Award Number: DAMD17-01-1-0360

TITLE: Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-I in Premenopausal Women

PRINCIPAL INVESTIGATOR: Nancy I. Williams, Sc.D.

CONTRACTING ORGANIZATION: The Pennsylvania State University University Park, Pennsylvania 16802-7000

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PREPARED FOR: U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012

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### Title and Subtitle
Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-I in Premenopausal Women

### Authors
Nancy I. Williams, Sc.D.

### Performing Organization
The Pennsylvania State University
University Park, PA 16802-7000
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### Performing Organization Report Number
Annual Summary (17 Sep 01 - 16 Sep 02)

### Funding Numbers
DAMD17-01-1-0360

### Abstract
This investigator has received a Career Development Award (DAMD17-01-1-0360) and an IDEA award (DAMD17-01-1-0361) to support her development as a breast cancer researcher, and to conduct a study to test whether a program of moderate aerobic exercise that is combined with a moderate level of dietary restriction will result in significant decreases in two biomarkers of breast cancer, circulating estrogens and IGF-I. The study will test whether a diet/exercise program will produce significant reductions in the peripheral production of estrone by adipose tissue through its impact on the reduction of fat mass. Lastly, validation studies for a novel method of assessing energy status will be performed. The annual summary for this study has been submitted with the IDEA award. The support Dr. Williams has received from the CDA award has allowed her release from 66% of her teaching responsibilities, provided support for travel to the Era of Hope meeting and supported a graduate student. These funds have therefore indirectly helped to support numerous research and training accomplishments that are listed in this report.

### Subject Terms
Breast cancer, menstrual cycle, IGF-1, estradiol, exercise
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Introduction

This proposal entitled "Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-I in premenopausal women" will provide important scientific contributions with respect to the primary prevention of breast cancer in women. Specifically, this study will examine potential mechanisms relating to the role of physical activity in the reduction of the risk of breast cancer by testing whether moderate aerobic exercise can reduce the levels of two hormonal biomarkers, circulating estrogens and insulin-like growth factor I (IGF-I). Since elevated levels of both of these hormones have been associated with an increased risk of breast cancer, and because exercise may modulate circulating levels, we wish to extend previous findings from epidemiological and cross-sectional studies by performing a tightly controlled, prospective clinical study that addresses previously unanswered questions related to the role of exercise in the modulation of estrogen and IGF-I. Although previous studies have shown that negative energy balance, and not other stressful aspects of physical exercise, can modulate reproductive function and therefore circulating estrogen levels, no studies to date have determined the magnitude of energy deficit required for these changes during long-term training, and no studies have attempted to differentiate between the exercise-induced changes in ovarian versus adipose sources of circulating estrogens. Since both estradiol (ovarian) and estrone (adipose tissue) are biologically active, and because the importance of estrone as a risk factor increases with age and adiposity, it is important to consider the degree to which exercise which creates a negative energy balance affects both of these sources of circulating estrogens. Circulating levels of IGF-I correlate with breast cancer risk, yet studies examining the responses of this hormone and its binding proteins to chronic exercise are lacking. Since IGF-I levels are very sensitive to nutritional status, previously reported stimulatory effects of exercise on IGF-I can be overridden if exercise is performed in the face of negative energy balance. In this regard, exercise that promotes weight loss can be viewed as a way to reduced levels of IGF-I, and therefore potentially reduce the risk of breast cancers. To date, no studies have addressed whether a program of moderate aerobic exercise and dietary restriction producing a negative energy balance that is carried out over a long duration will significantly alter IGF-I levels. Further the degree to which these levels might be altered in individuals of differing energy stores has not been addressed. Metabolic energy availability is an important contributing factor in the development of reproductive cancers. However, current methods for assessing energy availability, which include anthropometric measures, calculations of energy balance, evaluation of various serum and urinary biomarkers are prone to measurement error, not sensitive to alterations in energy availability, and are sometimes affected by disease states. The current project centers on the introduction of a novel approach to estimating energy status by measuring metabolic hormones in plasma: insulin, IGF-I, IGFBP-1 and leptin. Recently, dried blood spot (DBS) sample collection techniques have allowed for endocrine based population studies examining a wide variety of ecological factors that contribute to variation in human reproduction. In order to use the proposed method of energy status assessment in large population-based applications, such as those addressing the role of physical activity and or diet in the risk of breast cancer, the battery of metabolic hormones that comprise the proposed method must be amenable to collection and assays. Although the DBS technique has been partially validated for some hormonal assays, it has not yet been properly validated for insulin, IGF-I, IGFBP-1 and leptin, and it is unclear whether the technique is responsive to physiological changes of these compounds. Therefore, the current work calls for the validation of the DBS sampling technique for these assays under physiological conditions. The proposed studies will yield new and important information regarding the degree to which an exercise and diet program that results in an energy deficit will reduce the risk of breast cancer.

