

AEPCOS NEWSLETTER

ANDROGEN EXCESS & PCOS SOCIETY

Spring 2017 newsletter

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- This issue newsletter features a detailed summary of the AEPCOS/Endocrine Society Update Meeting, held in Orlando, Florida, USA on March 31.

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- * Details and Program for upcoming AEPCOS Annual Meeting!

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FORTHCOMING AEPCOS MEETINGS

- 15th AEPCOS Annual Meeting, San Antonio, Texas, USA, October 26-27, 2017
- Postgraduate course at ASRM (following AEPCOS Annual meeting), San Antonio, Texas, USA, October 29, 2017. Practical Management of PCOS: From Fertility to Long-term Health.

AEPCOS/Endocrine Society Update Meeting

Orlando, Florida, United States of America—March 31, 2017

Summarized by David Abbott, PhD, and Elisabet Stener-Victorin, PhD

This was the first AEPCOS Update meeting to be held in official collaboration with the Annual Meeting of the Endocrine Society, thanks to an initiative led by our Senior Executive Director, Ricardo Azziz (Albany, USA). Registration, abstract submission and hotel accommodation were arranged through the ENDO 2017 webpage, and for this year only, also through AEPCOS. In 2018, it is planned to fully integrate this process and meeting program within the ENDO webpage and smart phone meeting App.

The meeting, organized by the AEPCOS Board-appointed Update Meeting Program Committee of David Abbott (Chair; Madison, USA), Elisabet Stener-Victorin (Stockholm, Sweden) and Antoni Duleba (San Diego, USA), was designed to focus on “Gut, Microbiome and Fat: Origins of PCOS Metabolic Disease?”, have only oral presentations, and to push the envelope of clinical and basic science understanding surrounding the pathogenesis of metabolic disease in women with PCOS and in animal models. Just over 100 delegates attended and unsolicited positive feedback strongly encouraged continuing such topic-focused meetings affiliated with ENDO that intermingle clinical and basic presentations, generating audience-engaged discussion and debate.

The first session of the morning, “The Gut Microbiome and PCOS” was chaired by Elisabet Stener-Victorin. The first speaker was Bulent Yildiz (Ankara, Turkey), who gave an introduction and general overview to the field of gut microbiome in women with PCOS with his lecture “Gut-brain axis and metabolism in PCOS”. He described how gut, brain and metabolism are highly related with each other in obesity and diabetes, as well as in PCOS, and how the central nervous system regulates food intake through complex interactions of homeostatic and hedonic systems, with the gastrointestinal system contributing to food intake and metabolism via orexigenic and anorexigenic gastrointestinal hormones. Alterations in gut microbiota and possible interactions with gut-brain axis in PCOS is a topic of interest and preliminary data from animal models and humans suggest alterations in gut microbiota. He ended his talk with the statement that understanding the relationship between PCOS and homeostatic and hedonic systems, gastrointestinal hormones and gut microbiota, as well as potential effects of different therapeutic interventions on these systems, will provide further understanding and novel treatment opportunities for women with PCOS.

This lecture was followed by Lisa Lindheim (Graz, Austria), highlighting that as of March, 2017, there are only 8 publications related to gut microbiome in PCOS. Lisa’s group were the first to publish an original research paper demonstrating how alterations in gut microbiome composition and barrier function are associated with reproductive and metabolic defects in women with PCOS. They found a loss of fecal bacterial diversity and changes in bacterial community composition in women with PCOS. Further, increased intestinal permeability correlated with bacterial diversity. To get a better understanding of the mechanisms connecting the gut microbiome and PCOS,

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City of Orlando - Photo Credit: Javier C. Acosta

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she continued her studies in a mouse model of PCOS combining diet-induced obesity with prenatal androgenization. She found that both maternal androgen exposure and high-fat/high sugar (HF/HS) diet affect bacterial richness in a sex-dependent manner, whereas HF/HS diet, rather than androgen exposure, affects fecal bacterial profiles. By performing fecal microbial transplantation (FMT) from offspring exposed to maternal androgens and HF/HS diet with altered reproductive and behavior function, her group investigated whether dysbiosis of the gut microbiome causes these abnormalities. The FMT transferred bacterial richness and taxonomic features of the disease model, but did not transfer the PCOS-like phenotype observed in donor mice. This PCOS-like mouse phenotype was therefore not caused by a microbiome-dependent mechanism.

