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JUNE NEWSLETTER: FOCUS ON METABOLIC FLEXIBILITY IN PCOS

The June newsletter is dedicated to metabolic flexibility in PCOS.

Daniel Dumesic, Professor of Reproductive Endocrinology at UCLA, Los Angele, USA, previous President of AEPCOS Society and member of the editorial board, has interviewed Paolo Moghetti, M.D., Associate Professor of Endocrinology at University of Verona, Italy. Paolo is member of AEPCOS Society from its foundation in 2002 and has recently published a paper in JCEM (2013 June; 98:2581-8) on this issue. The first author of the paper is Dr. Daniela Di Sarra.

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@aesociety.org

The updated preliminary program of 11th Annual Meeting of AEPCOS Society is reported with some specific information about transportation to Newport.

Some information about next AEPCOS Update meeting in Brazil and a picture from AACE-AEPCOS joint session in Phoenix, AZ, USA are presented, too.

VOLUME 1, ISSUE 5	Editorial Board		
JUNE 30, 2013	Enrico Carmina, M.D., Palermo, Italy		
In this issue:	Tracy Bekx, M.D., Madison, WI, USA		
	Daniel Dumesic M.D., Los Angeles, CA, USA		
	Joop Laven, M.D., Rotterdam, The Netherlands		
* Metabolic flexibility in PCOS	Jan McAllister, Ph.D., Hershey, PA, USA		
* 11th AEPCOS Annual Meeting	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. A block of rooms at very competitive prices has been reserved for people attending the meeting. To get these special prices, rooms should be booked by AEPCOS office before September 16, 2013.

Abstract deadline is August 2, 2013. For abstract form, registration or hotel booking please connect to: www.ae-society.org or 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

Diagnosis and Treatment of Female Androgenic Hair Loss in PCOS and its frequent association with telogen effluvium

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

Improving randomized clinical trials in infertility

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— Is there a cardiovascular risk paradox in PCOS?

Alice Chang-Rochester, USA

Influence of aging on CVD risk in PCOS

Enrico Carmina—Palermo, ITALY

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

To be announced

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 AEPCOS ANNUAL MEETING

REGISTRATION ONLY

AEPCOS members \$260	Non AEPCOS members \$360
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NEWPORT HYATT REGENCY RESORT

	\$219 for night _	October 16	October 1	7October 18	i	
Payment amount: S				VISAMaster Expiration date:		
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Online payment	nline payment To safely pay online, connect to: www.ae-society.org neck payment Make checks payable to Androgen Excess Society					
Check payment Email, mail or fax the suite 10, 90139 Pale	e registration form	to: Androgen Exc	cess & PCOS	Society, via delle	Croci 47, 1st floor,	

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.

TRANSPORTATION TO/FROM NEWPORT

BY AIR

T.F. Green Airport - Warwick, RI (26 miles/35 minutes)

Airlines - Serviced by all major domestic airlines

Car Rental Agencies - Serviced by all major car rental companies

Public Transportation - Cozy Cab or RIPTA

Cozy Cab operates scheduled shuttle van service between T F Green Airport and Newport RI, with service every two hours from 7 am to 10 pm, and hourly service on Friday and Sunday. Additional trips run daily at 5 am and 12 midnight. Fare is \$20 per person, one-way. Call 1-401-846-2500 or 1-800-846-1502 for reservations.

BY RAIL

Amtrak Kingston Station - West Kingston, RI (18 miles/30 minutes)

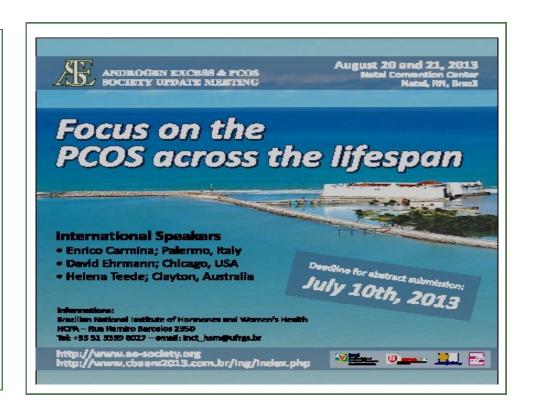
Public Transportation - Reserved Car Service (401) 295-1100 or RIPTA

BY CAR

From New York City, take I-95 to the third Newport exit, picking up Route 138 east (which joins briefly with Rte. 4) and crossing the Newport toll bridge slightly north of the downtown district.

From Boston (75 miles), take Route 24 through Fall River, picking up route 114.into town.

AEPCOS UPDATE MEETING NATAL, BRAZIL, AUGUST 20-21, 2013



A PICTURE FROM AACE/AEPCOS JOINT SESSION

The picture shows the participants to the AACE/AEPCOS joint session at the AACE Annual Meeting (Phoenix, AZ, USA, May 1-5, 2013).

