not receive an exogenous form (estrogen treatment). The subject in this group was expected to gain weight; however, she actually lost one pound which was probably due to decreased caloric intake and increased activity level. Thomas (1986) reported that ovary removal in the female rat was observed to cause weight gain due primarily to reduced activity level. If ovary removal has the same effect in humans, then the stable weight maintained by this subject could have been the result of physical activity.

Comments offered by subjects in the ovariohysterectomy group treated with estrogen included difficulty in losing weight, craving for
sweets, and desire for additional food. These observations reflect the symptoms documented by Gentry et al., (1976), Morton et al., (1953), Sherwin and Gelfand (1985), and Smith and Sauder (1969) that were indicative of low estrogen levels. The increased energy level noted by the majority of the subjects in this group was indicative of the restoration of energy that Wade (1972) observed in ovariectomized rats treated with estrogen. It appears that estrogen treatment produced inconclusive and conflicting results based on quantitative and qualitative data and the majority of comments expressed by this group of subjects. Further investigations over longer periods of time and with larger numbers of subjects are needed to determine the effect physiologically on weight maintenance.
CHAPTER V

SUMMARY AND CONCLUSIONS

Eight healthy females participated in this investigation to determine if estrogen (endogenous and/or exogenous) protects against weight gain in women as has been demonstrated in female animals. Additionally, weight data from the medical records of 19 retrospective subjects were included in the study to supplement that obtained from the prospective groups.

A three (groups) by three (time periods) repeated measures design was utilized as the basic experimental research model. Two subjects receiving a hysterectomy served as the control group. Six subjects having an ovariohysterectomy were assigned to one of the two experimental treatment groups according to prescribed hormone treatment; one group of five subjects received estrogen and the other group of one received no hormone therapy. The three variables, body weight, activity level, and caloric intake, were measured approximately two weeks prior to surgery, three months post-surgery, and six months post-surgery. Three day dietary records, food frequency checklists, activity and personal information forms were completed by the subjects.

Mean weight changes for the eight prospective subjects were calculated separately and combined with the retrospective data. No significant differences in mean weight changes between or among groups were found. However, a trend was observed in mean weight changes among the study groups. Specifically, the combined hysterectomy groups experienced the greatest degree of weight suppression by losing approximately two pounds; whereas the combined ovariohysterectomy groups with and
without estrogen treatment each experienced a weight gain of approximately two pounds.

Caloric intakes and exercise changes impacted on the weight changes but corresponding influences were obscured in some cases. Overall, it appeared that the ovariohysterectomy groups with and without estrogen treatment had to decrease caloric intake and increase activity level to a greater degree than the hysterectomy group to lose weight; weight loss appeared to be achieved with less effort by the hysterectomy subjects.

There were individual variations observed regarding food intake behavior and activity level in the prospective subjects. Information on individual subjects were presented as case studies. Many of the subjects practiced dietary limitations and most combined exercise programs with dieting for weight control. Several ovariohysterectomy subjects with estrogen treatment commented that weight control was difficult and that appetite changes were noted, especially the desire for sweets. This group also noted increased body fat, particularly in the abdomen region. The hysterectomy subjects observed less fat and more muscle tone in this area.

This study failed to indicate that the exogenous form of estrogen, which is normally prescribed to ovariohysterectomy patients, protected against weight gain as evidenced in animal studies. The results of this study revealed that the endogenous source of estrogen, as maintained in the ovaries of hysterectomy subjects, appeared to protect against weight gain in the sense that weight loss was achieved with greater ease considering activity level and caloric intake. This finding supports those of animal studies. Definitive results on weight changes in the
groups may not be truly representative due to the fact that three-fourths of these subjects were on diets during the course of the study.

