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THE EFFECTS OF TRAINING ON SELECTED STEROID HORMONES:
RESPONSE TO EXERCISE IN POSTMENOPAUSAL WOMEN

The Ohio State University

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THE EFFECTS OF TRAINING ON SELECTED
STEROID HORMONES: RESPONSE TO EXERCISE
IN POSTMENOPAUSAL WOMEN

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
The Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

by

Holly Jo Richardson-Lehnhard

The Ohio State University
1984

Reading Committee:
Dr. Robert L. Bartels
Dr. Timothy E. Kirby
Dr. Mary G. MacVicar

Approved by:

Robert L. Bartels
Department of Health, Physical Education, and Recreation
DEDICATION

To my husband and colleague, Robert Lehnhard. His unyielding support, relentless encouragement and endless patience have allowed me to grow and achieve in many aspects of my life.
ACKNOWLEDGEMENTS

My sincere appreciation is extended to my adviser, Dr. Robert L. Bartels, for sharing his wisdom, kindness and friendship over these years. I consider myself fortunate to have worked with such a fine individual.

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Special thanks to my subjects. Their time and dedication to this project made possible this study.

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VITA

March 7, 1955.................................................................Born Iowa City, Iowa

December 18, 1977..........................................................B.S., College of Liberal
Arts, University of Iowa, Iowa City, Iowa

June 1978 - July 1979..................................................Graduate Assistant,
University of Wisconsin-LaCrosse, LaCrosse, Wisconsin

December 20, 1979..........................................................M.S., University of
Wisconsin-LaCrosse, LaCrosse, Wisconsin

1980 - 1981.................................................................Coordinator of Adult
Fitness Methodist Hospital
Cardiac Rehabilitation, Houston, Texas

1981 - 1984.................................................................Teaching Associate and
Staff in Faculty Staff
Fitness/Outpatient Cardiac
Rehabilitation Programs,
The Ohio State University,
Columbus, Ohio

FIELDS OF STUDY

Major Field: Exercise Physiology
Studies in Exercise Science.
Professors Robert L. Bartels, Ph.D. and
Timothy E. Kirby, Ph.D.

Studies in General Physiology.
Professor James Grosse, Ph.D.

Studies in Cardiovascular Physiology.
Professor Robert L. Hamlin, D.V.M., Ph. D. and
William Muir, D.V.M., Ph.D.
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**Hypothalmus-Pituitary-Ovarian Axis**

**Steroid Biosynthesis**

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**Effects of Training on Maximal Oxygen Uptake**

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**Effect of Exercise and Training on Serum Concentration of DHEAS**

**Effect of Exercise and Training on Urinary levels of Adrenal 17-Ketosteroids**
CHAPTER I

INTRODUCTION

In the past 10 years there has been heightened awareness in women towards fitness-related activities. In addition to this concern over fitness, there is a concomitant increase in the number of women engaging in athletics. In 1978 only 78 women participated in the New York Leggs Mini Marathon, almost 60 times as many women ran the half marathon in 1983 with over 5,000 women competitors. As more women begin to exercise and train, there has been increasing concern over the effect of such activities on the health status of the participants and no area has come under investigation more than the gynecologic endocrine effects of training.

In up to 50% of premenopausal conditioned female athletes menstrual irregularities are noted. No conclusive evidence regarding change in ovarian hormones (estradiol, estrone) has been gathered. However acute exercise has been noted to increase adrenal androgen release and may in part contribute to changes in the hypothalamic-pituitary-ovarian axis.
With the graying of our society, larger number of older adults are also involved in fitness/conditioning programs. Exercise has been prescribed for everything from improvement in mental outlook to prevention of the climactic symptoms in postmenopausal women yet no data is available to examine the endocrine changes that might be playing a role in reduction of these symptoms. It is difficult to carry over data from the younger conditioned female to her older, postmenopausal, counterpart. In postmenopause the ovary becomes fibrotic and atrophic and 80-90% of the circulating estrogens reflect peripheral conversion of adrenal adrogens. It is thus the purpose of this study to evaluate the effect of acute exercise and chronic training program on hormonal profiles in postmenopausal women and relate these both to the possible mechanisms behind the alteration and the implication of such change.

Statement of the Problem

Much of the past research has evaluated the acute and chronic effects of exercise on hormonal concentrations of young premenopausal woman. However findings from studies on young women cannot be extrapolated to the older postmenopause woman. Both the production and biosynthesis of estrogens in the postmenopausal woman differ from the
premenopausal woman resulting in the different hormonal profile of the older woman.

The lack of research evaluating the effect of exercise on postmenopausal women, particularly in relation to hormonal profiles of the older woman, make this a unique population to investigate; therefore, it is important to determine what effect, if any, exercise and training has on the selected steroids in postmenopausal women.

**Purpose of the Study**

The purpose of this study was to determine 1) The effect chronic training has on plasma concentrations of the selected steroid hormones; estradiol, estrone, testosterone, and dehydroepiandrosterone sulfate (DHEA-S) and on 24 hour urine collections of adrenal hormones (17 ketosteroids). 2) The effect of acute exercise on the same parameters in trained and untrained postmenopause women. 3) Physiologic changes associated with training.

**Research Questions**

1. Does acute exercise have any effect on the plasma concentrations of estradiol and estrone in trained and untrained postmenopausal women?
2. Does acute exercise have any effect on the plasma concentrations of testosterone in trained and untrained postmenopausal women?

3. Does acute exercise have any effect on plasma concentrations of dehydroepiandrosterone sulfate (DHEA-S) in trained and untrained postmenopausal women?

4. Does acute exercise have any effect on urinary concentrations of 17-ketosteroids in trained and untrained postmenopausal women?

5. Does training result in baseline changes in the steroid hormones, estradiol, estrone, testosterone and DHEA-S?

**Research Hypotheses**

1. Acute exercise has no effect on plasma concentrations of estradiol and estrone in trained and untrained postmenopausal women.

2. Acute exercise has no effect on plasma concentrations of testosterone in trained and untrained postmenopausal women.

3. Acute exercise has no effect on plasma concentrations of DHEA-S in trained and untrained postmenopausal women.
4. Acute exercise has no effect on plasma concentrations of the 17-ketosteroids in trained and untrained postmenopausal women.

5. Training has no effect on the baseline concentration of estradiol, estrone, testosterone and DHEA-S.

Delimitations
1. Subjects were all volunteers, from the same geographical, socioeconomic area of Columbus, Ohio. Hence the subjects do not represent a random sample.