The morning session concluded with Varykina Thackray (San Diego, USA) demonstrating how adult, partial aromatase inhibition (AI) in female mice induces PCOS-like traits and altered gut microbiome. Letrozole-induced AI in exposed mice caused substantial reduction in bacterial richness and a decreased relative abundance of specific Bacteroidetes and Firmicutes. Of note, these observations are consistent with differences in gut microbiome between PCOS and healthy women reported by Lisa Lindheim in the immediately preceding talk.

Enrico Carmina (Executive Director and CEO; Palermo, Italy) and Bulent Yildiz then chaired the first short oral presentation session led off by Jennifer Hill (Toledo, USA). She employed a prenatal androgenization rat model to alter maternal microbiome and cause PCOS-like traits in adult female offspring with accompanying hypertension and delayed onset of puberty. Manuel Doblado (San Diego, USA) demonstrated that administering inflammatory response-inducing lipopolysaccharide (LPS) and interleukin 1-beta to human ovarian theca cells in culture enhanced expression of the androgen biosynthetic enzyme, CYP17A1, increased release of testosterone (T) and accelerated theca cell proliferation, suggesting a causal link between inflammatory response and ovarian hyperandrogenism. Oleg Varlamov (Beaverton, USA) reported on how pubertal onset of exogenous T treatment in female nonhuman primates, with or without accompanying Western-style diet, diminished lipolysis in both abdominal subcutaneous and visceral fat, likely contributing to increased body mass index and adiposity compared to control monkeys. Western style diet exaggerated increased adiposity and insulin resistance in T-exposed monkeys. Milana Kokosar (Gothenburg, Sweden) showed that a single bout of electroacupuncture causing muscle contractions, increased whole-body glucose uptake, an effect that in part was mediated via epigenetic and transcriptional changes in adipose tissue in women with PCOS. The effect could be partially blocked by administration of alpha and beta adrenergic receptor antagonists in female rats. Balasz Legesa (Bern, Switzerland) finished off the morning session demonstrating how metformin diminished the androgenic phenotype of a human adrenal cortex cell line in favor of increased glucocorticoid release, suggesting an additional beneficial outcome of such insulin sensitizer treatment in women with PCOS.



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To start the afternoon, Stephen Franks (London, UK) and Anuja Dokras (Philadelphia, USA) chaired the second short oral presentation session, led off by Emilia Koivuaho (Oulu, Finland) showing that in her study population, term birthweight was reduced in women who developed PCOS as adults, and that the more severe the adult PCOS symptomology, the lower the birthweight of the subjects. The women with more severe PCOS symptomology also exhibited earlier age at onset of growth and adiposity rebound childhood, and the earlier age of onset predicted increased BMI in adulthood, suggesting potential benefits may result from targeted early lifestyle intervention by pediatricians. Liv Guro Hanem (Trondheim, Norway) demonstrated the power of a 4-year follow-up study to reveal increased fetal and neonatal head and brain size in daughters of PCOS women who received the insulin sensitizer, metformin, during the 2nd and 3rd trimesters of pregnancy in comparison to daughters of PCOS women who did not. Whether this indicates prevention of modestly diminished brain size or metformin-induced enlargement remains to be determined. Kajalben Buddhev (Omaha, USA) illustrated how more rapid early weight loss following gastric sleeve gastrectomy best predicts long-term maintenance of weight loss in obese, mainly PCOS, women. Manuel Maliqueo (Santiago, Chile) guided us through how maternal obesity alters the circulating sex steroid profile as measured by LC-MS/MS, and placenta mRNA and protein expression of steroidogenic enzymes. Circulating testosterone was higher in obese women carrying a male fetus, both in first and third trimesters compared with normal-weight women, as well as diminished placenta protein expression of P450 aromatase. These results suggested that maternal obesity altered the sex steroid profile during pregnancy, which may be related to fetal gender and associated with modifications in the expression of placental steroidogenic enzymes.