Further research is needed using a larger number of subjects. Questions also remain concerning potential differences in younger versus older subjects as well as fatter versus thinner subjects, including a progesterone and estrogen treated group, and following the subjects for longer periods of time to enable longitudinal body weight differences to be assessed.
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APPENDIX A

PERSONAL DATA QUESTIONNAIRE
(Please Print)

Name ___________________________ Date ______________________

Street Address ____________________________________________

City ________________ State _______________ Zip Code ______

Home phone with area code ( ) __________________________

Business phone with area code ( ) _________________________

Where do you prefer to be contacted? Home _____ Work ________

When is the best time to contact you at this preferred number? ________

Do you have definite plans to move outside this geographic area within
the next six months? Yes ____ No _____

Birthdate _________ Weight ___________ Height ___________

Occupation ______________________________________________

Race (Please Circle): White Gross Yearly (Under $25,000)
Black Family Income ($25,000 - $40,000)
Hispanic (Circle) ($40,001 - $55,000)
Asian ($55,001 - $70,000)
Other (Over $70,000)

Highest grade completed in school: Grade School 1 2 3 4 5 6 7 8
(Circle the year denoted by no.) High School 9 10 11 12
College 13 14 15 16
Graduate School 17 18 18+

What is the name of your gynecologist? ______________________________________

Which type of surgery are you scheduled for: (Please check)

Hysterectomy (uterus removal) ______
Ovariohysterectomy (uterus plus ovaries removed) ______

Will you be receiving hormone treatment following surgery? Yes ____ No ____
APPENDIX A (cont.)

If yes, what specific hormone(s) will you be receiving? ____________

Do you experience any of the following on a regular basis? (check those that apply)

Irregular menstrual periods ___ Hot flashes ___ Dizziness ___
Stress ___ Inability to sleep at night ___

Have you previously undergone any type of surgery upon your uterus or ovaries? (check)

Yes ___ No ___ If yes, what was the reason for surgery and which organ was affected? _______________________________________

Briefly describe your disease history with emphasis on major illnesses:

_________________________________________________________________________

_________________________________________________________________________

What medication(s) are you currently taking and for what reason? ______

_________________________________________________________________________

Number of natural children and their ages: # ___ Ages ____________

Have you ever experienced a miscarriage? Yes ___ No ___ If yes, how many times? ____________

Do you do your own housekeeping? Yes ___ No ___

How many days per week do you normally exercise? ______________

How many minutes per day do you exercise? ______________

In which exercise(s) do you participate? Please circle all that apply.

walking  jogging  aerobics  swimming  other (specify) ______

Approximately how many calories do you normally consume daily? ______
APPENDIX B

POST CARD

(please print)

Patient's name _____________________________

Home phone with area code __________________

Work phone with area code ____________________

Gynecologist's name _________________________

Office phone with area code __________________

Surgery date ________________________________

Today's date _________________________________

Weight measurement taken today _______________
APPENDIX C

PATIENT CONSENT FORM

You have been selected to participate in a research project investigating the effects of hysterectomy (removal of the uterus) and ovariohysterectomy (removal of the uterus and ovaries) upon body weight. You are invited to be one of approximately twenty-five subjects chosen to take part in this research study because of your scheduled type of surgery. The information obtained from the data collected in this study will yield useful information for future women undergoing hysterectomy or ovariohysterectomy. This is a six-month study that is being conducted with the cooperation of The Fairfax Hospital and the Virginia Polytechnic Institute and State University.

If you decide to participate, you will be asked to meet with the investigator to discuss the study, fill out a personal data questionnaire form, correctly fill out dietary intake forms, activity level forms, and a food frequency checklist. You will be expected to complete and mail three-day dietary intake forms and activity level forms to me in a postage-paid envelope at the approximate time intervals: one week prior to surgery, three months post-surgery, and six months post-surgery. A computerized nutritional profile, based on your diet, shall be returned to you for your own reference. The completion of each set of activity level and dietary intake forms is estimated to take about one hour.

As part of normal post-operative procedure, appointments with your gynecologist are necessary at three months and six months following surgery. At that time your weight measurement will be taken. If
medication is prescribed by your gynecologist, it is most important that you carefully follow the prescription directions for correct usage and notify the doctor immediately if you intend to terminate usage of the drug. Possible risks associated with the administration of hormone treatment shall be discussed with you by your gynecologist and the important benefit of hormone treatment alleviating menopausal symptoms shall also be discussed. The only cost to you will be if you decide to call me or my advisor long distance. Alternate procedures are not appropriate for this experiment and the methods of data collection shall be carefully followed. No risks to anyone in the study are expected in the collection of data for this research project.

