AEPCOS NEWSLETTER

ANDROGEN EXCESS & PCOS SOCIETY

APRIL 2015 NEWSLETTER

GUIDELINES FOR ADOLESCENT PCOS

This issue newsletter is dedicated to Adolescent PCOS.

Enrico Carmina, M.D., Professor of Endocrinology at the Palermo University, Executive Director of AEPCOS Society and member of the Editorial Board, has interviewed Selma Witchel, M.D. about the new guidelines on diagnosis of PCOS during adolescence that have been jointly prepared by several societies of Pediatric Endocrinology, the Endocrine Society and AEPCOS Society. Selma is Associate Professor of Pediatric Endocrinology at the University of Pittsburgh and .Chairman of Annual Meeting Committee of AEPCOS Society.

The updated program and some practical information regarding 13th AEPCOS Annual Meeting that will be held in Siracusa, Sicily, Italy, October 4-6, 2015 are presented, too.

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APRIL 30, 2015

In this issue:

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FORTHCOMING AEPCOS MEETINGS

- **Update Meeting of AEPCOS Society, Gdansk, Poland, June 12-13, 2015**
- **Update Meeting of AEPCOS Society, Mumbai, India, August 15-16, 2015**
- **13th Annual Meeting of AEPCOS Society, Siracusa, Italy, October 4-6, 2015**
- **14th Annual Meeting of AEPCOS Society, Australia, November 2016**

13th ANNUAL MEETING OF AEPCOS SOCIETY

Next annual meeting of AEPCOS Society will be held October 4-6, 2015 in Siracusa, Sicily, ITALY. The conference venue is the Hotel des Etrangers, Passeggio Adorno 10-12, 96100 Siracusa, Italy.

The preliminary program, registration and hotel reservation form are available at: www.ae-society.org/annual-meeting.

It is strongly recommended to reserve the hotel as soon as possible because early October is high touristic season in Sicily.

The most convenient airport is Catania airport that is linked by many daily flights to most European cities. Hourly flights from Rome and Milan permit easy connections for flights arriving from USA, South America and Asia. A taxi from the Catania airport to the historical center of Siracusa takes 40 minutes and costs 50-60 euro. There is hourly bus service to Siracusa which costs 6.2 euro while all main rental car companies have their office at Catania airport.

For further information, please check our website or contact: enrico.carmina@ae-society.org

13th ANNUAL MEETING OF AEPCOS SOCIETY

OCTOBER 4th, 2015

3:30 – 3:45 pm	**ANUJA DOKRAS, M.D., Ph.D.** *President of AEPCOS Society* **SELMA WITCHEL, M.D.** *Chairman of Annual Meeting Committee*	**WELCOME**
3:45 – 4:10 pm	**SHARON OBERFIELD, M.D.** *Department of Pediatrics,,Division of Pediatric Endocrinology, Columbia University, New York, NY, USA*	**CAH IN CHILDREN AND ADOLESCENTS**
4:10 – 4:35 pm	**RICARDO AZZIZ, M.D.** *Department of Obstetrics and Gynecology, Georgia Regents University, Augusta, GA, USA*	**REPRODUCTION AND CAH**
4:35 – 5:00 pm	**SELMA WITCHEL, M.D.** *Pediatric Endocrinology, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh, Pittsburgh, PA, USA*	**PRENATAL TREATMENT OF CAH: TO TREAT OR NOT TO TREAT**
5:00 – 5:15 pm	**MARIA NEW, M.D.** *Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, USA*	**NON INVASIVE PRENATAL DIAGNOSIS OF CAH**

OCTOBER 5th, 2015

9:00 – 9:25 am	**PAULIINA UTRIAINEN, M.D.** *Department of Pediatrics, Kuopio University Hospital and University of Eastern Finland, Kuopio, Finland*	**PREMATURE ADRENARCHE**
9:25 – 9:50 am	**ETHEL CODNER, M.D.** *Institute of Maternal and Child Research, University of Chile, Santiago, Chile*	**PCOS IN ADOLESCENT GIRLS: DIAGNOSIS AND TREATMENT**
9:50 – 10:15 am	**VINCENT PREVOT, Ph.D.** *INSERM Research Team, University of Lille2, Lille, France*	**MICRORNA, GNRH, PUBERTY AND PCOS**
10:40 – 11:05 am	**JAN MCALLISTER, Ph.D.** *Department of Pathology, Pennsylvania State University, Hershey, PA, USA*	**DENND1A and PCOS**
11:05 – 11:30 am	**PAOLO MOGHETTI, M.D.** *Section of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Verona, Verona, Italy.*	**INSULIN RESISTANCE IN PCOS**
11:30 am -1:00 pm		**ORAL COMMUNICATIONS: BASIC**