The second afternoon session, “Altered Adipose in PCOS”, chaired by David Abbott commenced with a presentation from Anna Benrick (Gothenburg, Sweden) demonstrating how whole-body overexpression of adiponectin, an adipocyte derived hormone, protected female mice from pubertal onset, DHT-induced metabolic dysfunction, but not from anovulation. The findings hold promise for novel, adiponectin-based, anti-inflammatory therapeutic approaches to diminish the risk of cardiometabolic disease in PCOS women. Stephen Franks provided new evidence for reduced postprandial energy utilization in a prenatally androgenized sheep model for PCOS and that elevated circulating levels of DHT accompany diminished thermogenic function in brown fat. Zi-Chang Chen (Shandong, China) convincingly demonstrated that transplantation of brown adipose into rodent models of obesity or PCOS counteracted weight gain or PCOS-like traits, including LH and testosterone levels. These results provided additional evidence for a potential therapeutic role of increasing energy utilization in obese and overweight women to combat severity PCOS symptomology. Daniel Dumesic (Los Angeles, USA) rounded off the session illustrating how androgen receptor-mediated constraint and dysregulation of adipogenesis in abdominal subcutaneous white adipose in women with PCOS potentially diminishes their ability to safely store lipid as BMI increases, making PCOS women more susceptible to progressive insulin resistance and its cardiometabolic sequelae.

Antoni Duleba chaired a rousing closing debate between Hector Escobar-Morreale (Madrid, Spain) and Ricardo Azziz speaking, respectively, in support and against the motion “Altered gut microbiome contributes to metabolic disease in women with PCOS”. The cogent arguments, interspersed with highly appreciated humor, energized audience discussion and revealed how little we understand about the causes and consequences of differences in gut microbiome, and that we clearly need to demonstrate direct causal consequences for microbiome-induced impairments to cardiometabolic health. Enrico Carmina closed the meeting by inviting all to attend the 2017 Annual Meeting of AEPCOS in San Antonio on October 27-28, and the 2018 Annual Meeting in Stockholm, Sweden.

Thanks to all for a wonderful update meeting!

RESEARCHER HIGHLIGHT—Melanie Gibson-Helm, PhD

Delayed Diagnosis, Lack of Information & Dissatisfaction in PCOS Women

Can you tell me about your research interests in PCOS? My research interests in PCOS focus on identifying evidence-practice gaps in PCOS healthcare and ways to address them. I am also particularly interested in the psychological aspects of PCOS.

You and your co-authors had a paper published in JCEM on patient experiences with PCOS diagnosis.

What were the key findings of this paper? This international paper reports survey responses from 1385 women living in 32 different countries. Nearly half of the participating women saw three or more health professionals before a PCOS diagnosis was established and for one third this took longer than two years. Less than one quarter were satisfied with the information they were given at diagnosis about lifestyle management or medical therapy. Over half reported not receiving any information about long-term complications or emotional support and counselling. After taking into account time since diagnosis, age and world region of residence, we found that satisfaction with the information women received at diagnosis was associated with greater overall satisfaction with their diagnosis experience. Seeing ≥ 5 health professionals and a longer time to diagnosis (>6 months) were both negatively associated with diagnosis satisfaction. Women's leading concerns related to PCOS were difficulty losing weight, irregular menstrual cycles, infertility and hirsutism, although these varied with age and world region.

Reflecting on these findings, how can health care professionals improve patient experience in PCOS diagnosis? Delays in PCOS diagnosis are lost opportunities for management and prevention. Women with undiagnosed PCOS may see different healthcare providers depending on their primary concern. So it's important that general practitioners, dermatologists, nurses and allied healthcare practitioners are also aware of the features of PCOS, in addition to endocrinologists and gynaecologists.

Women want to receive good quality information about the full range of PCOS features at the time of diagnosis. But it is also important to provide a range of options for accessing information and support (multidisciplinary healthcare, websites, leaflets and support groups) so women can choose the information that is relevant to their individual needs, concerns and health literacy.

Another key aspect is asking women about their individual concerns, helping them to prioritise their concerns and using this discussion to guide the co-development of management strategies.

What support do health professionals need? Health professionals need support to know what information sources to which they can confidently refer women. There is a role for PCOS experts in rigorously evaluating the quality of currently available information and co-developing evidence-based resources with women with PCOS.

Reference: Gibson-Helm M, Teede H, Dunaif A, Dokras A. Delayed Diagnosis and a Lack of Information Associated with Dissatisfaction in Women with Polycystic Ovary Syndrome. *J Clin Endocrinol Metab* 2017 102(2): 604-12.



Melanie Gibson-Helm, PhD

Enhanced Partnership with ASRM

AEPCOS has entered into an enhanced partnership with the Androgen Excess Special Interest Group (AESIG) of the American Society of Reproductive Medicine (ASRM). Some highlights of the agreement include:

- AEPCOS will appoint an annual AESIG Chair
- AEPCOS will enlist a volunteer to act as moderator for an online androgen excess/PCOS community forum
- AEPCOS will work with AESIG to develop a Pre-Congress Course to be held prior the ASRM annual meeting
- AEPCOS will organize its Annual Meeting in conjunction with the ASRM Annual Meeting every other year, beginning in 2017 (details below!)
- AEPCOS/AESIG members may moderate relevant sessions during the ASRM Annual Meeting

FORTHCOMING MEETING: Call for Abstracts!