All information obtained about you shall remain strictly confidential and will be reported only as group data to the scientific community through journals and other related publications. Your participation is voluntary. You are free at anytime to withdraw from the project without prejudice. Please keep in mind, however, that the validity of this research study depends on your cooperation and conscientious participation. Conclusive results from the project are affected if subjects withdraw since this changes the design of the study and the number required for statistical analysis.

At the completion of this study, a summary of the results of the project will be forwarded to you at your request.

If you have any questions during the course of this study, please feel free to ask me. You may contact me anytime during the study or you
may call my faculty advisor.

Cynthia A. Held

( ) -
(Researcher)

Dr. Vera J. Wall
Wallace Hall
Virginia Tech
Blacksburg, VA 24061
(Advisor)

You are making a decision whether or not to participate in this research study. Your signature indicates that you have read the preceding information, have decided to participate, and will allow me to have access to your medical records in order to obtain necessary information for this study (i.e. age, weight, height, disease history) if necessary.

______________________________       ______________________________
Patient's signature                Date

______________________________       ______________________________
Investigator's signature           Date

Please mail me a summary of the results of the study.  
Yes ___  No ___

Please mail me a nutritional analysis of my dietary intakes at the completion of the study.  
Yes ___  No ___

I would like a free nutrition counseling session at the completion of this study.  
Yes ___  No ___
## APPENDIX D

### FOOD FREQUENCY CHECKLIST

Name __________________________

<table>
<thead>
<tr>
<th>Check The Frequency The Following Foods Are Consumed</th>
<th>Never (less than 1 time per week)</th>
<th>1-2 times per week</th>
<th>3-7 times per week</th>
<th>More than once a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dark green vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dark yellow vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other green vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Bread (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheat germ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cereal (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pasta (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other grain (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancakes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Citrus fruit or juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other fruits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tomatoes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dried fruits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Milk (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yogurt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Oil (type)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Margarine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salad dressing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacon and sausage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fried foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salt pork</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream, sweet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream, sour</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Beef, hamburger</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pork, ham</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunch meat</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Franks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 7. Candy

<table>
<thead>
<tr>
<th></th>
<th>Never (less than 1 time per week)</th>
<th>1-2 times per week</th>
<th>3-7 times per week</th>
<th>More than once a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pie, cake, cookies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato chips, pretzels, popcorn, etc.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Teas/sugar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coffee/sugar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soda pop</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kool-aid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard liquor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ice cream</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ice milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sherbert</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 8. Other foods not listed that you eat regularly

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APPENDIX E

INSTRUCTIONS FOR RECORDING FOOD INTAKE

1. Record food intake on two weekdays (Monday through Friday) and one weekend day. Please do not record on days you feel sick. At the end of each day on the dietary intake form, please check if appetite was usual or not in the space provided. Be sure to record everything you eat or drink and to be accurate.

2. Eat as you ordinarily would if no records were being kept. Please try and refrain from dieting because this does not represent a typical eating pattern and may cause confusion with dietary evaluation. If you must diet, please indicate so under remarks. Remember, I am making no judgments upon the nutritive content of your meals.

3. Helpful suggestions:

Type or kind of food — be as specific as possible.

If listing ingredients will help identify a specific dish (as casserole, salad, certain food combinations), please supply this information. If an unusual dish, tell me breakdown of ingredients because this is easier for me in analysis.

Additions to foods — in preparation or at the table.

Include sauces, catsup to meat, sugar, cream, butter to bread and potatoes, etc.

Method of preparation — especially for vegetables (boiled, fried, etc.); meat and fish (broiled, pot roast, baked, fried, etc.) and eggs (scrambled, hard-cooked, fried, etc.)

Don't forget to note additions, such as butter, fat, sauces, gravy, etc.

Brand names — help to identify foods, such as candy bars, (ex., Hershey Almond, etc.), salad dressings, diet margarines, dessert toppings, etc.

