AEPCOS NEWSLETTER

ANDROGEN EXCESS & PCOS SOCIETY

NOVEMBER 2014 NEWSLETTER

PRESIDENTIAL LETTER

This issue newsletter reports the letter to AEPCOS members of new President of the society, Anuja Dokras. Anuja is Professor of Obstetrics and Gynecology at Pennsylvania University, Philadelphia, PA, USA.
Information about the update meeting on AMH that will be held in San Diego next March and the 13th Annual Meeting of AEPCOS Society that will be held in Sicily, Italy, October 4-6, 2015 are also presented. A few pictures of last Annual Meeting have been added..

For the scientific section of the newsletter, Poli Mara Spritzer, M.D., Professor at Federal University of Rio Grande do Sul, Porto Alegre, Brazil and member of the editorial board, has interviewed Ricardo Azziz, M.D., about fat to lean mass ratio in PCOS. Ricardo is President of Georgia Regent University, Augusta, GA, USA.

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In this issue:

FORTHCOMING AEPCOS MEETINGS

- **Update Meeting of AEPCOS Society, San Diego, CA, USA, March 5, 2015**
- **Update Meeting of AEPCOS Society, Gdansk, Poland, June 12-13, 2015**
- **13th Annual Meeting of AEPCOS Society, Palermo, Italy, October 4-6, 2015**
- **14th Annual Meeting of AEPCOS Society, Australia, November 2016**

LETTER TO AEPCOS MEMBERS OF THE NEW

Dear AE-PCOS members,

It is an honor and privilege to be the President of the AE-PCOS Society for the 2014-2015 term. As you know, this is an international society whose membership includes foremost scientific and clinical leaders in the field of androgen excess and PCOS. Their expertise covers the entire female lifespan including prenatal androgen exposure; pediatrics; reproductive and post-menopausal age. Also, the Society provides a vital forum for researchers who study several animal models of androgen excess, conduct high quality bench studies, and engage in large scale clinical trials.

Since its inception, the AE-PCOS Society has had a tremendous impact on clinical practice by publishing several guidelines and recommendation papers. In its annual meetings, the Society provides opportunities for thriving scientific discussions; during its many satellite meetings, we organize updates on recent developments in the field. We have an exciting line-up of events for the upcoming year. Our update meeting will be held in March in San Diego, USA during the ENDO meeting, and our annual meeting will be held in October in Palermo, Italy. Please do mark these dates in your calendar.

I would like to dedicate this year as the "Year of the Patient."To further that message, we will engage in projects such as associating directly with patient support groups in different countries and via our website (that we will be updating). Our objective will be to participate in and support activities that increase an awareness of PCOS and improve access to its treatment. These efforts have already been started by the AE-PCOS society, with plans to reach out to patients across the globe.

I am counting on your enthusiastic support and contribution for a host of AE-PCOS Society activities this year.

Sincerely,

Anuja Dokras, MD., PhD.

Professor of Obstetrics and Gynecology

Director of PENN PCOS Center

University of Pennsylvania, Philadelphia, USA

AEPCOS UPDATE MEETING ON AMH IN ANDROGEN EXCESS DISORDERS

March 5, 2015, in San Diego, CA, USA, during the Annual Meeting of Endocrine Society, AEPCOS Society organizes an update meeting on AMH in Androgen Excess Disorders that will be held during a dinner cruise around San Diego Bay.

The cruise will start at 7:00 pm and will finish around 10:00 pm.

The preliminary program of the meeting includes lectures on AMH role in ovarian function and its measurement during infancy and puberty. A debate on use of AMH assay for PCOS diagnosis will conclude this update meeting.

Because the boat may accommodate only 120 seated passengers, pre-registration is requested.

Until February 15, 2015, registration fee for AEPCOS members is only $20 (the regular cost of the cruise without dinner is $110) while the fee for non AEPCOS members is $80. After February 15, 2015, for both members and non members, the registration fee will increase to $120.