- 15th Annual Meeting
- Valencia Riverwalk Hotel, San Antonio, TX USA—October 26-28, 2017
- Read on to peruse the preliminary program ...
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- **Abstract submission deadline: 23:00 PST July 23, 2017**
- Two Baumgartner-Azziz travel awards are available for top scoring abstracts by young researchers (<35 years).
- Abstract form available on AEPCOS website
- Abstracts should be sent to info@ae-society.org

This meeting is organized to precede the Annual Meeting of the American Society of Reproductive Medicine, also in San Antonio You may get more details at our website: www.ae-society.org

AEPCOS Annual Meeting Program

Thursday, October 26, 2017		
Time	Speaker	Topic
4:00 – 6:30 pm	REGISTRATION	
5:00 – 6:00 pm	TBA	MEET THE PROFESSOR SESSION
7:00 – 9:00 pm	WELCOME DINNER	

Friday, October 27, 2017		
Time	Speaker	Topic
7:30 - 10:00 am	REGISTRATION	-
8:30 - 8:40 am	ANTONI DULEBA <i>Chair of the Annual Meeting Committee</i> HELENA TEEDE <i>President of AEPCOS Society</i>	WELCOME
8:40 - 9:40 am	Chair: TBA	SESSION I: DEBATE: DOES PCOS LEAD TO ADVERSE CARDIOVASCULAR OUTCOMES?
8:40 - 9:00 am	ANUJA DOKRAS, M.D., Ph.D. <i>Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA</i>	YES, PCOS LEADS TO ADVERSE CARDIOVASCULAR OUTCOMES
9:00 - 9:20 am	RICHARD LEGRO, M.D. <i>Department of Obstetrics and Gynecology Pennsylvania State University School of Medicine, Hershey, PA, USA</i>	NO. PCOS DOES NOT LEAD TO ADVERSE CARDIOVASCULAR OUTCOMES
9:20 - 9:40 am	GENERAL DEBATE	

AEPCOS Annual Meeting Program

9:40 - 11:00 am	Chairs: TBA	SESSION II: ORAL PRESENTATIONS – TBA
11:00 - 11:30 am	COFFEE BREAK	
11:30 am -1:00 pm	Chairs: TBA	SESSION III: PATHOPHYSIOLOGY OF PCOS
	11:30 am- 12:00 pm	DAVID ABBOTT, Ph.D. <i>Wisconsin National Primate Research Center and Department of Obstetrics and Gynecology, University of Wisconsin, Madison, WI, USA</i>
	12:00 – 12:30 pm	WIEBKE ARTL, M.D., D.Sc. <i>University of Birmingham, Birmingham, UK</i>
	12:30 – 1:00 pm	ANTONI J DULEBA, M.D. <i>Department of Reproductive Medicine, University of California, San Diego, La Jolla, CA, USA</i>
1:00-2:30 pm		BREAK

2:30 - 3:30 pm	Chairs: TBA	SESSION IV: ORAL PRESENTATIONS - II
3:30 - 5:30 pm	Chairs: TBA	SESSION V: MANAGEMENT OF PCOS

AEPCOS Annual Meeting Program

	3:30 - 4:00 pm	KIRSTY WALTERS, Ph.D. <i>Women's and Children's Health at the University of New South Wales (UNSW), Sydney, Australia</i>	THE PURSUIT TO DEVELOP MECHANISM-BASED INTERVENTIONS FOR PCOS	
	4:00 - 4:30 pm	ANUJA DOKRAS, M.D., Ph.D. <i>Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, USA</i>	EFFECTS OF LIFESTYLE ON PCOS	
	4:30 - 5:00 pm	ANGELICA LINDEN HIRSCHBERG <i>Department of Obstetrics and Gynecology, Karolinska Institute, Stockholm, Sweden</i>	STEROID HORMONE RECEPTORS AND PROLIFERATION OF THE ENDOMETRIUM IN OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME - EFFECTS OF LIFESTYLE INTERVENTION	
	5:00 - 5:30 pm	RICHARD LEGRO, M.D. <i>Department of Obstetrics and Gynecology Pennsylvania State University School of Medicine, Hershey, PA, USA</i>	OCP AND PROGESTINS IN PCOS: BENEFITS AND HARMS	
	5:30 - 6:30 pm	POSTER SESSION		