Amount of foods — are very important and must be recorded. Record as:

1. Cups or fractions of cups (vegetables, coffee, juice, etc.)
2. Number (fruit, vegetables, bacon, bread, etc.)
3. Ounces (meat, juices, beverages)

   cup (c) = measuring cup = 8 oz.
   ordinary drinking glass = 3/4 c. = 6 oz.
   tall glass (iced tea) = 1 1/4 c. = 10 oz.

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APPENDIX E (cont.)

juice glass = 4 oz.
coffee or tea cup = 5 oz.

4. Tablespoons (tbsp.) -- cream cheese, gravy, peanut butter, etc.
5. Teaspoon (tsp.) -- butter, sugar, jelly, etc. 1 pat butter = 1 level tsp.

4. Individual foods and food groups:

A. Fruit

1. State number and size, such as: apple 1 med. (medium)
applesauce 1/2 cup (which is 1 small sauce dish)
grapefruit 1/2 medium, etc.

2. Juice in ounces.
3. Other - state kind and size of serving.

B. Cereal

1. State amount as measuring cup or fraction of cup.

C. Milk and beverages

1. Give kind -- whether whole, skim, buttermilk, etc.
2. If you list cream, denote whether light, medium or heavy
3. Measures: 1 cup refers to 1 measuring cup (8 oz.)
   1 glass refers to ordinary drinking glass, or
   3/4 cup (6 oz.)
4. Be sure to include additions to coffee and tea, as:
   lemon, sugar, cream, etc. (specify amount also)
5. Include soft drinks, even diet sodas.

D. Meats

1. Give in ounces and/or approximate size. Record as cooked weight.
   1 small serving (sm serv) meat or fish = 1 oz
   1 average serving meat or fish = 3 oz
   1 large serving meat or fish = 4 oz

E. Vegetables

1. Record as fraction of cups or pieces.
   potato -- baked 1 medium
   potatoes -- mashed, 1/2 c (with butter and milk)
   peas -- green, canned (or fresh), drained 1/2 c
APPENDIX E (cont.)

celery — raw, 1 stalk
asparagus — cooked, 3 stalks
broccoli — cooked, 3 stalks or chopped, drained 1/2 c

2. Be sure to list all additions as butter, sour cream, etc.

F. Sugar

1. Record as level teaspoons. If a sugar substitute such as nutrasweet is used, specify name of product and amount used.

G. Desserts

1. Average serving -- 1/2 cup
2. Milk, sauces, etc. -- should be recorded and amount stated.
3. Pies -- give dimensions or size, as 1/6 of 9 inch pie.
4. Cake -- give size and name, as:
   Angel food, yellow (or white), with chocolate icing
   Small, medium, or large serving.

H. Between meal snacks

1. Be sure all of these are included: soft drinks, coffee, tea, ice cream, candy bars, potato chips, pretzels, etc.

I. Meals away from home

Put note in purse and jot down items after eating; transfer to food record at home. Ask waiter or hostess about particular foods or amounts you aren't sure of. When recording foods eaten at fast food restaurants, simply record name of restaurant, name of food item (i.e. Big Mac) and amount.
### APPENDIX F