2. Subjects were all from one to 10 years postmenopausal, on no hormonal supplements and had both ovaries intact. Therefore, the sample does not represent postmenopausal population as a whole.

3. Subjects were less than 35% body fat.

Limitations
1. Error in volume measurements and gas analysis is inherent in determining VO$_2$ max. The extent of these errors can not be absolutely determined.
2. Although the specificity and sensitivity for the specific sex steroids is quite high there remains error in the determination of the hormones by radioimmunoassay. Intra and interassay coefficient of variation for the hormonal assays is 2.1 and 18.3%.

3. It was assumed that subjects collected all voids during the 24 hour collect times. Creatinine determination of the 24 hour collection will help to decide if the collection was adequate.

4. Changes associated with dirunal variation of hormone release will be controlled by collecting samples at the same time of day.

5. Based on the high estrone and DHEA-S concentrations obtained from the subjects in the present study, the women may reflect a perimenopause sample and may not in fact be true postmenopause as expected.

6. Additional exercise the subjects engaged in outside the eight week training program was not controlled for. This additional exercise may confound the data.
Definitions

1. Acute Exercise - Submaximal exercise consisting of 20 minutes of aerobic work at an intensity between 70-80% of an individual's maximal oxygen consumption ($V_O^2_{\text{max}}$).

2. Androgen - A C-19 compound known as a group of sex steroids. A substance that possesses masculinizing properties. Major androgens in the post menopausal women are androsterone, testosterone and DHEA-S.

3. Androstenedione - A C-19 androgen less potent than testosterone secreted by both the adrenal cortex and ovary. Called a "prohormone" since it is a precursor for estrone. Normal values for post menopausal women: 600 - 900 pg/ml.

structure of androstenedione:

4. Aromatization - A process by which a hydrogen atom is eliminated from an aromatic compound (43). It includes conversion of androstenedione to estrone and testosterone to estradiol.

5. Climacteric - A period of physiological failure of ovarian function during which there are endocrine, somatic and psychic changes.

structure of DHEA:


structure of estradiol-17:

9. Estrone (E1) - An oxidation product of estradiol. Circulating estrone is derived from peripheral metabolism of estradiol and androstenedione. In postmenopause, estrone is more potent than estradiol. Plasma concentration in postmenopausal women are approximately: 20-40 pg/ml.

structure of estrone:

10. Follicle Stimulation Hormone (FSH) - A gonadotropin hormone of the anterior pituitary. Stimulates growth of the ovarian follicle in the young female.

11. Gonadotropins - Follicle stimulating hormone and luteinizing hormone. Secreted by the anterior pituitary gland.

12. Luteinizing Hormone (LH) - Secreted by the anterior pituitary gland. Has its effects on the ovary, and is considered a gonadotropin. Acts with FSH to cause ovulation of mature follicles and secretion of estrogen.

13. Maximal Oxygen Uptake (\( \dot{V}O_2^{\text{max}} \)) - The maximal amount of oxygen an individual can consume. Expressed in liters/minute (l/min) or in milliliters/kilogram·minute\(^{-1}\) (ml/kg·min\(^{-1}\)).
14. Menopause - The final menstrual flow naturally occurring around the age of 50.

15. Osteoporosis - Abnormal loss of bone mass (unit bone per volume).

16. Perimenopause - The period beginning physiologic failure of ovarian function. Characterized by the increasing frequency of anovulatory cycles.

17. Postmenopause - The variable period of time from the last episode of menstrual bleeding. Usually occurs around 50 years of age.

18. Premenopause - Refers to the entire period from menarche to menopause.

19. 17-Ketosteroids - A specific group of adrenal steroids with a ketone at carbon number 17, the most abundant being androsterone and etiocholanolone. The oldest practical method for measuring adrenal steroids, employs the Zimmermann reaction for 17-KS (20). Testosterone, androstenedione, and DHEA are precursors of 17-KS.

20. Steroid Hormones - Includes sex hormones and adrenal cortical hormones. Compounds with a cyclopentenophenanthrene nucleus. Steroids consists of: 1) a cyclopentane ring:
2) A fused hydrogenated phenanthrene:


22. Testosterone - The principle androgenic male sex hormone. Also a C-19 compound. In peripheral tissue it is converted by aromatization to estradiol. Normal concentrations in postmenopausal women range from approximately 200 - 300 pg/ml.

Structure of testosterone:
CHAPTER II

REVIEW OF LITERATURE

With the public's increased interest in health and fitness which has transpired over the last few years, there has been a concomitant rise in the number of young and old women who engage in activities for health and fitness reasons. Not only is the number of women increasing in regards to fitness activities, the number of women engaged in training and competitive sports is also rising.

The position statement made by the American College of Sports Medicine concerning women and their participation in long distance running appeared to be an initial impetus from the scientific community for the promotion of women and distance running (4). The American College of Sports Medicine concerned itself with supportive information pertaining to participation of the female athlete in long distance running.

It is the opinion of The American College of Sports Medicine that females should not be denied the opportunity to
compete in long-distance running. There exists no conclusive scientific or medical evidence that long-distance running is contraindicated for the healthy trained female athlete (4).

Of particular concern was the high incidence of menstrual dysfunction in the active women. The incidence of menstrual irregularities has been reported to range from zero to 50% (8). The American College of Sports Medicine has reported that 33% of competitive female long-distance runners experience menstrual dysfunction for at least brief periods (4). The College did, however, note that there appeared to be no evidence to indicate that these dysfunctions are harmful to a woman's reproductive system. That this statement was limited to the training of females indicated the necessity for further investigations into gynecologic endocrine responses of exercise and training.

More women of all ages are pursuing numerous activities, including distance running, aerobic dance, power lifting and body building. With the promotion of women's fitness and participation in competitive sports, there has and continues to be interest addressing the gynecological considerations of the active female of all ages.

The natural aging process which produces changes
evident in the older female make postmenopausal women a unique group to study. As serum concentrations of estrogen decrease, the biosynthesis of estrogen is also altered, leading to certain endocrine, somatic and psychic changes. By studying changes in the hormonal profile related to the reproductive system the researcher can determine not only the hormonal responses which occur with training and exercise in the older women, but also gain insight into the possible mechanisms behind such responses. This review will cover the following topics: 1) General endocrine changes associated with postmenopause 2) Changes in related sex steroids of premenopause women associated with exercise and training. 3) Exercise and training in postmenopausal women.

