

Hot off the Press

HIRSUTISM

Azziz R, Sanchez LA, Knochenhauer ES, Moran C, Lazenby J, Stephens KC, Taylor K, Boots LR. *Androgen excess in women: experience with over 1000 consecutive patients.* J Clin Endocrinol Metab. 2004 Feb;89(2):453-62
Keegan A, Liao LM, Boyle M. *'Hirsutism': a psychological analysis.* J Health Psychol. 2003 May;8(3):327-45.

POLYCYSTIC OVARY SYNDROME

Bayram N, van Wely M, Kaaijk EM, Bossuyt PM, van der Veen F. *Using an electrocautery strategy or recombinant follicle stimulating hormone to induce ovulation in polycystic ovary syndrome: randomised controlled trial.* BMJ. 2004 Jan 24;328(7433):192.
Carbunaru G, Prasad P, Scoccia B, Shea P, Hopwood N, Ziai F, Chang YT, Myers SE, Mason JI, Pang S. *The Hormonal Phenotype of Nonclassic 3beta-Hydroxysteroid Dehydrogenase (HSD3B) Deficiency in Hyperandrogenic Females Is Associated with Insulin-Resistant Polycystic Ovary Syndrome and Is Not a Variant of Inherited HSD3B2 Deficiency.* J Clin Endocrinol Metab. 2004 Feb 1;89(2):783-794.
Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G. *Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome.* J Clin Endocrinol Metab. 2004 Mar;89(3):1273-6.
Gambineri A, Pelusi C, Genghini S, Morselli-Labate AM, Cacciari M, Pagotto U, Pasquali R. *Effect of flutamide and metformin administered alone or in combination in dieting obese women with PCOS.* Clin Endocrinol (Oxf). 2004 Feb;60(2):241-9.
Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. *Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome.* Fertil Steril. 2004 Jan; 81(1):19-25.

MEETINGS OF INTEREST

**Androgen Excess Society International
Satellite Meeting**
August 31, 2004
Lisbon, Portugal
www.androgenexcesssociety.org

**12th International Congress Endocrinology
(ICE) Meeting**
September 1 - 4, 2004
Lisbon, Portugal
www.ice2004.com

**60th Annual Meeting of the American
Society for Reproductive Medicine**
October 16-20, 2004
Pennsylvania Convention Center ~
Philadelphia, Pennsylvania
www.asrm.org

Center for Androgen-Related Disorders
8631 W. Third Street, Suite 930E
Los Angeles, CA 90048

Non-Profit
Organization
U.S. Postage
PAID
Permit 22328
Los Angeles, CA



8700 Beverly Boulevard,
South Tower, Suite 3611
Los Angeles, CA 90046
(310) 423-9964
www.csmc.edu/card

CARD Staff

Ricardo Azziz, MD,
MPH, MBA - *Director,*
Center for Androgen-
Related Disorders

Sheila Bolour, MD
Assistant Director

Glenn Braunstein, MD
Associate Director

Dennis Magoffin, PhD
Associate Director

Danielle Blum, MSN,
CNM, RNP - *Research
Nurse Coordinator*

In this issue...

- o Current CARD research*
- o Lecture Series ---
Mark your calendar!*
- o Charter Membership
opportunities - Join Now*
- o First Annual Patient
Care Conference*
- o Hot off the Press!*
- o From the Bench*
- o Clinical Review*

Center for Androgen-Related Disorders

Director's Welcome

June 2004 Vol. 1, Issue 1

Ricardo Azziz, MD, MPH, MBA

It has been very exciting to witness the development of the Center for Androgen-Related Disorders (CARD) at Cedars-Sinai Medical Center and its continued growth into what we are sure will be a regional and national resource for the study and treatment of women with androgen-related disorders. Overall, androgen excess and androgen deficiency affect between 7% and 10% of all women, making these disorders one of the most common endocrine abnormalities of man. This unique Center is the only one of its kind on the West Coast and is committed to:

- Fostering and focusing research in androgen-related disorders by creating an environment of collaboration among clinical and basic scientists and physicians who have an interest in treating these women.
- Raising sensitivity and awareness regarding these disorders among the lay and scientific communities and the medical profession.
- By developing, coordinating and completing clinical trials regarding the most promising treatments for these disorders.
- By serving to educate patients and their treating physicians regarding the latest advances regarding the nature, prevalence, and latest advances in the management of these disorders.
- Providing cutting edge diagnostic and treatment services for those effected women.