The joint meeting was dedicated to clinical aspects of PCOS syndrome, including diagnosis of PCOS in adolescence, cardiovascular risk in PCOS, and changes of ovarian function and cardiovascular risk from infancy to menopause

From left; Neil Goodman, M.D., Chairman of the session, Rhoda Cobin, M.D., Past President of AACE, Patricia Vuguin, M.D., Walter Futterweit, M.D., Past-Past President of AEPCOS Society and Enrico Carmina, M.D., Executive Director of AEPCOS Society.



ANDROGEN EXCESS & PCOS SOCIETY

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Paolo Moghetti, M.D.

METABOLIC FLEXIBILITY

IN PCOS

Daniel Dumesic, M.D., has interviewed Paolo Moghetti, M.D., Associate Professor of Endocrinology at the University of Verona, Italy, about his recent study on metabolic flexibility in PCOS.

1. Paolo, your research shows that impaired insulin-stimulated glucose oxidation (metabolic inflexibility) in PCOS women is related to both insulin resistance and hyperandrogenism. Why is metabolic inflexibility important in PCOS and do you think it plays a role in the control of body weight?

Our study demonstrated that PCOS women have an impairment in their metabolic plasticity, i.e. in the physiological ability of the body to modify the type of substrates selected for fulfilling tissue energy demands according to the conditions occurring at any specific time. Although it is not easy to have a comprehensive view of the implications of this defect in metabolic adaptation, a series of consequences can be hypothesized.

In other conditions characterized by insulin resistance, such as obesity and type 2 diabetes, this phenomenon has been linked to the metabolic syndrome, which is a common finding in PCOS women. Furthermore, it has been linked to non-alcoholic fatty liver disease, which also seems to be common in these women. Both these conditions have several, relevant clinical implications.

We do not know whether metabolic inflexibility is more specifically linked to PCOS. However, the independent association we have found between this metabolic abnormality and serum free testosterone levels, after adjusting for a number of potential confounders, such as age, total fat mass, fat distribution, indices of insulin resistance at both the muscle and adipose tissue level, and glucose tolerance, suggests that there may be some specific relationships. Although at present these relationships remain speculative, hopefully our findings will stimulate further research on this topic.

As regards the possible role of abnormalities in metabolic flexibility in the control of body weight, there is evidence that in obese individuals baseline fat oxidation is reduced, and switching from low- to high-fat oxidation in response to high-fat feeding is blunted. A decreased fat oxidation can lead in turn to the depletion of glycogen stores with stimulation of appetite and increased energy intake, thus favouring weight gain. Interestingly, it was found that ectopic rather than peripheral fat storage can be more strongly linked to a reduced metabolic flexibility. Another interesting issue is that physical activity enhances metabolic flexibility during a high-fat diet, suggesting that regular exercise could be particularly important in counteracting this phenomenon in PCOS women.

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2. Again we see an interesting "chicken-and-the-egg" relationship between PCOS-related metabolic dysfunction and reproductive as well as endocrine abnormalities. Do you think that metabolic inflexibility in PCOS is the cause or effect of insulin resistance and hyperandrogenism?

It is very difficult to answer this intriguing question. To observe an association does not necessarily mean there is a cause-effect relationship, and any attempt to establish a direction in these relationships is even more challenging. However, we can hypothesize a bi-directional link between metabolic inflexibility and both insulin resistance and hyperandrogenism.

In particular, this defect in metabolic adaptation may theoretically be both effect and cause of the impaired insulin action. As an example of the very complex and bi-directional relationships we are facing, an impaired response to insulin means also a reduced ability of tissues to increase carbohydrate oxidation during hyperinsulinemia, with reduced metabolic flexibility. However, it has been hypothesized that metabolic inflexibility may lead to ectopic fat accumulation, which in turn may cause further progression of insulin resistance.

Similarly, several experimental data support the hypothesis of a primitive effect of androgen excess on substrate oxidation. Nonetheless, we cannot rule out the hypothesis that abnormalities of androgen secretion may be triggered by metabolic alterations and/or changes in adipokine secretion linked to these alterations.

Overall, we must conclude that we are still in a brainstorming phase of knowledge about the role of metabolic inflexibility in PCOS subjects. I think we would need prospective studies starting at the very early stages in PCOS women lives to provide insight into the mechanisms underlying this phenomenon and its consequences. The abnormalities found in the chick and their changes over time may help us to understand the beginning and the end of the story.

3. I notice that metabolic inflexibility in PCOS is associated with several anthropometric, endocrine and metabolic features, including BMI, waist circumference and total-body fat mass. Did you notice a similar pattern of metabolic inflexibility in the subgroup of PCOS women who were non obese?

The sample size of our study was relatively small for this subanalysis. Nonetheless, in non obese women a similar pattern was observed for relationships between metabolic flexibility and insulin sensitivity. There was also a tendency for an association with free testosterone, although it did not reach statistical significance. Conversely, no relationships were found with anthropometric features.