**General Endocrine Changes Associated with The Menopause**

In order to understand the endocrine changes associated with the female reproductive system, it is important to outline the role of the hypothalamus-pituitary-ovarian axis. In the normal menstruating woman, the negative feedback, inhibitory effect of estrogen and progesterone on the hypothalamus, leads to the cyclical nature of both ovarian and pituitarian hormones. As the hypothalamus matures, it begins to secrete gonadotopin releasing hormone (GHRH)
which in turn stimulates the secretion of lutenizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary gland (16, 36). LH and FSH stimulate the growth and development of the ovarian follicle, and subsequent estrogen production. Combined with progesterone, the estrogen produced, through action on the hypothalamus and anterior pituitary, inhibits the production of LH and FSH, thus creating the cyclic rise and fall in these hormones (27) (See Figure 1).

Figure 1
Hypothalamus-Pituitary-Ovarian Axis
The climacteric is marked by the loss of the ovaries as a fully functional site of estrogen production. This physiological failure of the ovaries is attributed to the progressive loss of the ovarian follicles (52, 53, 54, 55) and results in diminished levels of estrogen in the body. The low estrogen level leads to a decreased inhibition of the hypothalamus-pituitary axis resulting in marked increases in LH and FSH (27). These higher levels of FSH and LH along with the diminished level of estrogen are two cardinal physiologic changes exhibited by the older women.

Besides decreased blood levels of estrogen, the functional loss of the ovaries causes a shift in the primary source of estrogen production to aromatization of adrenal androgens. This change in biosynthesis and metabolism of estrogens may be the most pronounced hormonal change in the menopause and postmenopause woman (53).

**Estrogens.** The principle function of the estrogens is to cause growth of sexual organs and other tissues needed in reproduction (27). Having effect on the fallopian tubes, uterus, and vagina, estrogens cause glandular tissue to proliferate, aiding in the development of the urogenital tract. Estrogens also play a role in increasing osteoblastic activity, aiding in skeletal growth (27).
With a decrease in estrogen levels, the older woman may experience the following symptoms: the urogenital tract (uterus, fallopian tubes, cervix, and vagina) may shrink in size and lose its muscle motility, the breasts may decrease in size and become increasingly flaccid and osteoporosis may occur (27). These latent symptoms contribute to the other more cognizant symptoms of hot flushes, irritability, and moodiness experienced by the menopausal and postmenopausal woman.

In the premenopausal woman most of the estradiol and estrone are from direct ovarian secretion with small contributions from extragonadal conversion. In the older woman the opposite appears to happen. Throughout the reproductive years the follicles of the ovary are progressively lost (62). With the climacteric, the ovum becomes smaller and fibrotic and begins to lose its physiological function. The endocrine changes (increase in LH and FSH and decrease in estrogen levels) and loss of ovarian structure (loss of follicles and theca interna cells) are reflected in the hormonal fluctuation of the estrogens and androgens. There appears to be an increase in plasma levels of androgens relative to the reduction in estrogen values (62). The amount of estrogen production, as well as the biosynthesis of estrogens, changes in the older
woman. The contribution of estradiol to total circulating estrogen becomes substantially reduced and no longer produces the associated cyclic changes. However, the concentration of estrone does not undergo such marked changes. The amount of production in estrogens varies widely with a mean decrease of around 90% for estradiol and about 70% for estrone (58). What estrogen remains appears to be produced from peripheral conversion of precursors.

Estrone, which is less estrogenic than estradiol accounts for the majority of estrogen produced during the menopause. Levels may range from 30 to 40 ug/ml in women 1-5 years in the postmenopause (58). With estrone being less potent than estradiol the estrogen target organs remain atrophic and quiescent. Estrone becomes the chief estrogen exceeding levels of estradiol.

The source of estrogen production has long been disputed by investigators. The adrenal cortex, ovarian stroma and extragonadal tissues were believed to be the major sources of estrogen production (24, 26, 28, 29, 32, 63). It is been determined that most estrone is consequence of a "prehormone mechanism" in which the adrenal gland secretes a "non-androgenic" precursor, androstendione, which is then converted by aromatization to estrone in extragondal tissue (58, 62).
With little direct glandular secretion of estrogen, the amount of estrogen produced depends on the available precursor and the extent of conversion. Adipose tissue has been identified as a site for extragondal aromatization, therefore, body weight may be a significant factor on steroid production (19, 40, 46). Longcope found that the subjects weight and menopausal status were major factors with regard to the amount of estrone and estradiol produced (40).

**Androgens.** Because of their role in acting as precursors for estrogen secretion, the levels of androgens are important. The androgens that appear to be significant for the synthesis of estrogen are the following: androstenedione, dehydroepiandrosterone, and testosterone. Androstenedione and DHEA are important precursors for estrone and are derived mainly from direct adrenal glandular secretion (10, 29, 32). In postmenopausal women, Vermulen noted that approximately 30% of androstenedione is contributed by the ovary and the rest by the adrenal gland (63). Older women have a decrease in circulating androstenedione levels of around 600 - 900 pg/ml compared with premenopause women with values of 1600 - 2000 pg/ml.
Conversion rates of androstenedione have been found to be as much as four fold after menopause (26).

Longcope recently investigated the importance of DHEA as a source of estrone in postmenopause women. He concluded that approximately 30 percent of the aromatization of DHEA to estrone occurred via the circulating blood pool of androstenedione. However, approximately 25% of estrone arose from the aromatization of DHEA to estrone in peripheral tissue without the immediacy of the blood pool of androstenedione (41). His data showed that in some postmenopausal women DHEA can be an important precursor to circulating estrogen.

Testosterone can be secreted by both the ovaries and to a lesser extent the adrenal gland (35, 63). About 50% of circulating testosterone can be attributed to the ovarian output (56). Peripheral conversion of androstenedione seems to account for a small part of the testosterone levels (58).

The following figure demonstrates the biosynthesis of estrone and estradiol from the presursors DHEA and androstendrone (see Figure 2).
Figure 2
STERIOD BIOSYNTHESIS

In summary, the major source of production for estrone in post menopausal women has been attributed to peripheral conversion of androstenedione with adipose tissue being a major site for aromatization. Estradiol production is mainly dependent on extraglandular formation from estrone, androstenedione and testosterone. There appears to be very little direct ovarian secretion of estradiol.

The following figure show sources of estrogen during reproductive and postmenopausal life (see Figure 3).
Figure 3

SOURCES OF ESTROGEN

OVARY

EXTRAGLANDULAR AROMATIZATION

ADRENAL

Androstenedione

secretion

Adipose

Estradiol

Estrone

Estradiol

Estrone

PREMENOPAUSE

POSTMENOPAUSAL

Based on the preceding discussion, it is evident that the endocrine system of the older women is different in many ways from her younger counterpart. Estradiol and estrone levels show considerable decrease whereas the androgens do not show such marked decrements. Altered metabolism of the estrogens parallel the decrease in circulating serum levels of the sex hormones.