OCTOBER 5th, 2015

3:00 – 3:25 pm	**MANUEL TENA-SEMPERE, Ph.D.** *Department of Cell Biology, Physiology and Immunology, Physiology Section, University of Córdoba, Córdoba, Spain*	**CONNECTING METABOLISM AND REPRODUCTION**
3:25 – 3:50 pm	**BULENT YILDIZ, M.D.** *Department of Medicine, Endocrinology and Metabolism Unit, Hacettepe University School of Medicine, Ankara, Turkey*	**GUT BRAIN AXIS AND METABOLISM IN PCOS**
3:50 – 4:15 pm	**HECTOR ESCOBAR-MORREALE, M.D.** *Diabetes, Obesity and Reproductive Endocrinology Unit, Hospital Universitario Ramón y Cajal. Madrid, Spain*	**ADIPOKINES, ADIPOSE TISSUE AND PCOS**
4:15 – 4:40 pm	**ENRICO CARMINA, M.D.** *Endocrinology and Metabolism Unit, University of Palermo, Palermo, Sicily, Italy*	**LONG TERM METABOLIC AND CARDIOVASCULAR FUTURE OF PCOS WOMEN**
5:10 – 6:30 pm		**ORAL COMMUNICATIONS: CLINICAL**

OCTOBER 6th, 2015

9:00 – 9:25 am	**VASANTHA PADMANABHAN, Ph.D.** *Department of Pediatrics, University of Michigan, Ann Arbor, MI, USA*	**DEVELOPMENT PROGRAMMING**
9:25 – 9:45 am	**DAVID ABBOTT, Ph.D.** *Wisconsin National Primate Research Center and Department of Obstetrics and Gynecology, University of Wisconsin, Madison, WI, USA*	**PCOS-LIKE TRAITS IN NATURALLY OCCURRING HYPERANDROGENIC FEMALE MONKEYS**
9:45 – 10:10 am	**ROGERIO LOBO, M.D.** *Department of Obstetrics and Gynecology, Columbia University, New York, NY, USA*	**NEW CONCEPTS IN OVARIAN FUNCTION IN PCOS**
410:10 – 10:30 am	**JACQUELINE BOYLE, M.D.** Faculty of Medicine, Nursing & Health Sciences, *Monash University, Clayton, Australia*	**ADVANCES IN MODELS OF CARE IN PCOS**
11:00 – 11:30 am	**ANUJA DOKRAS, M.D., Ph.D.** *Department of Obstetrics and Gynecology,, University of Pennsylvania, Philadelphia, PA, USA*	**UNDERSTANDING DYSLIPIDEMIAS IN PCOS**

OCTOBER 6th, 2015

11:30– 11:55 am	**RICHARD LEGRO, M.D.** *Department of Obstetrics and Gynecology, Pennsylvania State University, Hershey, PA, USA*	**WHAT WE HAVE LEARNED FROM MULTI-CENTER CLINICAL TRIALS?**
11:55 am – 12:10 pm	**ESZTER VANKY, M.D.** *Department of Obstetrics and Gynecology, Trondheim University, Trondheim, Norway*	**METFORMIN USE DURING PREGNANCY:** **RESULTS OF A MULTICENTER TRIAL**
12:10 -1:00 pm	**RICARDO AZZIZ, M.D.** *Augusta, GA, USA* **ROBERT NORMAN, M.D.** *Adelaide, Australia* **HELENA TEEDE, M.D.** *Clayton, Australia*	**PANEL DISCUSSION** **DEVELOPING GUIDELINES FOR EPIDEMIOLOGIC STUDIES WORLDWIDE**

You are invited to submit abstracts of your original research to be considered for presentation at the 13th Annual Meeting of the Androgen Excess & Polycystic Ovary Syndrome Society (AE-PCOS Society).

To be considered for presentation your abstract must be submitted no later than **SEPTEMBER 5th**, 2015, 11:00 pm (2300 hrs) PST.

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.

AEPCOS UPDATE MEETING

Gdansk, Poland, June 12-13, 2015

An update meeting on PCOS will be held in Gdansk, Poland, June 12-13, 2015.

Registration and hotel form may be found at: http://pcos.med.pl/#/en

The final program of the meeting is reported in the following page.

For further information, please contact: Prof. Dominik Rachon drachon@gumed.edu.pl

OTHER FUTURE MEETINGS

- EUROPEAN SOCIETY OF ENDOCRINOLOGY, DUBLIN, IRELAND, MAY 16-20, 2015
- ESHRE, LISBON, PORTUGAL, JUNE 14-17, 2015
- EUROPEAN SOCIETY PEDIATRIC ENDOCRINOLOGY, BARCELONA, SPAIN, OCTOBER 1-3, 2015
- ASRM, BALTIMORE, MD, USA, OCTOBER 17-21, 2015
- ENDOCRINE SOCIETY, BOSTON, USA, APRIL 1-4, 2016

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Selma Witchel, M.D.