For further information and registration form please consult our website: www.ae-society.org or contact enrico.carmina@ae-society.org or info@ae-society.org

13th ANNUAL MEETING OF AEPCOS SOCIETY

Next annual meeting of AEPCOS Society will be held October 4-6, 2015 in Sicily, ITALY.

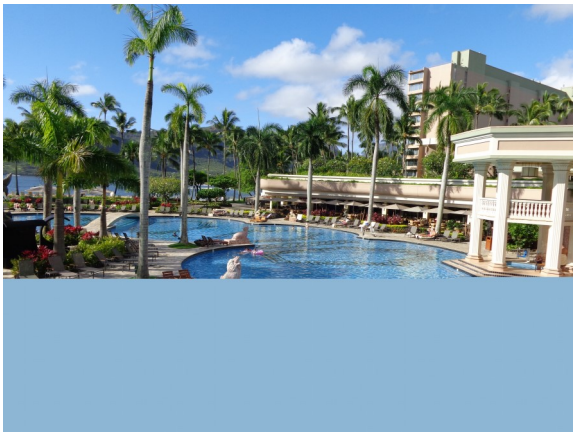
The exact venue and the preliminary program will be available from March 2015. For further information, please check our website or contact: enrico.carmina@ae-society.org

Pictures of Sicily, Italy

OTHER FUTURE MEETINGS

- Endocrine Society, San Diego, CA, USA, March 5-8, 2015
- Pacific Coast Reproductive Society, Rancho Mirage, CA, USA, March 11-15, 2015
- European Society of Endocrinology, Dublin, Ireland, May 16-20, 2015
- ESHRE, Lisbon, Portugal, June 14-17, 2015
- European Society Pediatric Endocrinology, Barcelona, Spain, September 9-12, 2015

PICTURES FROM 12TH ANNUAL MEETING OF AEPCOS SOCIETY



All pictures have been provided by Doctor Futterweit. From top: Daniel Dumesic giving his talk, David Abbott speaking, Walter Futterweit during a break, Walter Futterweit with Enrico Carmina and Rosa Alba Longo, one of the swimming pools of the resort.

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Ricardo Azziz, M.D., Ph.D.

FAT TO LEAN MASS RATIO AMD METABOLIC DYSFUNCTION IN PCOS

The scientific part of the newsletter is dedicated to a study on fat/lean mass ratio in PCOS. Editorial board member Professor Poli Mara Spritzer has interviewed Professor Ricardo Azziz who co-authored the paper recently published on Human Reproduction (*Ezeh U, Pall M, Mathur R, Azziz R. Association of fat to lean mass ratio with metabolic dysfunction in women with polycystic ovary syndrome. Hum Reprod. 2014; 29:1508-17)*

1. *Ricardo,What was the main question that motivated this study?*

Most (~70-75%) of women with PCOS have insulin resistance (IR) greater than wouldbe predicted by their body mass. In turn, the IR of PCOS is associated with compensatory hyperinsulinemia (HI), which is in part responsible for the hyperandrogenism of the disorder. In fact, hyperandrogenism, whether degree of hyperandrogenemia or hirsutism, is more closely associated with the degree of IR/HI than any other parameters, other than obesity. Understanding the mechanisms underlying the IR/HI of PCOS would then allow us to develop new and better targeted therapies for this and other IR-related disorders.

In a previous study (*Ezeh et al. J Clin Endocrinol Metab 98:1541–1548, 2013*), we demonstrated that PCOS women had lower mean insulin sensitivity (Si, reflecting whole-body insulin-mediated glucose uptake or IMGU), but similar glucose effectiveness (Sg, reflecting whole-body non-insulin-mediated glucose uptake or NIMGU), as assessed by the frequently sampled intravenous glucose tolerance test (FSIVGTT), as controls. However, the decreased IMGU in PCOS was not accompanied by a compensatory increase in NIMGU. As had others, PCOS women demonstrated a similar distribution in visceral (VAT) and subcutaneous adipose tissue (SAT) content as body mass-matched controls. In PCOS, VAT and SAT independently and negatively predicted Si and Sg, respectively. However, the association between Sg and VAT in PCOS was lost after adjusting for SAT, leaving SAT as the stronger independent and negative predictor of Sg (NIMGU) in these women. Alternatively, in PCOS, VAT was found to be the stronger independent determinant of Si (IMGU). In controls, SAT, but not VAT, correlated negatively with Si, and neither VAT nor SAT was an independent predictor of Sg.