Changes in Sex Steroids in the Premenopause Woman Associated with Training and Exercise.

In the mid 1970's the literature reporting research on the role of training and menstrual dysfunctions began to explore the etiology of such phenomena. Investigators began to study the gynecologic endocrine changes associated with exercise and training. A group of hormones that have been implicated in the development of menstrual irregularities are the sex steroids. Both androgens and estrogens are two groups of hormones that appear to undergo alterations with exercise and training in both pre and postmenopausal women.

Estrogen. The reports on exercise estrogen levels in reproductive age women, have in the past noted changes in both estradiol-17B and to a lesser extent, estrone.
Research yielded inconsistent findings. Investigators demonstrated increases (12, 33, 64), decrease (12) and no change (16), in plasma estrogen levels when looking at acute and chronic responses.

In a number of studies, acute exercise appeared to increase the levels of plasma estradiol (12, 33, 64) and remained somewhat elevated after the acute bout of exercise (64). Bonen noted that heavy exercise in untrained subjects increased estradiol concentrations, whereas no such increments were observed in trained subjects exercising at the same absolute work load (12). In a case study, Shandgold looked at chronic exercise and its effect on a runner's estradiol concentration, her data concurred with Bonen's, indicating slightly but not significantly higher estradiol levels (56). In another study, plasma estradiol was similar in runners immediately following a 10 mile run compared to samples collected between 12 and 24 hours after a run and with nonathletic females (9). In an in depth study, Dale noted estradiol concentrations were decreased in runners who were oligomenorrheic. In runners who were ovulatory, levels remained unchanged (17).

In addition to estradiol, estrone has also been addressed in the literature. The few reports which are available, show estrone levels associated with exercise may
remain unchanged with acute exercise in amenorrheic and eumenorrheic runners (42), or increase in regular menstruating women (60).

It has been speculated that changes in concentrations of ovarian hormones, estradiol and estrone associated with training may be influenced by peripheral conversions of androgens (17), to date, no data is available addressing the issue of aromatization in exercising women.

**Androgen.** Androgen concentration in the premenopause woman appear to be important in that they are a secondary source for estrogen synthesis (58). Until a few years ago exercise and its effect on androgens was limited to research pertaining to males and animal models. Early literature reported that the adrenal gland may adapt to adrenocorticotropic hormone (ACTH) with chronic exercise (61). Thus, including the hypothalamus-hypophysis-adrenal axis as a possible explanation for changes in androgens (61). Investigators are in disagreement as to the response of plasma androgen concentrations in young females.

A few investigators agree that adrenal androgens; testosterone, dehydroepiandrosterone and androstenedione increase after a submaximal aerobic work bout (9, 42). Hutchinson indicated that plasma concentrations of
androstenedione appear to be higher in anaerobically trained women than in aerobic trained women (30). In a recent study plasma testosterone increased linearly as a function of exercise in both trained and untrained women (34). In the same study, androstenedione and dehydroepiandrosterone increased in the trained but not in the untrained. Loucks noted increases in dehydroepiandrosterone with exercise but levels of testosterone remained unchanged prior to and on completion of acute exercise in amenorrheic runners (42).

For the premenopause woman there appears to be some adrenal and ovarian stimulation with exercise. However, because the lack of quantitative data and differences in research designs make it difficult to determine the extent to which levels change.

Exercise and Training in the Postmenopausal Woman

There exists little information about postmenopausal women in regards to exercise and training. The research which has been done on the older women has studied general cardiovascular responses to training and exercise (1, 7, 21, 51, 66). That the cardiovascular hemodynamic training responses of the older women appear to be similar to her younger counterpart, despite the decline in aerobic capacity with age are important considerations. However, there
exists a paucity of research addressing postmenopausal women and the gynecologic endocrine changes which may be associated with exercise and training.

Recent literature presents a school of thought which advocates exercise in postmenopausal women in an attempt to decrease the likelihood of developing musculoskeletal problems and associated symptoms of menopause. Osteoporosis is a major problem of postmenopausal women, and recent research has suggested that these women may very well benefit from physical activity by helping to prevent bone and muscle deterioration (6, 7, 25, 47).

There have been few studies which have investigated the changes in sex steroids of menopause or postmenopause women associated with exercise and training. One of the first investigations which addressed the issue of hormonal changes and exercise in the postmenopausal women was the work done by Wallace (64).

Estrone and estradiol levels were found to decrease in postmenopausal women (mean age 55 years old) after a low level of acute exercise (52% of VO$_2$ max) by five to four percent. Additionally, serum levels remained depressed for both steroids 30 minutes after the exercise.

In a later study initiated by Wallace, concentrations of testosterone were measured in addition to estradiol and
estrone during a training program (65). Estradiol increased significantly for the postmenopausal women even with a concomitant decrease in body fat. Paralleling this increment the E1/E2 profile of the postmenopausal woman changed to a "premenopausal" profile. Estrone levels decreased from 30 pg/ml to 25 pg/ml whereas estradiol levels significantly increased from 25 pg/ml to 75 pg/ml. The androgen profile prior to training was typical of the postmenopausal women but became typical of premenopause as the testosterone levels decreased with training. Androgen concentrations decreased from 450 pg/ml to 375 pg/ml in the older women compared to their younger counterparts with post training levels remaining stable for the premenopause women (380 pg/ml) (65).

The research completed by Wallace demonstrates the possibility of increasing estrogen levels (estradiol) and altering levels of androgens in postmenopause women with training. This investigation serves as an initial attempt to demonstrate the possible role exercise may have in altering the gynecologic endocrinology of the older women.

The design by Wallace can be improved upon. The conditioning program the subjects completed consisted of various activities; walk-jog, aerobic dance, swimming, aerobic games and weight lifting at 70% of maximal capacity
for a duration of 40 - 65 minutes for 6 weeks. The lack of one consistent type of exercise and the short conditioning program (6 weeks) may have confounded the results. In addition, the possible mechanisms for changes in the hormonal levels were inadequately addressed.

Possible clinical implications and mechanism behind such changes remain to be addressed in future investigations. The few aforementioned studies are evidence indicating the lack of research regarding exercise and the endocrine changes of the postmenopause woman.