Saturday, October 28, 2017		
Time	Speaker	Topic
8:30 - 9:30 am	Chairs: TBA	SESSION VI: ORAL PRESENTATIONS - III
9:30 - 10:00 am	Chairs: TBA	PRESIDENTIAL LECTURE
9:30 - 10:00 am	HELENA TEEDE, M.B.B.S., Ph.D. <i>President of AEPCOS Society</i>	TBA
10:00 - 10:30 am	COFFEE BREAK	

AEPCOS Annual Meeting Program

10:30 - 11:30 am		Chairs: TBA	SESSION VII: DEBATE: OVARY: A VILLAIN OR A VICTIM?
	10:30 - 10:50 am	RICARDO AZZIZ, M.D., M.B.A., M.P.H. <i>The State University of New York System Administration, Albany, NY, USA</i>	THE OVARY IS THE VILLAIN
	10:50 - 11:10 am	ROY HOMBURG, M.D. <i>Homenton University Hospital, Reproductive Medicine, Queen Mary, London University, London, UK</i>	THE OVARY IS A VICTIM
	11:10 - 11:30 am	GENERAL DEBATE	

11:30 am-12:30 pm		Chairs: TBA	SESSION VIII: GENETICS AND EPIGENETICS
	11:30 am-12:00 pm	CORRINE K. WELT, M.D. <i>Department of Internal Medicine, Utah University, Salt Lake City, UT, USA</i>	GENETICS OF MENOPAUSE AND PCOS
	12:00 - 12:30 pm	ELISABET STENER-VICTORIN, Ph.D. <i>Department of Physiology and Pharmacology, Karolinska Institute, Stockholm, Sweden</i>	TRANSCRIPTIONAL AND EPIGENETIC CHANGE IN ADIPOSE TISSUE AND SKELETAL MUSCLE IN WOMEN WITH PCOS
12:30 - 1:00 pm		Chair: RICARDO AZZIZ, M.D., M.B.A., M.P.H. <i>Chief Officer of Academic Health and Hospital Affairs, The State University of New York, Albany, NY, USA</i>	RICARDO AZZIZ DISTINGUISHED CAREER AWARD
	12:30 - 1:00 pm	RICARDO AZZIZ DISTINGUISHED CAREER AWARD RECIPIENT (TBA)	TBA
1:00 - 2:30 pm		BREAK	

AEPCOS Annual Meeting Program

2:30 - 3:30 pm	Chairs: TBA	SESSION IX: SPECIAL SESSION OF ORAL COMMUNICATIONS PEDIATRIC ENDOCRINOLOGY
3:30 - 4:30 pm	Chairs: TBA	SESSION X: PREGNANCY AND PCOS
	3:30 - 4:00 pm	ESZTER VANKY, M.D. <i>Department of Obstetrics and Gynecology, Trondheim University, Trondheim, Norway</i>
	4:00 - 4:30 pm	MANUEL MALIQUEO, M.D. <i>Department of Medicine, University of Chile, Santiago, Chile</i>
	4:30 - 5:00 pm	Chairs: TBA
	4:30 - 5:00 pm	SESSION XI: DEVELOPMENT OF INTERNATIONAL GUIDELINES FOR PCOS DIAGNOSIS AND TREATMENT
	4:30 - 5:00 pm	INTERNATIONAL PANEL Robert Norman, Michael Costello, Anuja Dokras, Joop Laven, Terhi Piltonen, Helena Teede
	5:00 - 5:20 pm	ENRICO CARMINA, M.D. <i>Executive Director and CEO AEPCOS Society</i>
	5:20 - 5:30 pm	ENRICO CARMINA, M.D. <i>Executive Director and CEO AEPCOS Society</i> ELISABET STENER VICTORIN <i>President-Elect of AEPCOS Society</i>
	5:30 - 6:15 pm	ENRICO CARMINA, M.D. <i>Executive Director and CEO AEPCOS Society</i> HELENA TEEDE <i>President of AEPCOS Society</i>
		PRESENT SUCCESS AND FUTURE CHALLENGES OF AEPCOS SOCIETY
		PRESENTATION OF 2018 AEPCOS ANNUAL MEETING STOCKHOLM, SWEDEN
		2017 AEPCOS SOCIETY, INC. ANNUAL BUSINESS MEETING