

### MARCH 2014 NEWSLETTER

#### DIMINISHED LIPID OXIDATION AND FAT SPARING PHENOTYPE IN PCOS

The March newsletter is dedicated to metabolic perturbations that may encourage obesity in women with PCOS. Professor Daniel Dumesic interviewed the President of the AEPCOS Society, David Abbott, Ph.D. Dave is Professor in the Department of Obstetrics and Gynecology and Senior Scientist at Wisconsin National Primate Research Center, University of Wisconsin, Madison, WI, USA. Dave has been a member of AEPCOS Society from 2004 and has extensively studied experimental induction of PCOS-like traits in primates by administering androgens during fetal life.

Some important information about the 12<sup>th</sup> Annual Meeting of the AEPCOS Society is included. The meeting site is the Kauai Marriott Resort Hotel and Beach Club, Kalapaki Beach, Kauai, HI, USA, October 22-23, 2014.

The abstract deadline is September 7<sup>th</sup>, 2014. Abstract forms are available from [www.society.org](http://www.society.org) or from contacting [info@ae-society.org](mailto:info@ae-society.org)

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#### Editorial Board

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#### FORTHCOMING AEPCOS MEETINGS

- 12th Annual Meeting of Androgen Excess & PCOS Society, Kauai Marriott Resort Hotel and Beach Club, Kauai, Hawaii, USA, October 22-23, 2014
- Update Meeting of AEPCOS Society, San Diego, CA, USA, March 4, 2015
- 13th Annual Meeting of AEPCOS Society, Palermo, Italy, October 4-6, 2015

## 12<sup>TH</sup> AEPCOS ANNUAL MEETING, KAUAI, HAWAII, OCTOBER 22-23, 2014

The 12th Annual meeting of the AEPCOS Society will be held at Kauai Marriott Resort Hotel and Beach Club, Kalapaki Beach, Kauai, Hawaii, USA, October 22-23, 2014, immediately after the Honolulu ASRM Annual Meeting. The venue of next annual meeting is a wonderful resort that is located in the very beautiful island of Kauai. The airport of Lihue, only one mile from the resort, may be reached by a



short 20 minutes flight from Honolulu. Several airlines serve this route with more than 10 daily flights. Lihue airport may be reached also by daily direct flights leaving from main Western USA and Canada cities including Los Angeles, San Francisco, Phoenix, Seattle and Vancouver. We have negotiated a very good rate at the Kauai Marriott that will be available to all registered guests for the duration of the meeting and for the following three days. Resort fee is optional but registration includes free shuttle bus from the airport. **As a special bonus for pre-registered (before October 1, 2014) AEPCOS and ASRM members flying to Lihue from Honolulu, we will reimburse \$100 of the ticket price (actual cost of the return ticket is \$103). AEPCOS members flying directly to Lihue from continental USA will get \$50 reimburse.**

The meeting program will include invited lectures, meet the professor sessions and oral communications

# REGISTRATION FORM

## 12TH AEPCOS ANNUAL MEETING

### REGISTRATION

\_\_\_\_\_ AEPCOS members \$260 \_\_\_\_\_ Non AEPCOS members \$360

### KAUAI MARRIOTT RESORT HOTEL AND BEACH CLUB

\$219 for night

\_\_\_\_ October 22 \_\_\_\_ October 23 \_\_\_\_\_ Number and dates of additional nights

Payment amount: \$\_\_\_\_\_ Credit card payment: \_\_\_\_\_ VISA \_\_\_\_\_ MasterCard \_\_\_\_\_ AMEX

Credit card number \_\_\_\_\_ Expiration date: \_\_\_\_/\_\_\_\_ CVV \_\_\_\_\_

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Online payment \_\_\_\_\_ to safely pay online, connect to: [www.ae-society.org](http://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](mailto:info@ae-society.org)

Registration includes transportation from/to airport, lunch and 2 coffee breaks. Price of the room is for single or double garden view room but does not include taxes (13.42%). Add \$30 for partial ocean view. The same hotel rate will be applied for up to 3 additional nights. Resort fee (\$30 daily) is optional.