Summary

From the previous pages, one can appreciate the complexity of the gynecologic endocrine system of the postmenopausal women. Differences in estrogen production and biosynthesis are for the most part responsible for the hormonal profile of the older woman as compared to her younger counterpart.

The fact that these women have different hormonal profiles and because there has been limited research concerning exercise and training in postmenopausal women, this subpopulation constitutes a unique group to investigate. Research concerning itself with the possible
hormonal changes associated with exercise and training in these women is warranted. Furthermore, mechanisms responsible for possible changes induced by exercise and training as well as implications associated with activity in the postmenopausal woman need to be addressed.
CHAPTER III

METHODS AND PROCEDURES

The purpose of this study was to determine what effect, if any, exercise and training has on selected steroid hormones in postmenopausal women. Subject participation involved a maximal graded exercise test, a 20 minute submaximal work bout, 8 weeks of aerobic training, a second maximal graded exercise test, and a second 20 minute submaximal work bout.

Subjects

The subjects were nine untrained, natural or surgically induced postmenopausal women with intact ovaries: no less than one year postmenopause and no greater than 10 years postmenopause. All subjects were free of any chronic disabling illness or prescribed medical regimen.
### Table 1
**Subjects Profile**

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<th>Subject</th>
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<th>Yrs Post Menopause</th>
<th>Height (in)</th>
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<tr>
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</tbody>
</table>

**Range**
- 50-115
- 62-134
- 21-35
- 87.2-109

**Mean**
- 54.4
- 5.4
- 64.6
- 134
- 28.1
- 95.9
- 38.1

**S.D.**
- 3.3
- 2.8
- 2.1
- 13.9
- 5.08
- 7.23
- 10.25

* (N) = natural (age) induced menopause  
(S) = surgically induced menopause

**Conditions of Testing**

All physiological measurements and blood drawing were conducted at The Ohio State University Laboratory of Exercise Physiology. Urine samples were collected by the subjects and returned to The Laboratory of Exercise Physiology. Blood samples were collected at the same time of day prior to and upon completion of the training regime. All hormonal assays were determined in laboratories associated with the Clinical Research Unit of The Ohio State University Hospitals and The Ohio State University College.
Research Design

The research was based on a one group pretest - posttest experimental design with repeated measures. Subjects served as their own controls. The hormonal concentrations served as dependent variables. The acute exercise bout and training regime were the independent variables.

Methods

Each subject completed two volitional maximal graded exercise tests on the treadmill. These tests served as a screening for participation in the study, and were also used to determine the women's appropriate exercise prescription. A 12-lead EKG and blood pressure were monitored prior to, during, and following this test. Oxygen consumption was determined during this test using open-circuit spirometry. Based on the results of the first maximal test each subject was placed on an eight week walk/jog training program, of appropriate intensity, following the guidelines set forth by The American College of Sports Medicine (3).
Prior to, and following completion of the eight week training program, each subject completed the following testing: 1) A pre-work bout 24 hour urine collection. 2) A 35 ml blood sample taken 20 minutes prior to work bout. 3) Performance of a 20 minute work bout on the treadmill at a setting which elicited a 70 percent maximal effort. 4) A 35 ml blood sample taken 5 minutes following work bout. 5) A post-work bout 24 hour urine collection. In addition to these aforementioned tests, body composition was assessed prior to and upon completion of training.

The blood and urine samples were appropriately processed and analyzed for the selected steroid hormones, in accordance with the Clinical Research Unit of The Ohio State University Hospital and the College of Medicine Obstetrics and Gynecology Laboratory, Division of Reproductive Biology.

Procedure

Informed Consent and Physicians Clearance. Before testing all subjects obtained clearance from their personal physician, indicating that they had no health problems and that a regular exercise program was not contraindicated for them. Prior to the initial testing all subjects read and signed an informed consent explaining procedures and
possible risks involved in testing, blood drawing and training. The subjects were reassured that all information was to be confidential.

**Maximal Exercise Test.** Prior to and upon completion of an eight week training program, all subjects completed a volitional maximal exercise test conducted in accordance with guidelines set forth by The American College of Sports Medicine and conducted under supervision by a physician (3). These maximal tests followed the standard Bruce protocol, utilizing a Quinton research treadmill (14). A Marquette-CASE (computerized assisted system for exercise) 12-lead electrocardiograph was used to monitor the subject's heart rate at rest, during submaximal workloads, during maximal effort, and during recovery. Blood pressure measurements were taken prior to, during, and following exercise by auscultation using a sphygmomanometer and stethoscope. Oxygen consumption was determined by open-circuit spirometry using the Erich Jaeger metabolic cart. Calibration of the gas analyzers and minute volume was done prior to each testing session.

**Exercise Prescription.** Exercise prescription was based on the results of the maximal tests, and followed the
guidelines set forth by The American College of Sports Medicine (2, 3). Each subject's prescription involved an exercise intensity which had the subject working at 70% of her maximal capacity and corresponding heart rate for 20 continuous minutes. The exercise prescription was incorporated into an eight week training program for the subjects, as well as being used to determine the work performed in the following tests.

**Submaximal Acute Exercise Bout.** Prior to and upon completion of training, each subject completed a single, submaximal work bout on the treadmill with the following urine and blood samples being taken. A 24 hour urine collection was made before performing the work bout. Beginning at 8 a.m. one day prior to the acute exercise all urine was collected, the collection was complete at 8 a.m. the following day after the first void. Twenty minutes prior to the work bout a 35 ml blood sample was drawn. A 20 minute work bout on the treadmill was then performed at a speed and grade prescribed to elicit a 70% maximal effort. Five minutes following the work bout a second 35 ml blood sample was drawn. A post exercise 24 hour urine collection was made following performance of the work bout.
**Body Composition.** Body composition was assessed prior to and following the training program. Using Lafayette skinfold calipers, sites of the tricep, suprailiac and right thigh were summed and fat percentages were calculated according to Pollock et al (49). Specific anatomical sites for the skinfolds were as follows: tricep; vertical fold on the posterior midline of upper arm halfway between the acromion and olecranon process, suprailiac; diagonal fold on crest of the ilium at the midaxillary line, thigh; vertical fold on the anterior aspect of the thigh midway between the hip and knee joint (47).

**Training.** Following the first submaximal test, the subjects were placed on an eight week walk/jog training program, involving a 20 minute exercise session three days per week: Monday, Wednesday, Thursday. Each exercise session was at an intensity that required 70 percent of maximum effort. The eight week training program was in accordance with the American College of Sport Medicine recommendations (2, 3).