As we look forward to our continued growth, serving to provide the research community, the medical profession, and affected patients as a resource in the development of cutting edge investigations and promising therapies in androgen excess and androgen deficiency. Please do not hesitate to contact us if you would like any further information by calling me at (310) 423-7433 or April Moore at (310) 423-4887.

Sincerely,

CARD Calendar of Events

September 8, 2004

LECTURE SERIES

David Ehrmann, MD - Associate Professor of Medicine
University of Chicago

November 3, 2004

LECTURE SERIES

Andrea Dunaif, MD - Division Chief
Division of Endocrinology, Metabolism and Molecular Medicine
Northwestern University

January 5, 2005

LECTURE SERIES

Richard S. Legro, MD - Associate Professor
Department of Obstetrics & Gynecology
Hershey Medical Center @ Penn State University Medical School

*All CARD Lectures will be held in Harvey Morse Conference Rooms 4 & 5 at CSMC.
The CARD business meeting will begin at 6:00 PM and the Lecture will begin at 6:30 PM.*

From the Bench



Dennis Magoffin, PhD

Research related to androgen abnormalities, like all research, is dependent on the ability to generate high quality data. In the Center for Androgen-Related Disorders we are committed to establishing resources with which Center investigators can generate the highest quality data. To this end, Dr. Ida Chen heads the steroid assay core lab with special emphasis on measurement of androgens in clinical samples. The Kevin Bacon law states that everyone is linked by no more than six degrees of separation. In our case, however, there are only two degrees of separation between the CARD research team and the original steroid radioimmunoassays developed by Dr. Guy Abraham.

As Dr. Frank Stanczyk so elegantly presented in the first CARD research seminar, there are a variety of potential problems with measuring androgens accurately, particularly the low levels circulating in women. Commercial assay kits are designed to measure the higher concentrations of androgens in men and do not yield the accuracy demanded of research, especially research involving women. Therefore in order to get accurate androgen levels in women, it is necessary to perform a number of additional steps in addition to a simple immunoassay.

As you are well aware, the majority of androgens circulate complexed to proteins in the blood. Accurate measurement of androgens requires that they be separated from these proteins so that the antibody of the immunoassay has free access to the steroid molecule. In some cases this can be accomplished by a pH change, but the best method is to use organic extraction. Organic extraction is a nonspecific process that isolates all steroid molecules. The accuracy of immunoassays is dependent on the selectivity with which the antibody recognizes the androgen of interest once the androgen is removed from the proteins. All antibodies recognize structurally similar steroid molecules and their conjugates to varying degrees. If this cross-reactivity is sufficient to affect the accuracy of the measurement, a chemical separation step can be employed to purify the steroid prior to assay with the antibody. The CARD assay core laboratory has the capability to perform extraction and purification of samples prior to assay. These validated assays for testosterone, androstenedione and dehydroepiandrosterone yield excellent results. In addition the core lab performs validated assays for sex-hormone binding globulin (SHBG) and free (or bioavailable) testosterone.

Obtaining high quality data is only part of the story. How does one interpret the results? To understand the results, normative data for the populations being studied are required and CARD is in the process of establishing normative data for each of our assays. If any of you have a specific population that is relevant to your research interests, you can contact Dr. Ida Chen to discuss establishing normative values.

The steroid assay core is only one of the high quality tools available within CARD to foster optimal research and collaboration. In the coming newsletters, we will discuss some

of the research projects being conducted by CARD investigators and highlight additional state-of-the-art technologies being used by CARD investigators to understand the causes of and the treatments for androgen-related disorders.

CARD Research

Danielle Blum, MSN, CNM, RNP

CARD Clinical Trials

The genetics and etiology of PCOS, the epidemiology and features of androgen excess, particularly in different ethnic groups, and optimum treatment are some of the questions that remain unanswered despite the high prevalence and morbidity of these disorders.

An integral aspect of the Center for Androgen Related Disorders is research designed to answer these questions. Currently, there are more than ten active studies that are taking place in CARD. Each CARD newsletter will highlight a different research study. The study for this newsletter is the Clinical Repository.

Clinical Repository

Goals of the clinical repository are to (1) Establish an umbrella procedure for enrolling, using, and storing samples and data of study participants with Androgen Excess (2) Establish a procedure to allow us to contact the enrolled participants and their blood relatives for future studies (3) Develop a repository of blood samples coupled with clinical data, medical history and family history

The subjects are individuals with clinically demonstrated Androgen Excess, individuals who are thought to have Androgen Excess, and their family members (blood relatives).