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Overall, this study indicated that the IR of PCOS was not associated with differences in VAT and SAT distribution with controls, nor was it associated with differences in NIMGU, except for those PCOS with severe insulin resistance where NIMGU was also compromised. Thus, we then asked the question, perhaps the difference in IR between PCOS and body mass-matched controls lies in differences in their total fat to lean body mass (F/L), considering that we and others have observed possible evidence of abnormal adipogenesis in PCOS, the well documented evidence that excess total fat mass is strongly associated with increased IR.

2. Could you state your most important findings?

Our results indicate firstly that, compared to body mass-matched controls, women with PCOS demonstrate abnormal body composition characterized by a greater percent body fat, body fat mass, and increased ratio of fat to lean mass(F/L ratio), which is independently associated with differences in the values of metabolic dysfunction in basal state (fasting insulin, HOMA-IR and HOMA-%β-cell) between PCOS and controls, suggesting that the higher degrees of metabolic dysfunction in PCOS patients may be, at least in part, be attributable to their higher F/L ratio.

Secondly, these findings were confirmed by assessment of metabolic dysfunction in dynamic state (using an FSIVGTT) whereby Si and acute insulin response to glucose (AIRg), were negatively and positively related to the F/L ratio in both PCOS and controls. Only in PCOS women did the F/L tend to negatively correlate with Sg, although this association did not reach significance. Thirdly, although the F/L ratio and WHR are highly confounded, our data indicate that the F/L ratio predicted metabolic dysfunction more effectively than WHR in multivariate models.

Of note, the increased F/L ratio observed in PCOS compared to controls was relatively modest, indicating that this difference in body composition alone is not sufficient to account for the significantly increased IR observed in PCOS.

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In fact, other studies from our laboratory have indicated that while the degree of obesity observed in PCOS is exaggerated through referral bias (*Ezeh et al. J Clin Endocrinol Metab. 2013;98:E1088-96*), adipose tissue itself, at least that which is subcutaneous, is highly dysfunctional in PCOS, with significant defects in adipocytokines regulation, micro-RNA function, and GLUT-4 content and expression, among other defects (*Chazenbalk et al, J Clin Endocrinol Metab. 2010;95:935-42; Chazenbalket al. J Clin Endocrinol Metab. 2012;97:E765-70; Chen et al. Diabetes. 2013;62:2278-86;Wu et al. J Clin Endocrinol Metab. 2014, Epub ahead of print*).

3. *What could be the implications of your findings to daily practice regarding the use of the F/L ratio for weight management recommendations of PCOS patients?*

Our report highlights the limitations of the body mass index (BMI) as a marker of metabolic dysfunction dues to its inability to distinguish between fat and lean body mass, and highlights the possible use of the F/L ratio as an alternative surrogate marker of IR.
Our report further suggests that efforts to increase lean body mass, through strength training, and the like, could have a greater beneficial effect in PCOS women than normal.
Furthermore, this report suggest that perhaps wider use of total body bioelectrical impedance analysis (BIA), an easy office-based procedure to perform, could be used to assess F/L and so better target life-style counseling for PCOS patients.

4. *What additional studies would be needed?*

These data need to be confirmed in larger studies. Furthermore, a more detailed assessment of the contribution of regional adipose tissue sub-compartments to the disparity in F/L is also needed.
Finally, prospective controlled comparative clinical trials assessing the effects of weight training aimed at increased muscle (lean) mass on insulin sensitivity and metabolic status, and the benefit of using BIA to select such patients, is needed