**Blood and Urine Assays.** After separation of serum, hormonal concentrations of estrone, estradiol, testosterone and DHEA-S were determined by radioimmunoassay (RIA). Serum
for testosterone, estrone and estradiol were properly extracted with cold diethyl ether, and assayed following the procedures outlined by Powell and Stevens (50). DHEA-S was measured by RIA using a kit from Nuclear Medical Systems (45).

Urinary levels of the 24 hour 17-ketosteroids were determined following the procedures outlined in a kit manufactured by Biochemical/Diagnostic, Inc. (11). Steroid sulfates were first hydrolyzed, and estimated colorimetrically by the Zimmerman reaction (20).

Statistical Methods

The data for each of the plasma concentrations of the steroid hormones and the urinary levels of 17-ketosteroids were statistically treated with analysis of variance (ANOVA) and the Student-Newman-Keul test for multiple comparisons. The alpha level was set at $P < .05$. 
CHAPTER IV

RESULTS

The following results will be divided into two sections. The first set of results will address the pre and post training data obtained from the physiologic, psychologic and performance variables; \( \dot{V}O_2 \text{max}, \) body composition and duration of the maximal tests. The second part of the results will present data on blood serum levels of estrone, estradiol, testosterone and DHEA. In addition, data on the adrenal 17 Ketosteroids and 17 Hydroxysteroids will be presented.

Maximal Oxygen Uptake

Maximal oxygen uptake (\( \dot{V}O_2 \text{max} \)) when expressed in relative terms (ml/kg/min\(^{-1}\)) was significantly higher (\( P < .05 \)) after training (25.7±1.5 to 28.4±1.4). The overall improvement in \( \dot{V}O_2 \text{max} \) was 10.8 percent. When interpreting the absolute (l/min) maximal oxygen consumption data the same significant improvement was noted (1.5±1.1 to 1.72±.1) (see figure 4).

40
Figure 4
Effects of Training on Maximal Oxygen Uptake

\[ \dot{V}O_2^{\text{max}} \]
(ml/kg/min)

\( \dot{V}O_2^{\text{max}} \)
(l/min)

I = Untrained (pre 8 weeks training)
II = Trained (post 8 weeks training)

Brackets represent mean ± SEM

\( PR > T = 0.0019 \)

\( PR > T = 0.0078 \)

* Significant difference \( (P < .05) \)
Body Composition

There was no significant difference (P < .05) in percent body fat (28.6±1.5 vs 29.2±1.5 %) or lean body weight (95.2±2.3 vs 94.3±2.7 lbs.) after training. Fat weight (38.8±3.2 vs 39.4±3.1 lbs.) did not change significantly with training (see figure 5).

Time on Treadmill

Duration of the maximal tests was compared. There was a significant increase (P < .05) in exercise time (6.7±.5 to 7.4±3 min) following training (see figure 6).

Estradiol

Pre exercise levels of estradiol were significantly lower (P < .05) after eight weeks of training (25.0±1.70 to 20.3±1.5 pg/ml). Post exercise concentrations of estradiol showed similar significant (P .05) decrements (27.2±1.5 to 21.2±1.8 pg/ml) after training (see figure 7).

Estrone

In the untrained subjects pre exercise estrone levels were significantly higher (P < .05) than post exercise levels (120.5±16.0 to 89.3±6.0 pg/ml). After the eight week training program, pre exercise levels showed significant decreases (P < .05) when compared to the pre exercise untrained data (120.5±1.5 to 87.0±7.5 pg/ml) (see figure 8).
Figure 5
Effects of Training on
Body Composition

Brackets represent mean ± SEM
I = Untrained (pre 8 weeks training)
II = Trained (post 8 weeks training)
Figure 6
Effects of Training on Maximal Time on the Treadmill

Time on Treadmill (min)

I = Untrained (pre 8 weeks training)
II = Trained (post 8 weeks training)

(PR > T = 0.0387)

Brackets represent mean ± SEM

* Significant difference (P < .05)
Figure 7
Effect of Exercise and Training on Serum Concentration of Estradiol

Estradiol
(pg/ml)

Brackets represent mean ± SEM

I = Pre Exercise, Untrained
II = Post Exercise, Untrained
III = Pre Exercise, Trained
IV = Post Exercise, Trained

*III is significantly different (P < .05) from I and II.
** IV is significantly different (P < .05) from I and II.
Figure 8
Effect of Exercise and Training on Serum Concentration of Estrone

Brackets represent mean ± SEM

I = Pre Exercise, Untrained
II = Post Exercise, Untrained
III = Pre Exercise, Trained
IV = Post Exercise, Trained

*II is significantly different (P < .05) from I.
**III is significantly different (P < .05) from I.
**Testosterone**

Concentration of testosterone showed no significant changes \((P<.05)\) with exercise or training (see figure 9).

**DHEA**

Serum concentrations of DHEA showed no significant changes \((P<.05)\) with exercise or training (see figure 10).

**17-Ketosteroids**

The 24 hour urinary 17 Ketosteroids showed no significant changes with exercise before or after training \((7.3 \text{ vs } 7.2 \text{ mg/TV})\) and \((4.8 \text{ vs } 6.6 \text{ mg/TV})\) respectively \((P<.05)\) (see figure 11).
Figure 9

Effect of Exercise and Training on Serum Concentration of Testosterone

Brackets represent mean ± SEM

I = Pre Exercise, Untrained
II = Post Exercise, Untrained
III = Pre Exercise, Trained
IV = Post Exercise, Trained
Figure 10

Effect of Exercise and Training on Serum Concentration of DHEA-S

Brackets represent mean ± SEM

I = Pre Exercise, Untrained
II = Post Exercise, Untrained
III = Pre Exercise, Trained
IV = Post Exercise, Trained
Figure 11

Effect of Exercise and Training on 24 hour urine concentration of 17-ketosteroids

Brackets represent mean ± SEM

I = Pre Exercise, Untrained
II = Post Exercise, Untrained
III = Pre Exercise, Trained
IV = Post Exercise, Trained
The purpose of this study was to determine the effects of exercise and training on steroid hormones in postmenopausal women. The subjects served as their own controls entering the study in an "untrained" state. They were initially tested and then placed on an eight week training program. It was imperative to the present investigation that a training effect take place. This was demonstrated by significant increases in post training $\dot{V}O_{2}\text{max}$ (ml/kg·min$^{-1}$ and l/min) and maximal exercise duration (time on treadmill, min).