Body

Study Design: The study utilizes a prospective, randomized design that tests the effects of a moderate exercise program (4X/wk; 4 months) combined with moderate dietary restriction that results in an average daily energy deficit of -20%-30% kcals (Figure 1). Previously sedentary, eumenorrheic women aged 25-35 years will be assigned to exercise or control groups. Both normal weight (BMI 21-25 kg/m²) and overweight (BMI 26-30 kg/m²) will be assigned to either exercise or control (no exercise, no dietary restriction) groups; 4 groups, n=15
Subjects will be studied for a total of six menstrual cycles, i.e., 2 control followed by 4 cycles with training and dietary restriction.

**Recruiting/Screening**
- Beck Depression Inventory (BDI)
- Eating Disorder Inventory (EDI)
- Medical History
- Menstrual History
- Physical Activity
- Food Frequency Questionnaire

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<tr>
<th>Recruiting/Screening</th>
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<th>Control 2</th>
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**Figure 1. Study Design**

**Progress According to the Approved Statement of Work:**

**Note:** Human Subjects Approval obtained from DOD October, 2001

**Proposed Month 1**
1. Recruitment of subjects for year 1 of study (n=5 in each of 4 groups)
   a. Place ads in local newspapers, on tv, radio, announce study on email lists, post signs
   b. Train research staff to take phone interviews
2. Get organized
   a. Make up subject notebooks with instructions for all aspects of study
   b. Prepare individual subject files and labels and storage for urine collection devices
   c. Meet with GCRC staff and review study procedures

**Actual Month 1:** September, 2001

Recruitment was delayed due to delay in human subjects approval. We prepared ads, trained staff to take phone interviews, drew up data forms, made subject notebooks, prepared subject files, and met with GCRC nurses, physicians, and dietary staff to set up procedures.

**Proposed Month 2**
1. Ongoing recruitment
2. Begin subject information sessions
3. Begin subject screening/initial testing

**Actual Month 2:** October, 2001

The subjects were recruited from the local Centre County, PA area using multiple advertising methods. Newspaper ads ran for one week in the local newspaper. Additionally, advertising incorporated flyers and ads on a local rolling news station. As a result, approximately 55 phone and e-mail contacts were made. Four one-hour "Informational Sessions" were held for the subjects to learn more about the study.

**Proposed Month 3**
1. Ongoing recruitment/information sessions
2. Continue subject screening/initial testing

**Actual Month 3:** November, 2001
Due to limitations in laboratory personnel, recruiting and sign-up was delayed and a “second phase” of recruiting was planned. Contact was maintained with potential participants through phone and email.

**Proposed** Months 4-12
1. Continue recruitment efforts only if necessary
2. Continue subject screening/initial testing
3. Complete subject exercise training/experimental testing

**Actual** Month 4; December, 2001

Due to limitations in laboratory personnel, recruiting and sign-up was delayed and a “second phase” of recruiting was planned. Contact was maintained with potential participants through phone and email.

**Actual** Months 5-6; January and February, 2002

Second phase of recruitment began. We re-contacted our pool of initial contacts, and placed ads in the local newspaper again. We held two more information sessions, and then began study sign-ups. We signed up 20 individuals who were willing to complete the study during Year 1. We had difficulty signing up subjects who would serve as controls, i.e., subjects who would go through all the procedures in the study except receiving dietary counseling to have their food intake reduced and participating in the exercise sessions. Many individuals indicated upon phone screening that they would not participate if they weren’t going to lose weight and get in shape. Therefore, we decided to postpone the recruitment of control subjects until our Year 2 cohort. We plan to recruit subjects during Year 2 differently, so that can successfully sign-up women who will not exercise or have their calories reduced, and women who will participate in the diet and exercise groups. We will do this by increasing our recruitment efforts over a longer time period with more ads, and by placing ads that emphasize the other health benefits of the study besides exercise and caloric reduction.

**Actual** Months 7-11; March-July, 2002

We began exercise training and dietary counseling for several subjects in late February and March, after screening procedures had been completed, and documentation of normal menstrual cyclicity for two complete menstrual cycles with daily urine samples and corroborative testing for ovulation and adequate progesterone levels had occurred. The last woman completed exercise training and post-testing in July, 2002.

**Actual** Month 12, August, 2002

In August we began aliquotting urine samples from the subjects’ collections, preserving the urine samples, and measuring specific gravity. We also began data entry for initial survey and demographic data, daily training, weekly food exchanges, body weight, body composition, resting metabolic rate and diet and physical activity logs.

**Actual** Month 13, September, 2002

We continued aliquotting and processing urine samples and data entry.

**Actual** Month 14, October, 2002

We have completed data entry and are beginning preliminary data analysis. We began assaying urine for E1G and PDG, and are beginning to assay metabolic hormones, i.e., insulin, leptin, T3, and IGF-I. We are also preparing data reports for subjects that completed the study, and getting ready to recruit for Year 2.
Preliminary Results From Year 1:

Subjects: Our subjects were previously sedentary, eumenorrheic women (ovulatory menstrual cycles with circulating mid-luteal phase progesterone levels>5 ng/ml) 25-35 years old. They had the following characteristics: non-smoking; not using hormonal contraceptives for at least 6 months prior to the study; gynecological age greater than or equal to 13 years of age; no history of depression, disordered eating, or other affective disorders; no history of weight loss; no apparent disease; not aerobically trained (less than 1 hour a week of aerobic activity); weight stable (less than or equal to 2.5 pound change) in the last year; no medication incompatible with hormonal analyses, exercise or caloric restriction. Out of 30 subjects that signed informed consents, 20 subjects made it through the screening procedures and began the control phase of the study. The twenty women described their ethnicity as the following: 14 Caucasian, 3 Asian, 2 African-American and 1 Other.

