

MAY NEWSLETTER: FOCUS ON ALTERED CORTISOL METABOLISM INSIDE OVARIAN FOLLICLES IN PCOS

The May newsletter is dedicated to altered steroid metabolism inside ovarian follicles in PCOS. The Editor, E.C., has interviewed Helen Mason, Ph.D., Professor of Reproductive Endocrinology at St. George's University of London, United Kingdom. Helen is member of AEPCOS Society from 2005 and has recently published a paper in JCEM (published online May 15, 2013) on this issue. The first author of the paper is Dr. Anthony Michael who has collaborated with Helen Mason also in the answers reported in the present Newsletter.

Because the treated issues are often controversial, we encourage comments from our members and will publish these in future newsletters. If you wish, you may send a letter to: enrico.carmina@ae-society.org

The new preliminary program of 11th Annual Meeting of AEPCOS Society is reported, too.

For any information about all AEPCOS meetings, you may contact: info@ae-society.org

VOLUME 1, ISSUE 5

MAY 31, 2013

In this issue:

- * Mechanisms of anovulation in PCOS
- * 11th AEPCOS Annual Meeting

Editorial Board

Enrico Carmina, M.D., Palermo, Italy
Tracy Bekx, M.D., Madison, WI, USA
Daniel Dumesic M.D., Los Angeles, CA, USA
Joop Laven, M.D., Rotterdam, The Netherlands
Jan McAllister, Ph.D., Hershey, PA, USA
Poli Mara Spritzer, M.D., Porto Alegre, Brazil

FORTHCOMING AEPCOS MEETINGS

- Update on PCOS, Natal, Brazil, August 20-21, 2013
- Update on PCOS, Quito, Ecuador, September 25, 2013
- **11th Annual Meeting of Androgen Excess & PCOS Society, Newport, Rhode Island, USA, October 17-18, 2013**

ANNUAL MEETING OF AEPCOS SOCIETY

Newport, Rhode Island, USA,



11th Annual Meeting of AEPCOS Society will be held at the HYATT REGENCY RESORT HOTEL, 1 Goat Island, Newport, Rhode Island 02840, USA, October 17-18, 2013. The meeting will start October 17 at 4 PM to permit to people attending IFFS/ASRM meeting in Boston (that meeting is scheduled to finish October 17, at 1 PM) to can participate to AEPCOS meeting sessions. Newport is located 72 miles from Boston Convention Center (about 1 hour and 20 minutes by MA-24S). Transportation from Boston Convention Center to Newport Hyatt Regency Resort will be provided (bus leaving at 1:30 PM) but has to be reserved at least 15 days before.

The venue of 11th AEPCOS Annual meeting, Hyatt Regency Resort Hotel, is situated on Goat Island. Surrounded by Narragansett Bay, the hotel offers the seclusion of a private island, just minutes to downtown Newport. The resort provides water shuttle (and van shuttle) to/from downtown Newport.

Abstract deadline is August 2, 2013. For abstract form and preliminary program, please connect to: www.ae-society.org or contact: info@ae-society.org

Newport may be easily reached by car, by flight (25 miles from International T.F. Green/airport— PVD) or by train (18 miles from West Kingston railway station —along New York-Boston railway). A shuttle bus operates from both airport and train station to Newport hotels. For information or reservation on transportation, contact: info@ae-society.org

ANNUAL MEETING PRELIMINARY PROGRAM

DAILY SCHEDULE

THURSDAY, OCTOBER 17

AFTERNOON

4:00—4:15 pm **WELCOME**

4:15—5:15 pm **AEPCOS GUIDELINES FOR HIRSUTISM**

Diagnosis of hirsutism: what is there new?

Hector Escobar-Morreale—Madrid, Spain

Treatment of hirsutism: what is there new?

Paolo Moghetti - Verona, Italy

5:15—6:30 pm **AEPCOS-AACE JOINT SESSION:
CLINICAL PROBLEMS IN ANDROGEN EXCESS DISORDERS**

Utility of AMH evaluation in Androgen Excess Disorders

Neil Goodman—Miami, USA

Special problems in treatment of diabetic PCOS women

Jennifer Glueck - Miami, USA

Clinical Diagnosis and Medical Treatment of Female
Androgenic Hair Loss

Walter Futterweit —New York, USA

7:00-9:00 pm **WELCOME RECEPTION**

FRIDAY, OCTOBER 18

MORNING

8:00—9:20 am **OBESITY and PCOS**

Mouse model: Maternal obesity results in obese offspring

Rebecca Simons—Philadelphia, USA

Animal models of obesity and PCOS

David Abbott—Madison, USA

Nutritional influences and metabolic outcome in offspring

Mari Elizabeth Patti—Boston, USA

9:20—9:50 am **PRESIDENTIAL LECTURE**

Richard Legro—Hershey, USA

9:50—10:20 am **COFFEE BREAK**

10:20—11:40 am **CONTROVERSIES IN TREATMENT OF
INFERTILITY IN PCOS**

Clomiphene versus low dose FSH as first line treatment

Roy Homburg—Tel Aviv, Israel

Ovarian function after gastric bypass surgery

Samantha Butts—Philadelphia, USA

Do women with PCOS have an extended ovarian window?