In the present study, serum estrone concentrations prior to training decreased significantly after an acute submaximal exercise. These data are in agreement with Wallace et al who demonstrated estrone levels dropping as much as 5% after acute exercise (52% $\dot{V}O_{2}\text{max}$) (64). The present study showed a mean decrease of 26% in estrone concentrations and may reflect the higher working intensity (70% $\dot{V}O_{2}\text{max}$). Resting estrone levels after training exhibited similar significant decreases (120 to 87 pg/ml) which concur with a later study by Wallace (37 to 25 pg/ml) (63). The higher estrone values obtained in the present study may indicate the subjects were perimenopause and not menopause as we expected.
There was a trend which showed an increase in estradiol levels after acute exercise in both the trained (20.3 to 21.2 pg/ml) and untrained (25 to 27.2 pg/ml) subjects, this however was not significant and was in contrast to a previous study which demonstrated a 4% decrease in estradiol levels (64).

Training resulted in significantly lower resting estradiol levels (25 to 20.3 pg/ml) and lower post acute exercise concentrations (27.2 to 21.2 pg/ml). A previous investigation showed significant increases in resting estradiol levels, our data contrasts these findings. (65).

The androgen profile for the subjects in the present study did not show any significant changes with exercise or training. DHEA-S concentrations appeared to decrease after training (1.42 to 1.19 mg/ml) and is in accordance with findings of Wallace which also demonstrated decreases in androgens (100% testosterone and 70% Dihydrotestosterone).

Testosterone levels after an acute exercise bout in trained and untrained subjects set a trend by increasing in both. Resting levels of testosterone after training showed very little change (.7 to .68 ng/ml).

Adrenal activity as measured by urinary 17-ketosteroids showed no significant increases or decreases with exercise or training. The 17-ketosteroids did however, decrease after training (7.33 to 4.78 mg/TV) (see figure 11).

It is difficult to compare our androgen data with findings of Wallace because the lack of specificity and breakdown of androgens in the previous author's study. Our data concerned itself with
testosterone and DHEA-S which appear to have different origins, testosterone produced by the ovary (50%) and adrenal gland, while the majority of DHEA is secreted from the adrenal gland (58). These origins are important when discussing the possible mechanism behind the changes which were exhibited in the present study.

In the postmenopausal woman, the main source of estradiol is its conversion from estrone. The increase, although nonsignificant, in estradiol concentration following acute exercise in the untrained subjects may, in part, be an explanation for the significant decrease in estrone concentration during the same period. Although not specifically measured in this study, the results indicate a possible increase in the conversion of estrone to estradiol during exercise in the untrained postmenopausal woman.

The significant decrease in basal levels of both estradiol and estrone following training present interesting findings. In a previous study a positive correlation has been shown between an individual's amount of body fat and estrogen production (40). With this in mind, along with the decreases in estrogens shown here, it would be reasonable to expect a concommittant decrease in the subjects' body fat. This did not occur. Mean percent body fat and mean absolute fat weight showed slight increases of 28.5 to 29.1 percent and 38.8 to 39.4 pounds respectively (see figure 5). Neither of these increases were significant. These results indicate that the decreases in estrogens shown with training are not due to any decrease in their conversion from
androgens in peripheral (fat) tissues.

A possible explanation of the demonstrated drop in estrogens with training is offered by the decreases also shown in testosterone and DHEA-S (see figure 9 and 10). Although not statistically significant, the amount of decrease exhibited by these androgens may have been sufficient to create the significant decreases in the estrogens for which they are precursors. If this is true, then focus must now be placed on the adrenal gland, the primary source of androgen production in the postmenopausal woman.

Adrenal activity and androgen production were determined in this study by measuring the 17-ketosteroids in the urine, DHEA-S concentration in the blood, and to a lesser extent testosterone concentration in the blood. The trend, in all three of these parameters was to show a decreased concentration following training. This indicates a possible reduction in activity of the adrenal gland with training. If adrenal activity is diminished as a result of training, it may be due to a change in the adrenal gland's stimulation by adrenocorticotropic hormone (ACTH).

ACTH is secreted by the pituitary gland and stimulates the adrenal cortex causing the secretion of cortisol and testosterone. It is also responsible for the maintenance of enzymes active in adrenal steroidogenesis (ie, 17-B estradiol dehydrogenase) (38). With an acute bout of exercise, cortisol, testosterone, and androstenedione levels increase in men (13, 18, 37, 59). The subjects in this study showed a
similar response (see figure 9). This increase in hormone production is thought to be due to an increase in adrenocortical stimulation caused by an increased level of ACTH which in turn is caused by acute exercise (61). In this present study DHEA-S, testosterone and urinary levels of 17-ketosteroids decreased after eight weeks of training. These reduced levels seen with training may be caused by a decrease in adrenocortical stimulation due to reduced secretion of ACTH by the pituitary gland, or by a reduced "sensitivity" of the adrenal cortex to ACTH. The reduction of ACTH secretion and/or the reduced "sensitivity" of the adrenal gland to stimulation by ACTH may be an adaptation of this system to the "chronic stress" of training (61).

Summary

The present study demonstrated significant decreases in basal concentrations of estrone and estradiol after eight weeks of training in postmenopausal women. These changes may possibly be explained by the concomitant decreases in basal levels of DHEA-S, testosterone and urinary 17-ketosteroids. The mechanisms behind such changes may be influenced by the hypothalamus-hypophysis-adrenal axis and the adaptation of this axis to the chronic stress of training. It is difficult to extrapolate the previous studies which address the adrenocortical response for exercise and training because such studies have used males and animals as subjects. In the postmenopausal woman,
the adrenal gland serves as a major source for androgens which in turn serve as precursors for estrogens. The importance of the hypothalamus-hypophysis-adrenal axis in the active postmenopausal woman remains unclear.
Previous literature addressing effects of exercise and training on the gynecologic endocrine response of older women has been limited, and in no respect conclusive. The hypothalamus-hypophysis-adrenal axis in the active postmenopausal woman appears to mediate the production of steroid hormones important to the gynecologic endocrinology of the individual. It was the purpose of this study to determine, what effects, if any, acute exercise and training have on selected steroid hormones.

Nine postmenopausal women ages 51-59 volunteered to participate in an eight week training program. Prior to and on completion of the training program all subjects were tested to determine their maximal oxygen consumption. An exercise prescription was developed to elicit effort 70% of the woman's maximal capacity. Corresponding heart rate was used as an indication of this level of work. This 70% level was used during training and as the level for the 20 minute exercise bout on the treadmill.