Samples

These samples will be used to conduct clinical and laboratory studies (genetic and biochemical, immunologic and/or molecular) designed to understand the causes of and improve the treatments for Androgen Excess. It is our goal to use these samples at CARD, as well as to collaborate with other Androgen Related Disorders researchers.

The clinical repository will house resources that will be developed from the samples and clinical information registry are:

- * DNA and Lymphoblastoid Cell Line Repository
- * Serum Repository
- * Clinical Information Registry/IBD Database

For more information on CARD Research Studies contact Danielle Blum at (310)423-6412 or dblum@cshs.org. Ms. Blum is the Research Nurse Coordinator for the Center for Androgen-Related Disorders and the Center for Reproductive Medicine.

Female Androgen Insufficiency Syndrome: Fact or Fiction?



Sheila Yafai Bolour, MD

Despite the paucity of randomized clinical trials on the effects of androgen therapy in women with low libido and female sexual dysfunction, clinicians have been treating women with various forms of androgen therapy for many years. Until recently, there has been a lack of data and a lack of understanding of the physiological action of androgens, and androgen therapy, in women.

In recent years, testosterone receptors have been identified in vaginal and clitoral tissue, the brain, muscle and bones, heart and vasculature, and breast tissue. In females, androgens are the immediate precursors of estrogen. Androgens are produced by both the ovaries and the adrenal glands. Androgens include the hormones testosterone, dihydrotestosterone, androstenedione, DHEA and DHEA-sulfate. Androgen levels do not decline through the menopausal transition, but do decline as women age. Levels of serum testosterone concentrations decrease by almost 50% between the ages of 20 and 40 years in women. Androgen levels can also decline with glucocorticoid therapy, and free testosterone levels decrease with oral estrogen therapy because of an increase in sex-hormone binding globulin.

In 2001, the Princeton Consensus Conference was convened in order to provide an overview of the science and clinical implications of the role of androgens in women. They developed a consensus statement on the definition, diagnosis and management of androgen insufficiency in women and identified areas were further research and investigation needed to be pursued. The participants of this conference recognized that Female Androgen Insufficiency Syndrome exists. They defined Female Androgen Insufficiency Syndrome as the presentation of the following symptoms in a woman who has had an event associated with decreased androgen production. These symptoms include: low libido with global decrease in sexual desire or fantasy; persistent unexplained fatigue; and decreased sense of well-being. Signs of Female Androgen Insufficiency Syndrome include: thinning or loss of pubic hair, decrease in lean body mass, and osteopenia or

osteoporosis. Conditions that are associated with Androgen Insufficiency in women include: hypothalamic-pituitary abnormalities, premature ovarian failure (including oophorectomy), adrenal insufficiency, glucocorticoid therapy, and exogenous estrogen administration.

If a woman fits the clinical definition of androgen insufficiency outlined above, it is important to assess whether she has adequate estrogen levels as estrogen deficiency can lead to vaginal dryness and dyspareunia. Therefore, patients should be well-estrogenized before being treated for Androgen Insufficiency. If the symptoms persist in a postmenopausal women despite normal amounts of estrogen therapy, then other potential causes of the patient's symptoms should be ruled out including: depression, anemia, thyroid disease, or systemic illness. If symptoms cannot be explained by these illnesses, an evaluation of androgen levels should be undertaken. Caution should be exercised in assessing androgen levels in women as accuracy of androgen measurements in women is not guaranteed in every laboratory. Furthermore, normative ranges for androgen levels at various ranges are not well defined making the diagnosis more difficult.

Members of the Center for Androgen Related Disorders are investigators in clinical trials evaluating the efficacy of androgen therapy and other therapies for Female Androgen Insufficiency Syndrome. These therapeutic options will be presented to the FDA for approval in the near future. In the meantime, other therapies are being utilized by our staff to treat patients with this syndrome and to help improve the quality of their lives.

For more information about the treatment of Androgen Insufficiency, please contact the Center for Androgen-Related Disorders at (310) 423-9964.

Weblinks

PATIENT EDUCATION RESOURCES

American Society for Reproductive Medicine
www.asrm.org/Patients/mainpati.html

American College of Obstetricians & Gynecologists
www.acog.org

Polycystic Ovary Syndrome Association
www.pcosupport.org

Polycystic Ovary Syndrome Doctors
www.pcos-doctors.com

The Hormone Foundation
www.hormone.org