**SAMPLE DIETARY INTAKE FORM GUIDE**

**SET I - DAY 1**

<table>
<thead>
<tr>
<th>Food and Beverage Description</th>
<th>Kind</th>
<th>How prepared, size, etc.</th>
<th>Amount Consumed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breakfast:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>English Muffin</td>
<td>Whole wheat.</td>
<td>1 whole (2 halves)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with butter.</td>
<td>1 tsp.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with grape preserves</td>
<td>1 tsp.</td>
<td></td>
</tr>
<tr>
<td>Cereal</td>
<td>Raisin Bran.</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td></td>
<td>with sugar</td>
<td>1 tsp.</td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td>2% - white</td>
<td>1 oz.</td>
<td></td>
</tr>
<tr>
<td>Coffee</td>
<td>Black.</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Morning snack:</td>
<td>Juice</td>
<td>Orange, frozen</td>
<td>1/2 cup</td>
</tr>
<tr>
<td>Donut</td>
<td>Glazed, 5&quot; round</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Lunch:</td>
<td>Hamburger</td>
<td>McDonald's (regular)</td>
<td>1</td>
</tr>
<tr>
<td>French fries</td>
<td>McDonald's (regular size)</td>
<td>1 bag</td>
<td></td>
</tr>
<tr>
<td>Diet Coke</td>
<td></td>
<td>8 oz.</td>
<td></td>
</tr>
<tr>
<td>Afternoon snack:</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Dinner:</td>
<td>Chicken</td>
<td>Baked, breast.</td>
<td>3 oz.</td>
</tr>
<tr>
<td></td>
<td>w/barbeque sauce</td>
<td>2 tbsp.</td>
<td></td>
</tr>
<tr>
<td>Rice</td>
<td>Brown, long grain.</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td></td>
<td>w/butter</td>
<td>1 tsp.</td>
<td></td>
</tr>
<tr>
<td>Green Beans</td>
<td>Fresh w/no seasoning</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td>2% - white</td>
<td>8 oz.</td>
<td></td>
</tr>
<tr>
<td>Night snack:</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

**Appetite:**
- Less than normal [ ]
- Normal [x]
- More than normal [ ]

**Remarks (i.e. if dieting, indicate so; include any useful information concerning changes in eating patterns you may have noticed)**

---

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APPENDIX G
DIETARY INTAKE FORM
SET II - DAY 3

Name ____________________________________________
Code Number (leave blank) ____________________________
Date ___________________ Day of Week ____________________

<table>
<thead>
<tr>
<th>Food and Beverage</th>
<th>Description</th>
<th>Kind</th>
<th>How prepared, size, etc.</th>
<th>Amount Consumed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morning snack:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunch:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Afternoon snack:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night snack:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Appetite: Less than normal ___ Normal ___ More than normal ___

Remarks (i.e. if dieting, indicate so; include any useful information concerning changes in eating patterns you may have noticed)

______________________________
APPENDIX G (cont.)

Have you noticed a change in your current activity level as compared with your activity level before having surgery?

Yes ___ No ___

If yes, are you more or less active?

More ___ Less ___

Currently, how many minutes are you exercising per week? ____________
APPENDIX H

SUPPLEMENTAL PERSONAL DATA QUESTIONNAIRE

Although some of the questions may seem repetitive of the first questionnaire, the answers are of significance to the investigator. The term "surgery" in this questionnaire refers to hysterectomy.

Please check the appropriate response unless otherwise indicated.

1. Surgery type: _____ hysterectomy (uterus removal only)
   _____ hysterectomy plus one ovary removed
   _____ hysterectomy plus both ovaries removed

2. Were you prescribed hormones following surgery? Yes ____ No ____
   If yes, specify type, dosage and time period: __________________________

3. Did you discontinue use of hormone therapy for more than seven days at any point during the course of this study (excluding the typical five day monthly disuse period)? Yes ____ No ____. ____
   If yes, specify length of time off, approximate dates, and reason for disuse: __________________________

4. If applicable, describe your hormone medication history prior to surgery: __________________________

5. Are you aware of having a metabolic disease? Yes ____ No ____
   If yes, specify type (ex. thyroid disease): __________________________

6. Do you smoke cigarettes now? Yes ____ No ____
   If yes, how many cigarettes do you smoke on a daily average? #____
   If no, how long has it been since you last smoked? _____ years
   _____ months
   When you were smoking, about how many cigarettes did you smoke daily? #____

7. Do you currently have any physical limitations or did you during the course of this study (excluding first two months following surgery)? Yes ____ No ____ If yes, please specify: __________________________
8. Have you observed any changes in your skin elasticity or body shape following surgery? Circle those that apply.

   arms  chest  back  hips  buttocks  thighs  feet
   no changes observed

Please describe the changes that took place, if any: ________________________________

9. Were your daily dietary selections influenced by having to record your food intake? Yes ___ No ___
   If yes, how? ________________________________

10. Were you on a diet during any phase of this study? Yes ___ No ___
    If yes, during which month(s) after surgery did you diet? ______
    State your reason for your diet and briefly explain your diet plan.