Anuja Dokras—Philadelphia, USA

ANNUAL MEETING PRELIMINARY PROGRAM

DAILY SCHEDULE

FRIDAY, OCTOBER 18

11:40 am—1:00 pm **ORAL COMMUNICATIONS: BASIC**

1:00—2:00 pm **LUNCH and POSTER SESSION**

2:00—3:20 pm **LONG TERM CO-MORBIDITIES IN PCOS**

Chronic inflammation and CVD diseases

Nehal Mehta—Bethesda, USA

Subclinical atherosclerosis and PCOS

Alice Chang—Rochester, USA

Influence of aging on CVD risk in PCOS

Roger Lobo—New York, USA

3:20—3:50 pm **KEYNOTE LECTURE**

Genetic analyses of PCOS – the good, the bad and the ugly

Andrea Dunaif - Chicago, USA

FRIDAY, OCTOBER 18

3:50—4:10 pm **COFFEE BREAK**

4:10—5:10 pm **ORAL COMMUNICATIONS: CLINICAL**

5:10—5:40 pm **AEPCOS GUIDELINES FOR PCO MORPHOLOGY**

New thresholds in follicle count and ovarian size for defining Polycystic Ovaries

Enrico Carmina—Palermo, Italy

5:40—6:10 pm **CLINICAL RESEARCH IN PCOS: REPORTS FROM RINDIAN AEPCOS RESEARCH GROUP**

Duru Shah—Mumbai, India

Ashraf Ganie—New Delhi, India

6:10—6:20 pm **PRESENTATION OF NEW AEPCOS PRESIDENT**

6:20—6:45 pm **BUSINESS MEETING**

Enrico Carmina—Palermo, Italy

REGISTRATION FORM

11TH AEPCCS ANNUAL MEETING

REGISTRATION ONLY

_____ AEPCCS members \$260 _____ Non AEPCCS members \$360

NEWPORT HYATT REGENCY RESORT

\$219 for night ___ October 16 ___ October 17 ___ October 18

Payment amount: \$_____ Credit card payment: ___ VISA ___ MasterCard ___ AMEX

Credit card number _____ Expiration date: ____/____

Cardholder
name _____

Online payment _____ To safely pay online, connect to: www.ae-society.org

Check payment _____ Make checks payable to Androgen Excess Society

Email, mail or fax the registration form to: Androgen Excess & PCOS Society, via delle Croci 47, 1st floor, suite 10, 90139 Palermo, Italy. Fax: +39-091328997, Email: info@ae-society.org

Only written cancellation by fax or e-mail will be accepted. For cancellations until September 1, 2013, a 50% fee will be applied. No refund will be given after that date. Registration includes welcome reception, lunch (Oct 17) 2 coffee breaks. Hotel prices include \$20 Resort Fee (parking, in room high-speed internet, water shuttle or van shuttle to/from Downtown Newport, resort activities, access to fitness center, 2 bottled waters for night) but do not include 13% combined city and state occupancy taxes.

The certificate will be issued to the name of the accredited participant.

To get registration form in word, please contact: info@ae-society.org

ABSTRACT SUBMISSION FOR 11TH AEPCOS ANNUAL MEETING

You are invited to submit abstracts of your original research to be considered for presentation at the 11th Annual Meeting of the Androgen Excess & Polycystic Ovary Syndrome Society.

To be considered for presentation your abstract must be submitted no later than August 2nd, 2013, 11:00 pm (2300 hrs) PST. All abstracts must be submitted by email in word to: info@ae-society.org. The presenter is required to register for 11th Annual Meeting of the AE-PCOS Society on submission of the abstract

The Baumgartner-Azziz AE-PCOS fund will award 2 Travel Awards (\$750 each) to the best abstracts presented by young (<35 years) investigators.

All abstracts will be reviewed by a blinded scientific committee nominated by AE-PCOS Annual Meeting Committee.

JOB OPPORTUNITY

UNIVERSITY OF MICHIGAN INTERDISCIPLINARY FACULTY INITIATIVE IN REPRODUCTIVE SCIENCES

The Reproductive Sciences Program (RSP) at the University of Michigan seeks exceptional scholars for tenure-track positions in research areas that include: gonadal biology; stem cells and development; reproductive genetics and epigenetics; reproductive medicine; maternal-fetal interactions and medicine; bioengineering in reproduction; and reproductive endocrinology. Positions feature substantial hard money salary support and are available at the Assistant, Associate or Full Professor levels in the Medical School Departments of Cell and Developmental Biology, Obstetrics & Gynecology, Pediatrics, Physiology, Urology, and in the School of Engineering Department of Biomedical Engineering. Candidates should have M.D., and/or Ph.D., degrees with relevant postdoctoral or fellowship training, a strong track record of published work in reproductive sciences (non-cancer), and exceptional potential for conducting Interdisciplinary Translational and Fundamental Research in the Reproductive Sciences. Applications should be sent by July 1, 2013 and should include a curriculum vitae, a 1-2 page summary of research plans, and 3 letters of support. Send applications to:

Gary Smith and Sue Moenter, c/o Kelly Studer

RSP Interdisciplinary Faculty Cluster Hire Search Committee, 6428 Medical Science I, 1301 East Catherine St, Ann Arbor, Michigan, 48109-0617, USA

Email: UMReproductiveScience@med.umich.edu

website: <http://www.med.umich.edu/obgyn/research/rsp/index.htm>

**ANDROGEN
EXCESS &
PCOS SOCIETY**

12520 Magnolia Boulevard,
North Hollywood,
CA 91607, USA

Email :
info@ae-society.org

www.ae-society.org



Helen Mason, Ph.D.