Subject Attrition and Compliance: Nine women dropped out at various times during the study for the following reasons: 1 for menstrual abnormality, 5 medical (2 were exercise-related injuries), 3 self (time, intervention, etc.), and 2 for noncompliance. Compliance in the study was excellent, with women completing 3.9 out of 4 workouts per week, and over 85% of their scheduled visits (every other week) with the dietician. Subjects followed the diet as is evidenced by the significant weight loss achieved. Adherence to other testing procedures was excellent, and urine collections were completed with less than 3% of samples missing.

Table 1. Subject Characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yrs)</th>
<th>Weight (kg)</th>
<th>Height (kg)</th>
<th>BMI (kg/m²)</th>
<th>% Fat</th>
<th>VO₂ max (ml/kg/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low BMI</td>
<td>31 ± 3</td>
<td>63 ± 6</td>
<td>165 ± 6</td>
<td>23 ± 2</td>
<td>32 ± 4</td>
<td>33 ± 4</td>
</tr>
<tr>
<td>High BMI</td>
<td>32 ± 2</td>
<td>75 ± 8</td>
<td>165 ± 6</td>
<td>28 ± 2</td>
<td>39 ± 5</td>
<td>32 ± 6</td>
</tr>
</tbody>
</table>

Values are mean ± SD

Subjects met our initial targets for weight, age, BMI and fitness levels. Average menstrual cycle length was 29.7 ± 5 days, and did not change significantly in either Low or High BMI group. Aerobic exercise training was 4 times per week for four consecutive menstrual cycles at 77 ± 3 % of maximum heart rate for 40-60 minutes, resulting in an average of 22% increase in aerobic capacity as defined by VO₂ max (32.6 ± 4.7 to 40.0 ± 10 ml/kg/min; P < 0.05 pre vs post, Figure 2). Dietary intake was successfully reduced using the food exchange system (Low BMI = 1889 ± 354 to 1214 ± 239 kcals; High BMI = 2125 ± 287 to 1450 ± 264 kcals; P < 0.05 pre vs post in both groups). The combination of moderate exercise and diet produced significant weight loss in both groups (Low BMI -3.3 %; High BMI -7.6% P< 0.05, Figure 3). Significant changes in percent body fat occurred in both groups (Low BMI 32 ± 4 % to 25 ± 8 %; High BMI 39 ± 5 to 32 ± 6 %; P < 0.05, Figure 4).

Figure 2. Changes with exercise training in VO₂ max (ml/kg/min)
Preliminary Analysis of Urinary Steroid Metabolites

Figure 5 shows the profiles generated by our assays for E1G and PDG, urinary metabolites for estrogen and progesterone, respectively. We should complete these assays for our Year 1 subjects, in addition to those for metabolic hormones insulin, T3, leptin, IGF-I, and IGFBP-1 in the next two–three months.
Overall Results from Year 1:

We achieved excellent results from our dietary and exercise intervention. Our only anticipated changes for Year 2 include an expanded recruitment period, and a change in recruitment strategy to attract women who will agree to participate without the diet and exercise intervention. To do this we will structure the advertisements to highlight other aspects of the study from which subjects will benefit. These include diet counseling for non-weight loss purposes. We have developed several educational modules on nutrition topics of interest that do not advocate weight loss. Additionally, we will draw attention to the benefits of learning about one’s body composition, fitness level, and reproductive status.

KEY ACCOMPLISHMENTS

Summary of Year 1 of “Effects of moderate aerobic exercise combined with caloric restriction on circulating estrogens and IGF-I in premenopausal women”:

This study will test whether a program of moderate aerobic exercise that is combined with a moderate level of dietary restriction will result in significant decreases in two biomarkers of breast cancer, circulating estrogens and IGF-I. We will also test whether this type of diet/exercise program will produce significant reductions in the peripheral production of estrone by adipose tissue through its impact on the reduction of fat mass. Lastly, validation studies for a novel method of assessing energy status will be performed. To date we have completed our first year of the three year study protocol. Our cohort for Year 1 consisted of 20 women (25-35 yrs) divided into high (26-30 kg/m²) and low BMI (21-25 kg/m²) exercise groups. Aerobic exercise training was 4 times per week for four consecutive menstrual cycles at 77±3 % of maximum heart rate for 40-60 minutes, resulting in an average of 22% increase in aerobic capacity as defined by VO2 max (P < 0.05 pre vs post). Dietary intake was successfully reduced using the food exchange system (Low BMI = 1889 ± 354 to 1214 ± 239 kcals; High BMI = 2125 ± 287 to 1450 ± 264 kcals). The combination of moderate exercise and diet produced significant weight loss in both groups (Low BMI -X%; High BMI -X% P<0.05). Significant changes in body composition occurred in both groups (Low BMI 32 ±4 % to 25 ± 8 %; High BMI 39 ± 5 to 32 ± 6 %; P < 0.05). As expected, menstrual cycle length in these reproductively mature women did not change significantly with training and weight loss. We are currently conducting biochemical determinations of urinary estrone-3 glucuronide and pregnanediol-3 glucuronide, LH, and FSH, and serum IGF-I, Insulin, T3, Leptin, IGFbp-1, estrone and estradiol. Data reduction and analyses are being completed for dietary intake, energy expenditure, resting metabolic rate. We will begin recruiting for our Year 2 cohort in December, 2002.