    ________________________________

   Did you lose weight? Yes ___ No ___
   If yes, how much weight did you lose? ______

11. Has your energy level changed since surgery? Yes ___ No ___
    If yes, how? ________________________________

12. Before surgery, by how many pounds did your weight normally fluctuate in a year's time? (Circle selection)

   0  1  2  3  4  5  6  7  8  9  10  11 or more

Comment if desired: ________________________________

13. Was your weight of ____ pounds just prior to surgery a typical weight for you? Yes ___ No ___
    If no, explain: ________________________________

14. Have you observed any obvious changes in your eating habits since your surgery? Yes ___ No ___ If yes, specify: ________________________________
APPENDIX H (cont.)

15. If you did experience weight gain during the six month time period following surgery, to what do you attribute this weight gain?
   ______ Less active
   ______ Consumed more food
   ______ Unexplained weight gain

16. If you experienced a weight loss during the six month period following surgery, to what do you attribute this weight loss?
   ______ More active
   ______ Consumed less food
   ______ Unexplained weight loss

   Please make any additional comments you think will be helpful.

_________________________________________________________________________

_________________________________________________________________________

_________________________________________________________________________

THANK YOU for your help and participation - it is greatly appreciated:

A summary of the study results as well as a computerized nutrient analysis of your completed dietary intake forms will be mailed to you upon evaluation completion.
<table>
<thead>
<tr>
<th>Subject Code</th>
<th>Age</th>
<th>% of Ideal Body Weight</th>
<th>(in lbs.) Weight Measurements</th>
<th>Overall Weight Change</th>
<th>(kcal/day) Caloric Intakes</th>
<th>(hrs./wk.) Activity Level</th>
<th>Pre-post Surgery Activity Level Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>31</td>
<td>94.4</td>
<td>123.5 136.5 133</td>
<td>-2.0</td>
<td>2190</td>
<td>1900</td>
<td>0</td>
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<tr>
<td>2A</td>
<td>40</td>
<td>147.3</td>
<td>149.5 135.5 136.5</td>
<td>-1.0</td>
<td>2190</td>
<td>1900</td>
<td>+4.5</td>
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<tr>
<td>3A</td>
<td>31</td>
<td>86.6</td>
<td>120.5 132.0 131.0</td>
<td>+3.0</td>
<td>2190</td>
<td>1900</td>
<td>+4.5</td>
</tr>
<tr>
<td>4A</td>
<td>40</td>
<td>138.5</td>
<td>193.5 196.5 190.5</td>
<td>+4.0</td>
<td>2190</td>
<td>1900</td>
<td>-2.0</td>
</tr>
<tr>
<td>5A</td>
<td>30</td>
<td>130.0</td>
<td>168.0 170.0 174.0</td>
<td>+5.0</td>
<td>2190</td>
<td>1900</td>
<td>-2.0</td>
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<tr>
<td>6A</td>
<td>40</td>
<td>117.5</td>
<td>130.0 131.75 126.5</td>
<td>+3.5</td>
<td>2190</td>
<td>1900</td>
<td>-2.0</td>
</tr>
<tr>
<td>7A</td>
<td>43</td>
<td>110.7</td>
<td>132.0 133.0 135.0</td>
<td>+2.0</td>
<td>2190</td>
<td>1900</td>
<td>-2.0</td>
</tr>
<tr>
<td>8A</td>
<td>46</td>
<td>125.7</td>
<td>138.5 126.5 127.0</td>
<td>-11.5</td>
<td>2190</td>
<td>1900</td>
<td>-2.0</td>
</tr>
</tbody>
</table>

Prospective Study Group:
A = Hysterectomy
B = Ovariohysterectomy without hormone treatment
C = Ovariohysterectomy with estradiol treatment

Retrospective Study Group:
AA = Hysterectomy
BB = Ovariohysterectomy without hormone treatment
CC = Ovariohysterectomy with estradiol treatment

* 3 + 6 mo. - 0 mos. - pre-post surgery hour

Unit of 1.0 for activity level - 1 hour

APPENDIX I

BODY WEIGHTS, CALORIC INTAKES, AND ACTIVITY LEVELS OF SUBJECTS
The vita has been removed from the scanned document