One day prior to and one day after the training regime, subjects were exercised on a treadmill for 20 minutes at a speed and grade eliciting a 70% effort. Blood was drawn prior to and upon completion of the exercise bouts. Urine was collected 24 hours before and after the exercise bouts. Serum concentrations of DHEA-S, testosterone, estrone and estradiol were determined by radioimmunoassay.
Urine levels of 17-ketosteroids were determined using the Zimmerman reaction.

The present study showed significant decreases in basal levels of estrone and estradiol after training. This study also demonstrated significant decreases in estrone concentrations after acute exercise in the untrained women. No significant changes in DHEA-S, testosterone or 17-ketosteroids were shown, however, there was a trend which showed means for all three, decreasing after training.

Possible explanations for these changes in estrogens and androgens with training may be associated with the hypothalamus-hypophysis-adrenal axis. It is postulated that the adrenal gland may adapt to the stress of training and become less sensitive to stimulation by ACTH. Reduction of ACTH secretion as a result of training may also play a role in a decreased adrenocortical response.

The present study was an attempt to determine the effect of exercise and training on selected steroids in postmenopausal women. The possible effects and mechanisms behind such changes remain unclear. Further research is needed to clarify the effects and clinical significance of such changes.
Conclusions

Within the limitations of this study, the following conclusions were derived:

1. Estrone concentrations significantly decrease after acute exercise in the untrained postmenopausal woman.

2. Basal concentrations of estrone and estradiol decrease significantly after an eight week aerobic training program in postmenopausal women.

3. DHEA-S and testosterone levels do not significantly change with acute exercise, prior to or upon completion of training.

4. Urinary levels of adrenal 17-ketosteroids do not change significantly with acute exercise prior to or upon completion of eight weeks of training.

5. The results of this investigation cannot be extrapolated to include all postmenopausal women.

Recommendations

Possibilities for further investigations are numerous and should include:

1. Determination of ACTH and cortisol levels with exercise and training in the older woman to demonstrate possible hypophysis-adrenal stimulation.
2. Repeated exercise and training studies involving larger number of women with different postmenopausal status, ie, those that have had one or both ovaries removed.
3. Bone mass and mineral determinations of postmenopausal women undergoing a training program.
4. Time serial determinations of steroid hormones during a training regime.
5. Attempts to determine the possible change in metabolism of the sex steroids during training. (ie the amount of conversion, secretion, production, and clearance rate).
6. It is recommended that future studies involving this age population use a less stringent protocol for maximal tests. Although increases in VO₂ were demonstrated, a smaller incremental stepwise protocol may better indicate such improvements.
APPENDIX
### Analysis of Variance for Estradiol

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<th>MS</th>
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*(P < .05)*

---

### Analysis of Variance for Estrone

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*(P < .05)*
### Analysis of Variance for Testosterone

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### Analysis of Variance for Dehydroepiandrosterone (DHEA)

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<td>8</td>
<td>2.40</td>
<td>35.74</td>
<td>0.0001</td>
</tr>
<tr>
<td>Treatment</td>
<td>0.36</td>
<td>3</td>
<td>0.12</td>
<td>1.77</td>
<td>0.1791</td>
</tr>
<tr>
<td>Error</td>
<td>1.61</td>
<td>24</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>21.20</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Analysis of Variance for 17-Ketosteroids

<table>
<thead>
<tr>
<th>Source</th>
<th>SS</th>
<th>df</th>
<th>MS</th>
<th>F-ratio</th>
<th>PR &gt; F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects</td>
<td>120</td>
<td>8</td>
<td>15.0</td>
<td>1.85</td>
<td>0.1163</td>
</tr>
<tr>
<td>Treatment</td>
<td>38</td>
<td>3</td>
<td>12.7</td>
<td>1.56</td>
<td>0.2260</td>
</tr>
<tr>
<td>Error</td>
<td>195</td>
<td>24</td>
<td>8.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>353</td>
<td>35</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
### Plasma Concentrations of Selected Sex Steroids

(ng/ml)

<table>
<thead>
<tr>
<th></th>
<th>Premenopause</th>
<th>Postmenopause</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estradiol</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Follicular</td>
<td>25-75</td>
<td>9-15</td>
</tr>
<tr>
<td>Late Follicular</td>
<td>200-600</td>
<td></td>
</tr>
<tr>
<td>Mid Luteal</td>
<td>100-300</td>
<td></td>
</tr>
<tr>
<td><strong>Estrone</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Follicular</td>
<td>25-50</td>
<td>20-40</td>
</tr>
<tr>
<td>Late Follicular</td>
<td>150-200</td>
<td></td>
</tr>
<tr>
<td>Mid Luteal</td>
<td>70-100</td>
<td></td>
</tr>
<tr>
<td><strong>Testosterone</strong></td>
<td>200-400</td>
<td>200-300</td>
</tr>
<tr>
<td><strong>Androstenedione</strong></td>
<td>1600-200</td>
<td>600-900</td>
</tr>
<tr>
<td><strong>Dehydroepiandrosterone (DHEA)</strong></td>
<td><strong>=4900</strong></td>
<td>* = 1500</td>
</tr>
</tbody>
</table>


GYNECOLOGIC HISTORY

1. AGE

2. ARE YOUR POSTMENOPAUSE? yes no
   A. NATURALLY INDUCED
   B. SURGICALLY INDUCED
      ____ TOTAL Hysterectomy (uterus & cervix removed)
      ____ SUBTOTAL Hysterectomy (uterus removed)

3. OVARIES IN TACT? yes no
   one
   both

4. HOW MANY YEARS HAVE YOU BEEN POSTMENOPAUSE (since last episode of menstrual bleeding, excluding spotting)

5. WERE YOUR EVER ON HORMONE MANAGEMENT? yes no
   if yes, what type of treatment was it
   how long has it been since last management

6. DO YOU EVER EXPERIENCE SPOTTING? yes no
   if yes, how frequent (ie - once a day, once a week)
is interested in participation in a doctorate research study, "The Effects of Exercise on Selected Steroid Hormones in Untrained and Trained Postmenopausal Women". The research procedures include a physician supervised symptom limited graded exercise test, assessment of body composition, and an eight week supervised training program. All testing policies and procedures follow the guidelines set forth by the American College of Sports Medicine and The Ohio State University Human Subjects Review Committee.

Please indicate the suitability of your patient to participate in this evaluation.

_____ I know of no reason why she may not be tested.

_____ I feel she may be evaluated but urge caution due to ____________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

_____ This patient's present history contraindicates fitness evaluation.

_____________________________   ____________
PHYSICIAN'S SIGNATURE           DATE

(type or print name)

(address)

(city, state, zip)
BIBLIOGRAPHY


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