Only written cancellation by fax or e-mail will be accepted. For cancellations until September 1, 2014, a 50% fee will be applied. Only taxes will be refunded after that date. **Pre-registered (before October 1, 2014) AEPCOS and ASRM members flying the route Honolulu-Lihue will get reimburse of \$100 of air ticket price. Pre-registered AEPCOS members flying directly to Lihue from continental USA will get reimburse of \$50.** Reimburses will be available at the meeting.

## ABSTRACT SUBMISSION FOR 12<sup>TH</sup> AEPCOS ANNUAL MEETING

You are invited to submit abstracts of your original research to be considered for presentation at the 12th Annual Meeting of the Androgen Excess & Polycystic Ovary Syndrome Society. For abstract form, connect to: [www.ae-society.org](http://www.ae-society.org) or contact: [info@ae-society.org](mailto:info@ae-society.org)

To be considered for presentation your abstract must be submitted no later than September 7th, 2014, 11:00 pm (2300 hrs.) PST. All abstracts must be submitted by email in word to: [info@ae-society.org](mailto:info@ae-society.org). The presenter is required to register for 12th Annual Meeting of the AE-PCOS Society on submission of the abstract

All abstracts will be reviewed by a blinded scientific committee nominated by AE-PCOS Annual Meeting Committee. Accepted abstracts will be published on the abstract book and presented as oral communications.

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

## OTHER MEETINGS

- European Society of Endocrinology: May 3-7, 2014, Wroclaw, Poland
- Pediatric Endocrine Society: May 3-6, 2014, Vancouver, Canada
- Endocrine Society: June 21-24, 2014, Chicago, IL, USA
- ESHRE: June 29-July 2, 2014, Munich, Germany
- European Society for Pediatric Endocrinology: September 18-20, 2014, Dublin, Ireland
- ASRM: October 20-22, 2014, Honolulu, HI, USA
- 12th Annual World Congress on Insulin Resistance Diabetes and Cardiovascular Disease: November 20-22, 2014, Sheraton Hotel Universal City, Los Angeles, CA, USA





David Abbott, Ph.D.

## DIMINISHED LIPID OXIDATION IN PCOS

In this month's Newsletter, Dan Dumesic interviewed Dr. David Abbott, who commented on his recent publication in *Current Metabolomics* 2013; 1: 269-278, entitled, "**METABOLIC EVIDENCE OF DIMINISHED LIPID OXIDATION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME.**" Authors: Whigham LD, Butz DE, Dashti H, Tonelli M, Johnson LK, Cook ME, Porter WP, Eghbalian HR, Markley JL, Lindheim SR, Schoeller DA, Abbott DH, Assadi-Porter FM.

This study suggests a shift from lipid oxidation to amino acid utilization for energy production that may increase lipid accumulation and partially explain obesity tendencies in PCOS women.

### 1. Dave, what was the objective of your study?

David Abbott: We formed a multi-disciplinary working group, led by Drs. Fariba Assadi-Porter (Texas Tech University, USA) and Leah Whigham (Paso del Norte Institute for Healthy Living, TX, USA), to discern a molecular signature for PCOS. We hoped to gain insight into PCOS metabolic perturbations that encourage increased obesity. We recruited 10 women with PCOS, diagnosed from all three Rotterdam criteria, and 10 healthy women comparable in age (18-38 years) and body mass index (lean to obese). None appeared to be challenged in terms of glucoregulation or lipidemia. At the onset of a menstrual cycle or during an anovulatory period, as determined from serum progesterone levels and ultrasound exam, women were provided with 3-day's worth of meals comprising 35% of calories from fat, 15% from protein and 50% from carbohydrate. Total daily calories were adjusted to approximate energy balance for each woman. A similar meal provision continued on the 4th day, when each woman spent an overnight stay (~26 hours) in our hospital's human respiratory chamber. The standardized nutrient intake was designed to diminish dietary effects. Exhaled breath contains  $^{13}\text{CO}_2$  and  $^{12}\text{CO}_2$ , a mixture of stable carbon isotopes that reliably reflect cellular respiration and can be quantified by cavity ring-down spectrometry. As lipid is enriched with  $^{12}\text{C}$  because of the isotopic bias of pyruvate dehydrogenase against  $^{13}\text{C}$  during lipid synthesis, fat oxidation diminishes the ratio of  $^{13}\text{CO}_2$  to  $^{12}\text{CO}_2$  in exhaled breath compared to oxidation of protein or carbohydrate.