ALTERED CORTISOL METABOLISM INSIDE OVARIAN FOLLICLES IN PCOS

The Editor has interviewed Helen Mason, Ph.D., Professor of Reproductive Endocrinology at St. George's University of London, London, Helen Mason and her group have recently published the following study:

1. Helen, can you summarize your findings?

We are interested in the metabolism of the adrenal steroid hormone cortisol within reproductive tissues, and specifically in the ovary. Having previously established in animal models (cow and pig) that ovarian metabolism of cortisol by the 11β HSD enzymes increases during the growth of antral follicles, and having noted decreased metabolism of cortisol in bovine and porcine spontaneous ovarian cysts, we set out to establish if local ovarian metabolism of cortisol is decreased in follicles from women with polycystic ovaries relative to size-matched follicles from normal ovaries. We were also interested to see if the same was true of granulosa-lutein cells from PCOS patients undergoing oocyte retrieval for IVF. Using ratios of cortisol:cortisone measured in follicular fluid as an index of local cortisol metabolism by 11β HSD enzymes, we found that the intra-follicular cortisol:cortisone ratio was significantly increased (by 50%) in women with polycystic ovaries, consistent with decreased metabolism of cortisol to cortisone. Moreover, on sub-analysis, this elevation in cortisol:cortisone ratio (i.e. decreased cortisol metabolism) was confined to those patients with anovulatory PCOS (mean cortisol:cortisone ratio = 2.1) but did not differ between patients with ovulatory PCO versus normal ovaries (1.6 vs 1.2, respectively).

In patients undergoing treatment for infertility by IVF, the metabolism of cortisol to cortisone in isolated granulosa-lutein cells was significantly lower in patients with PCOS than in patients with any other cause of infertility (tubal infertility, endometriosis, male factor or idiopathic infertility). When isolated granulosa-lutein cells were challenged with various hormonal treatments acutely or chronically (for 4 or 24 hours, respectively), neither insulin nor metformin, alone or in combination, had any significant effect of cortisol-cortisone metabolism, whereas the metabolism of cortisol could be suppressed in a dose-dependent fashion by androgens at physiological concentrations. The most potent of the tested androgens was 11β -hydroxy-androstenedione, concentrations of which are known to be elevated in PCOS follicles.

Hence, we concluded that failure of folliculogenesis in PCOS is associated with a decrease in the local enzymatic inactivation of cortisol by 11β HSD enzymes, and that this might reflect local inhibition of cortisol metabolism by 11- and/or 7-oxy-metabolites of DHEA and androstenedione or by testosterone.

**ANDROGEN
EXCESS &
PCOS SOCIETY**

12520 Magnolia Boulevard,
North Hollywood,
CA 91607, USA

Email :
info@ae-society.org

www.ae-society.org

2. What may be the importance of this mechanism in pathogenesis of anovulation of PCOS women? Is it the main mechanism of ovulatory dysfunction or is it part of a more complex pathophysiology?

Previous studies have established that a sub-set of patients with PCOS symptoms present with changes in cortisol-cortisone metabolism in their liver and possibly kidneys (as reflected by urinary steroid metabolites).

This study establishes that the enzymatic inactivation of cortisol by 11β HSD in the ovary may also be changed locally at the level of the antral follicle. Available evidence from our labs and others suggests that impaired metabolism of cortisol-cortisone might be expected to impact on follicle growth, oocyte maturation, and follicle rupture at ovulation. Given that ovulation is an inflammatory cascade characterised by elevated levels of prostaglandins and activation of the matrix metalloproteinases, changes in the local metabolism of an anti-inflammatory steroid, cortisol, could impede the ovulatory mechanism. Changes in cortisol metabolism will also alter negative feedback within the HPA axis and may reset the endocrine drive between CRH, ACTH and adrenal androgens as well as circulating cortisol input to the ovaries.

Further studies are required to address the complex mechanisms via which cortisol might participate in the pathogenesis of anovulation in PCOS. It is likely that this is one of a number of dysregulated endocrine systems that contribute to disordered follicle growth in this syndrome.

3. Is there a relationship between dysfunctional 11β HSD activity and altered early folliculogenesis characteristic of PCOS?

Drawing on our prior studies of follicle growth in cows and pigs, it would appear that low levels of cortisol metabolism are associated with the anovulatory state of both early antral follicles and cystic follicles in other mammals, but additional studies would be required to draw this parallel to women and the pathogenesis of PCOS.