Figure 5. Urinary steroid metabolites for an individual subject during a control cycle and then four menstrual cycles thereafter where caloric restriction and exercise training occurred.
REPORTABLE OUTCOMES

Presentations:
The following presentations have resulted from work in N. Williams’ laboratory, since funding from DOD. Note: Funding from DAMD17-01-1-0361 was used to directly support only presentation #5.


MANUSCRIPTS

The following manuscripts have been generated from Dr. Williams’ laboratory since DOD funding was awarded.

PUBLISHED MANUSCRIPTS


Whipple TJ, Petit Moira, Sharkey N, Demers L, Williams NI. Leptin and the skeleton. (Accepted, Clinical Endocrinology for publication, 2002)

MANUSCRIPTS IN REVIEW


Williams, NI, Flecker KL, McConnell. Weight and Diet Concerns in Female Athletes: Association with Menstrual Cycle Length (submitted to Int J Sports Nut Exerc Metab, September, 2002)


Williams, NI. Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies (Invited publication of symposium presented at American College of Sports Medicine Meeting, St. Louis, MO, May, 2002; for publication in Med Sci Sports Exerc)

ABSTRACTS/PRESENTATIONS

The following abstracts and presentations have been generated from Dr. Williams’ laboratory since DOD funding was awarded.


Senior MK, Williams NI, McConnell HJ, Clark KC. Screening for subclinical eating disorders in female athletes: validation of an indirect interview technique. (Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001).


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FUNDING APPLIED FOR

The following grant proposals have been generated from Dr. Williams' laboratory since DOD funding was awarded:

Penn State University
College of Health and Human Development
Interdisciplinary Seed Grant Program, 1999-2000; $6000

Co-Investigator: (PI Jay Hertel)
"Changes in risk factors of anterior cruciate ligament ruptures in female collegiate athletes across the menstrual cycle"
Pathology Initiation Grant
Hershey Medical Center, Dept. Pathology
January 2002-January 2003 5%
$15,170

Co-Investigator (PI is Williams' Doctoral student, Thomas Whipple, MS, PT)
"The Role of Resistance Exercise and Energy Availability on Bone Metabolism"
Children's Youth and Family Consortium
Penn State University, CHHD
January 2002-January 2003 5%
$13,925

Co-Principal Investigator (with Moira Petit, PhD (PSU-Hershey))
"Designing Intervention Programs to Optimize Bone Development: Application of Bone Markers to Monitor the Short-term Response to Exercise"
NIH
1 RO1 HD39245-01 (Williams) 5/1/01 - 4/30/04 30%
PHS/NICHD
$1,538,361

Principal Investigator:
"Bioenergetics of Exercise-induced Menstrual Disturbances"
Goal is to test to determine the mechanism whereby low energy availability modulates reproductive function in exercising women
Pending Support
National Institutes of Health (NIH)
1 RO1 (PI is Hartman, Terryl J.) 7/01/02 - 6/30/07 15%
PHS/NICHD
$811,610

Co-Investigator:
"Nutrition, Fertility and Oxidative Stress"
National Institutes of Health (NIH)
HD-02-012 Cooperative Reproductive Science Research Centers at Minority Institutions
Co-Investigator:
$1,160,204 5%
"The efficacy and safety of metformin and lifestyle factors in the amelioration of hyperandrogenemia and its associated symptomology"

DEGREES IN PROGRESS

The following graduate students are receiving training in Dr. Williams' laboratory:

2000  Heather McConnell, MS (In progress) (Physiology)
2002  Megan Senior " MS(Completed) Screening for Subclinical Eating Disorders in Female Athletes: The Use of an Indirect Interview Technique " (Nutrition)
2002  Michael Perry MS (In progress) (Kinesiology)
2002  Kelly Dougherty  MS (In progress) (Kinesiology)
2002  Brian Frye  MS (In progress) (Kinesiology)
The following undergraduate students are receiving training in Dr. Williams’ laboratory:

2002  Erica Richard, BS Biology (in progress)
2003  Chrissy Rezk, BS Chemistry (in progress)
2004  Meredith Snook, BS Nutrition (in progress)

Conclusions:

See Overall Results from Year 1.