### 2. Can you summarize your findings?

David Abbott: As expected on waking, normal women provided breath samples enriched with  $^{12}\text{CO}_2$ , reflecting increased reliance on lipid oxidation when hepatic glycogen reserves became depleted during nighttime fasting. Subsequent meals markedly increased their breath  $^{13}\text{CO}_2$  content for the remainder of the day. In contrast, women with PCOS showed little  $^{12}\text{CO}_2$  enrichment in their breath sample on waking, and little change in  $^{13}\text{CO}_2$  content across the remainder of the day, despite receiving comparable nutrition to controls and remaining in the same controlled environment. PCOS women thus exhibited a form of metabolic inflexibility, or a diminished ability to switch from protein and carbohydrate to fat oxidation, a key feature of metabolically challenged conditions, such as type 2 diabetes mellitus and many cancers, but also of normal physiological states, such as the luteal phase of the menstrual cycle. Interestingly, PCOS women show a positive correlational trend between nighttime urinary nitrogen excretion and circulating testosterone, suggesting amino acids as preferential carbon sources for energy metabolism when lipid utilization diminishes and hyperandrogenism prevails.

**ANDROGEN  
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Untargeted nuclear magnetic resonance (NMR) metabolomics were additionally used to obtain unbiased identification and quantification of small molecules in overnight fasted serum samples and following a standard 2-hour oral glucose tolerance test (2hOGTT). Molecular concentration differences showed subtle, but distinct, differences in lipid and amino acid/glucose metabolism, with increased energy substrate use of ketogenically derived amino acids and glucose in PCOS women after an overnight fast. 2hOGTT metabolite changes were suggestive of impaired glucose and fat metabolism in PCOS.

3. What do you think is the importance of this finding in the mechanism of PCOS pathogenesis?

David Abbott: The diminished use of lipid as an energy substrate suggests a fat sparing phenotype for PCOS women. As circulating testosterone levels were positively linked to amino acid oxidation, a compensatory energy substrate for lipid, I'm afraid fat sparing could be either an originating pathology in PCOS or a consequence of hyperandrogenism. Fat sparing certainly provides a new twist in support of the thrifty genotype or phenotype origins that have long been linked to PCOS. I don't think the molecular insight we gained, however, provides a unique signature for PCOS. Fat sparing appears to occur when there is high demand for lipid synthesis, shunting glucose metabolism more towards cholesterol synthesis than energy metabolism, hence the compensatory engagement of amino acids as fasting energy substrates.

4. How do you think that such PCOS-related changes in metabolism alter fat accumulation and distribution, and contribute to lipotoxicity?

David Abbott: A fat sparing phenotype should increase lipid accumulation. Its distribution may well depend on a variety of factors, including sex, age, reproductive condition and family history. However, as compensatory use of amino acids as fasting energy substrates positively associates with circulating testosterone levels in PCOS women, and androgens impair adipogenesis, increased lipid accumulation occurring in tandem with diminished capacity for lipid storage could lead to ectopic lipid accumulation in organs such as the liver and pancreas, and widespread lipotoxicity. In the ovary, fat sparing could diminish use of lipid as an energy substrate during oocyte maturation and compromise the quality of eggs obtained during natural or IVF-related cycles.