References—none

Appendices—Curriculum Vitae
NANCY I. WILLIAMS
Curriculum Vitae

University Address
Department of Kinesiology
Room 267Q Recreation Building
Penn State University
University Park, PA 16802

Phone: 814-865-1346
Fax: 814-865-1275
Email: niwl@psu.edu

EDUCATION

1984
B.S. Biology, Bucknell University, Lewisburg, PA

1986
M.S. Exercise Physiology, The Ohio State University, Columbus, OH

1992
Sc.D. Applied Anatomy & Physiology, Boston University, Boston, MA

1992-1996
Postdoctoral fellowship, University of Pittsburgh School of Medicine, Center for the Study of Reproductive Physiology (Judy L. Cameron PhD, mentor)

PROFESSIONAL EXPERIENCE

1997-present Assistant Professor
Department of Kinesiology and Noll Physiological Research Center
Joint Appointments:
- Intercollegiate Program in Physiology, Department of Nutrition, Life Science Consortium (Nutrition Science Option)
  Penn State University
  University Park, PA

1996-1997 Visiting Assistant Professor
Human Anatomy & Physiology
Department of Biological Sciences
Ohio University
Athens, Ohio

1992-1996 Postdoctoral Fellow
Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

1987-1992 Graduate Fellow: Department of Health Sciences
Sargent College
Boston University
Boston, Massachusetts

Research Projects:
- NIH grant: "Effects of exercise on pituitary hormone secretion"
- NIH grant: "Exercise as an adjunct therapy for persons with mental illness"

Health/Fitness Center Coordinator: Faculty/Staff Fitness Program
1986-1987  
**Project Director:** Exercise Physiology Laboratory  
Department of Exercise Science  
The Ohio State University  
Columbus, Ohio  
NIH Grant: "Effects of chronic exercise training on aging"

1984-1986  
**Research Assistant:** Exercise Physiology Laboratory  
Department of Exercise Science  
The Ohio State University,  
Columbus, Ohio  
NIH Grant: "Effects of chronic exercise training on aging"

**HONORS AND AWARDS**

Fellowship Status: American College of Sports Medicine, 1998

NIH Individual National Research Service Award (NRSA), 1994-1996

Endocrine Society; Women in Endocrinology Travel Award, 1995

Association of Women in Science Education Foundation Award, 1990

American Association of University Women Predoctoral Fellowship, 1990

American College of Sports Medicine, New England Chapter Scholarship Award; 1989

Phi Sigma Biological Honor Society; 1984

Scholar/Athlete of the Year, Southern New Jersey Courier Post, 1980

**PROFESSIONAL MEMBERSHIPS**

- American College of Sports Medicine: 1984-present
- Endocrine Society: 1996-present
- Association for Women in Science: 1987-1992
- Mid-Atlantic Chapter ACSM: 1997-present

**TEACHING**

**COURSES TAUGHT AT BOSTON UNIVERSITY:**

- HS 276 *Physiology of Exercise Laboratory*
- HS 302 *Exercise Physiology (Lecture)*
- HS 535 *Clinical Fitness Evaluation*
- HS 573 *Physiology of Activity (Lecture)*
- HS 573 *Physiology of Activity (Laboratory)*
COURSES TAUGHT AT OHIO UNIVERSITY:

BIOS 450/550  *Principles of Endocrinology* (section on neuroendocrinology)
BIOS 446/546  *Exercise Physiology Laboratory*
BIOS 345  *Human Physiology*
BIOS 346  *Human Physiology Laboratory*

COURSES TAUGHT AT PENN STATE UNIVERSITY:

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<td>Scientific basis of Exercise for Older Adults</td>
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### COURSES TAUGHT ...cont.

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*Supervised the writing of new laboratory experiment and handout for Kines 456
**Supervise studentS who work in my laboratory on research project examining the interactions between reproductive function disturbances, eating habits, and body image

### STUDENT TRAINING

**Preceptor**

NIH GM08619-07 Research Training in Physiological Adaptations to Stress. National Institute of General Medical Sciences, 1996-2005. Director is PA. Farrell, PhD, Noll Physiological Research Center, Penn State University

**Mentor**

(Pending) Building Interdisciplinary Research Careers in Women's Health; Principal Investigator is Jay Moskowitz, MD, Penn State College of Medicine, Hershey, PA

**Committee Chair- Undergraduate Honors Thesis**

- 2000 Kathleen Flecker - Shreyer's Honor's College: "Weight and diet concerns among female athletes with menstrual cycle irregularities" (Winner 3rd place Undergraduate Research Exhibition)
- 2002 Chrissy Rezk - Shreyer's Honor's College: "Cognitive restraint and urinary cortisol in athletes with menstrual cycle disturbances"
- 2002 Meredith Snook- Shreyer's Honor's College: To be determined

**Committee Chair- Masters Students**

- 1999 Paula Wilkins "Body Image, Social Physique Anxiety, and Menstrual Dysfunction in the Female Athlete" (Physiology)
- 2000 Heather McConnell "Determining the validity of ovulation detection methods in an athletic population" (Physiology)
2000   Angelique Matuch "Quantifying physiological responses prior to competitive exercise" (Kinesiology)
2002   Megan Senior "Screening for Subclinical Eating Disorders in Female Athletes: The Use of an Indirect Interview Technique" (Nutrition)
2002   Michael Perry (In progress) (Kinesiology)
2002   Kelly Dougherty (In progress) (Kinesiology)
2002   Brian Frye (In progress) (Kinesiology)

Committee Chair - Doctoral Students
1999   Jill Bush "Proenkephalin peptide F concentrations in different blood bio-compartments: The effect of an acute resistance exercise protocol" (Kinesiology)
2000   Heather McConnell, MS (In progress) (Physiology)
2001   Thomas Whipple, MS, PT, (In progress) (Kinesiology)

Committee Member - Masters Students
1997   Scott Mazetti "The influence of direct supervision of heavy resistance training on muscular performance and hormonal responses" (Kinesiology)
1998   Sang Kyung Kim "The effects of menstrual function on plasma peptide F immunoreactivity in response to high intensity cycle exercise" (Kinesiology)
1998   Jennifer DeSanto "Body Composition and energy balance: Comparison between eumenorrheic and amenorrheic athletes" (Kinesiology)
1998   Wallace Baker "Characterization of leukocyte infiltration after muscle damage" (Kinesiology)
1998   Steve Tokeshi "Maximal isokinetic force generation in upper body musculature during concentric and eccentric actions: a gender comparison" (Kinesiology)
1999   Jannell MacAulay "Submaximal cycle ergometry as a predictor of maximal aerobic capacity in women on oral contraceptives" (Kinesiology)
2000   Brittney Salkeld "The effect of oral contraceptive use on measures of fatigue and energy metabolism" (Kinesiology)

Committee Member - Doctoral Students
1998   Jeff Volek "Fasting and postprandial serum lipoprotein responses to a hypocaloric low carbohydrate diet rich in monounsaturated fat and supplemented with n-3 fatty acids" (Kinesiology)
2002   Greg Daniels "Walking and running: Information and energetics" (Kinesiology)
2002   Nancy Johnston "Bio-markers of pre-term labor" (Nursing, Physiology minor)

Undergraduate Research Advising:
Summer 1998 University Minority High School Student Research Apprentice Program at Penn State
*Mentored student who helped with research projects in laboratory

Fall 98 to present WISE program; Women in Science in Engineering
*Have averaged two female students per year who have worked in laboratory

Summer 2001 Minority Access to Research Careers (MARC)
*Mentored student who helped with research projects in laboratory

Summer 2002 McNair Scholars Programs
*Mentored first generation college student who performed research project

Research
INTRAMURALLY FUNDED GRANTS
Sargent College of Allied Health Professions
Boston University, Boston, Massachusetts

**Principal Investigator:**
"Effects of exercise and caloric restriction upon luteinizing hormone secretion"

Penn State University
College of Health and Human Development
**Interdisciplinary Seed Grant Program**, 1997-1998; $5000

**Principal Investigator:**
"Prevalence of Female Athlete Triad Disorders: Estimation by Questionnaires and Subsequent Follow-up with Clinical and Laboratory Assessments of Physiological Status"

Penn State University
College of Health and Human Development
**Interdisciplinary Seed Grant Program**, 1998-1999; $6000

**Principal Investigator:**
"Disturbances in Reproductive Function caused by Metabolic Stress: Possible Increased Susceptibility in Individuals with Elevated Levels of Perceived Psychological Stress"

Penn State University
College of Health and Human Development
**Interdisciplinary Seed Grant Program**, 1999-2000; $6000

**Co-Investigator:** (PI Jay Hertel)
"Changes in risk factors of anterior cruciate ligament ruptures in female collegiate athletes across the menstrual cycle"

Pathology Initiation Grant
January 2002-January 2003  5%
Hershey Medical Center, Dept. Pathology  $15,170

**Co-Investigator (PI is Williams' Doctoral student, Thomas Whipple, MS, PT):**
"The Role of Resistance Exercise and Energy Availability on Bone Metabolism"

Children's Youth and Family Consortium
Penn State University, CHHD
January 2002- January 2003  5%
$13,925

**Co-Principal Investigator (with Moira Petit, PhD (PSU-Hershey)):**
"Designing Intervention Programs to Optimize Bone Development: Application of Bone Markers to Monitor the Short-term Response to Exercise"

**EXTRAMURALLY FUNDED GRANTS**

NIH National Research Service Award (NRSA), 1994-1996
Center for the Study of Reproductive Physiology
School of Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

**Principal Investigator:**
"Metabolic cues governing reproductive hormone secretion"
Pharmavite Corporation, Seattle, Washington
Research Grant-in-Aid, 1998-1999; $20,000

**Principal Investigator:**
"Consumer Taste and Education of a Nutritional Sports Supplement"

**US Army Medical Research and Materiel Command**
**US Army Breast Cancer Program**
1998-2001
$292,539

**Co-Investigator:**
"Use of Exercise to Increase CD4 Lymphocytes following Chemotherapy Treatment for Breast Cancer"

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**Principal Investigator:**
"Bioenergetics of Exercise-induced Menstrual Disturbances"
Goal is to test to determine the mechanism whereby low energy availability modulates reproductive function in exercising women

**US Army Medical Research and Materiel Command**
**US Army Breast Cancer Program (IDEA AWARD)**
9/17/01-9/16/04
$408,878

**Principal Investigator:**
"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (IDEA Award)"

**US Army Medical Research and Materiel Command**
**US Army Breast Cancer Program (CAREER DEVELOPMENT AWARD)**
9/17/01-9/16/05
$312,081

**Principal Investigator:**
"Effects of Moderate Aerobic Exercise Combined with Caloric Restriction on Circulating Estrogens and IGF-1 in Premenopausal Women (Salary Only)

**Retirement Research Foundation**
2000-2001
$56,832

**Co-Investigator:** (PI is J.L. Cameron, PhD)
"Physical Exercise and Brain Aging"

**Pending Support**
**National Institutes of Health (NIH)**
1 ROI (PI is Hartman, Terryl J.)
7/01/02 - 6/30/07
$811,610

**Co-Investigator:**
"Nutrition, Fertility and Oxidative Stress"

**National Institutes of Health (NIH)**
HD-02-012 Cooperative Reproductive Science Research Centers at Minority Institutions
Co-Investigator: $1,160,204
5%
"The efficacy and safety of metformin and lifestyle factors in the amelioration of hyperandrogenemia and its associated symptomology"
RESEARCH REPORTS

Williams NI, Christante DH, Swavely K, Laufer E, McBrearty C, and Clark KC. Penn State University JogMate Study: Product Effectiveness and Consumer Appeal
Submitted to Pharmavite Corp, Seattle, WA, July 15, 1999

PUBLISHED MANUSCRIPTS


MANUSCRIPTS IN PRESS

Whipple TJ, Petit Moira, Sharkey N, Demers L, Williams NI. Leptin and the skeleton. (Accepted, Clinical Endocrinology for publication, 2002)

ACCEPTED MANUSCRIPTS

MANUSCRIPTS IN REVIEW


Williams, NI. Experimental disruptions of the menstrual cycle: Lessons from long-term prospective studies (Invited publication of symposium presented at American College of Sports Medicine Meeting, St. Louis, MO, May, 2002; for publication in Med Sci Sports Exerc)

MANUSCRIPTS IN PROGRESS

Williams NI, Berga SL, Cameron JL. Mild metabolic stress potentiates the suppressive effect of psychological stress on reproductive function in female cynomolgus monkeys

Williams NI, Galucci AN. Physiological indicators of psychological stress prior to competitive exercise

Williams NI, McConnell HJ, Galucci AN, Clark KL. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up physiological studies.

Hertel J, Williams NI, Gribble PA, McConnell HJ, DiPasquale AA, Putukian M. Changes in risk factors of ACL injuries across the menstrual cycle.

ABSTRACTS

N.I. Williams, K.A. Greaves, G.R. Brodowicz, T.E. Kirby, and D.R. Lamb, FASCM. Cardiovascular effects of endurance training during submaximal exercise in elders. Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the Midwest American College of Sports Medicine Winter Meeting, Boyne Mountain, Michigan, February, 1986)

N.I. Williams, K.A. Greaves, and D.R. Lamb, FACSM. “Cardiovascular function in lean and obese children during acute submaximal exercise”. Exercise Physiology Laboratory, The Ohio State University, Columbus, Ohio, 43210. (research abstract presented at the Midwest American College of Sports Medicine Winter Meeting, Boyne Mountain, Michigan, February, 1987)


Miles MP, Mackinnon LT, Williams NI, Bush JA, Marx JO, Mastro AM, Kraemer WJ. NK cell activity and LFA-2 expression after running (presented at the American College of Sports Medicine Annual Meeting, Seattle, WA June 3-6, 1999)


Mackinnon LT, Miles MP, Grove DS, Williams NI, Bush JA, Marx JO, Kraemer WJ. Effects of prolonged exercise on expression of perforin mRNA in peripheral blood natural killer (NK) cells (presented at Sports Medicine Australia, 1999)


Flecker KA, Williams NI. Body Image, disordered eating and menstrual status in collegiate athletes. (presented at the National Conference for Undergraduate Research (NCUR), University of Montana, Missoula, Montana, April 27-29, 2000)


23

Senior MK, Williams NI, McConnell HJ, Clark KC. Screening for subclinical eating disorders in female athletes: validation of an indirect interview technique. *(Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001).*

McConnell HJ, Williams NI, O'Connor KA, Clark KL, Putukian M. Menstrual irregularities and disordered eating in female athletes: survey vs follow-up clinical and physiological studies. *(Presented at the 24th Annual meeting of the Mid-Atlantic Regional Chapter of the American College of Sports Medicine, Bushkill, PA, November 2-3, 2001).*


Dougherty, K., Galucci AN, McConnell HJ, Williams NI. Cortisol and testosterone levels prior to competitive exercise. (Submitted for presentation at the 2003 American College of Sports Medicine Annual Meeting, San Francisco, CA, June, 2003).


**INVITED PRESENTATIONS**

"Cardiovascular/Medical Applications for Aerobic Exercise", *Aerobics and Fitness Association of America (AFAA), National Primary Certification Workshop,* Boston, Massachusetts, October 3, 1987.

"Principles and Benefits of Exercise Training for Seniors", *Annual Health Program, Leo Yasenoff Jewish Community Center,* Columbus, Ohio, June 6, 1987.


"Exercise and Female Hormones: What are the Health Risks and Benefits?" *American College of Sports Medicine Health Fitness Summit,* April 14-18, 1999, New Orleans, LA

"Women's Health and Fitness Issues" Panel Discussion at*American College of Sports Medicine Health Fitness Summit,* April 14-18, 1999, New Orleans, LA

"Modulation of Reproductive Function by Metabolic Cues", invited speaker for *Bucknell University Biology Department Seminar Series,* March 3, 2000. Bucknell University, Lewisburg, PA

"Career Development for Women" Women and Sciences and Engineering (WISE) program for potential college students from surrounding area and other states, June 19, 2000, Penn State University

24

"Physiological Connections Between Factors of the Female Athlete Triad" Penn State Athletic Training Conference", April 12, 2002, Penn State University, University Park, PA

"Exercise and Women's Health: Lessons from the Female Athlete Triad", Department of Health and Exercise Science, April 25, 2002, Wake Forest University, Winston-Salem, NC

"Subclinical Eating Disorders and Menstrual Cycle Irregularities in Female Athletes" Eating Disorders on Campus, The Institutional Response, June 7, 2002, Eighth Annual Conference, Penn Stater Conference Center Hotel, Penn State University, University Park, PA

SYMPOSIUM PRESENTATIONS


SERVICE

PROFESSIONAL SERVICE

COMMITTEES

American College of Sports Medicine Student Affairs Committee, Student Representative for New England Chapter, 1988-1990

American College of Sports Medicine Executive Committee, Member at Large, New England Chapter, 1990-1991

American College of Sports Medicine, Strategic Health Initiative Committee: Women, Sporte and Physical Activity, June 2000-2002

REVIEWER

Journals

Journal of Applied Physiology, ACSM Health Fitness Journal

Grants


Editorial Board

American College of Sports Medicine Health and Fitness Journal (2002-present)

Fellow

American College of Sports Medicine, June, 1998

Participant

"Biopsychology of Infertility Workshop"
Sponsored by National Institutes of Health (National Institute of Child Health and Human Development); September 21-22, 1995; NIH Campus, Bethesda, Maryland

UNIVERSITY SERVICE

Advisory Board: The Tremin Trust Research Program on Women's Health, Penn State University, University Park, PA, 2001-present
University Committees
Faculty Senate (Spring 2002-present)-Senate Committee on Intra-University Relations

College Committees (College of Health and Human Development)
College of Health and Human Development Seed Grant Review Committee (Fall 00)
Faculty Council (Fall 00- present)

Intercollege Program Committee (Physiology)
Candidacy Exam Committee (Intercollege Program in Physiology) (Spring 01-present)

Department Committees (Department of Kinesiology)
Curriculum Committee Fall, 1998 to present
Candidacy Committee Fall, 1998 to 2002
Search Committee Fall, 1998
Search Committee (Noll Laboratory Exercise Physiology positions) Spring 99
Search Committee (General Education Fitness Position)
Search Committee Fall 01-Spring 02
Search Committee (Department of Kinesiology Chair)
Curriculum Revisions (ad hoc) Spring 01-Spring 02
Advisory Committee for Fitness Assessment Program Spring 02-present

University Presentations
Fall 1997 Kinesiology Proseminar “Professional Development”
Fall 1998 Kinesiology Proseminar “Professional Development”
Fall 1997 Nutrition Ingestive Behavior Journal Club “Reproductive disturbances and low energy availability: aberrant eating habits”
Fall 1997 Kinesiology Colloquium “Low energy availability and the female athlete: Clinical and Hormonal Effects”
Fall 1997 Population Research Institute “Modulation of Reproductive Function by Metabolic Cues”
Spring 1998 Nutrition Dept. Colloquium “Modulation of Reproductive Function by Metabolic Cues”
Spring 1998 Biobehavioral Health Dept. Colloquium “Reproductive disturbances caused by low energy availability: Interaction with psychological stressors”

OTHER SERVICE
News article, Kinesiology Today, Spring 1999 issue, “Study links Body Image to Athletes’ Fertility”
Interview/article, The Penn Stater, September/October 1999 issue “Research and Discovery Section” by Nick McCarthy
Interview/article, The Penn Stater, 2000 issue of undergraduate research, “Research and Discovery”
Interview/article, Intercom, July, 1999. featured in “Focus on Research” article, by Barbara Hale.

2000 Undergraduate Exhibition
Served as Judge for the 2000 Undergraduate Exhibition in April, 2000.