GUIDELINES ON DIAGNOSIS OF PCOS IN ADOLESCENCE

In this issue, Enrico Carmina has interviewed Selma Witchel about the new guidelines on diagnosis of PCOS in adolescence that have been published in the April issue of Hormone Research in Paediatrics. The consensus paper has been written by expert providers in pediatric endocrinology and adolescent health who were selected as the representatives of established professional societies.

Witchel SF, Oberfield S, Rosenfield RL, Codner E, Bonny A, Ibáñez L, Pena A, Horikawa R, Gomez -Lobo V, Joel D, Tfayli H, Arslanian S, Dabdghao P, Garcia Rudaz C, Lee PA. The Diagnosis of Polycystic Ovary Syndrome during Adolescence. Horm Res Paediatr. 2015 Apr 1

Selma, what led to this publication?

The diagnostic criteria for PCOS in adolescence are controversial, primarily because the typical features used in adult women, e.g. acne, irregular menses, and PCOM, may be normal pubertal physiological events (2). The goal of this consensus committee was to define criteria with sufficient evidence to be used for the diagnosis of PCOS in adolescents. For this process, evidence available in the literature was graded according to the AGREE criteria (3).

Which organizations contributed to this consensus paper?

In alphabetical order, the contributing professional societies were Androgen Excess-PCOS Society (AE-PCOS), Australasian Pediatric Endocrine Group (APEG), Asia Pacific Pediatric Endocrine Society (APPES), African Society for Pediatric and Adolescent Endocrinology (ASPAE), European Society for Pediatric Endocrinology (ESPE), Japanese Society for Pediatric Endocrinology (JSPE), Japanese Society of Obstetrics and Gynecology (JSOG), Latin American Society for Pediatric Endocrinology (SLEP), North American Society of Pediatric and Adolescent Gynecology (NASPAG), Pediatric Endocrine Society (PES).

What are the criteria for evidence of clinical and biochemical hyperandrogenism in the adolescent girl?

The clinical features suggestive of androgen excess include unwanted hair growth in a male-like pattern (hirsutism), moderate to severe inflammatory acne, and/or menstrual irregularities. Girls with these symptoms should be evaluated for the presence of hyperandrogenemia before initiation of any medical therapies. Importantly, isolated mild hirsutism should not be considered clinical evidence of hyperandrogenism in the early postmenarcheal years. Nevertheless, hirsutism may be progressive and may be devastating for an adolescent girl. As recommended for adult women, other disorders associated with androgen excess, e.g., congenital adrenal hyperplasia, need to be excluded from diagnostic consideration.

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Selma Witchel, M.D.

The diagnosis of biochemical hyperandrogenism in symptomatic women is based on documentation of elevated serum androgens using reliable assays with well-defined normal ranges. Due to the variability in the results of testosterone assays and the limited data available on the normal developmental fluctuations in testosterone levels during puberty, no clear cutoff testosterone concentrations applicable to the broad adolescent population are available. For adolescents, testosterone concentrations may be considered to be elevated when they are persistently greater than the adult female normative values according to assays performed by specialty laboratories with well-defined reference intervals. In general, total testosterone concentrations >55 ng/dl are likely consistent with hyperandrogenism when measured by an radioimmunoassay using an extraction step (4). Total testosterone concentrations >42 ng/dl using a LC-MS/MS assay may indicate hyperandrogenism (5) Currently, no data are available indicating for how long hyperandrogenemia must continue to accurately predict persistence and development of PCOS in adulthood.

What Are the Criteria for Evidence of Oligo-Anovulation in Adolescents?

Menstrual irregularity and anovulatory cycles are common among adolescents due to the immaturity of the hypothalamic-pituitary-ovarian axis. Available evidence suggests that symptoms of PCOS develop during the peripubertal years. The clinician is challenged to distinguish between adolescents with "physiological adolescent anovulation" and those with true ovulatory dysfunction.

The median age at menarche, between 12 and 13 years, has remained relatively stable across well-nourished populations in developed countries (7). By 3 years after menarche, Legro et al. (8) reported that over 90% of adolescent females have 10 or more menstrual cycles per year.

After taking into consideration the clinical context for the individual patient, the persistence of menstrual irregularities appears to be a good indicator of possible underlying pathology. Yet, for how long does adolescent oligomenorrhea need to persist to indicate the development of PCOS? Available data indicate that most adolescents establish a menstrual interval of 20–45 days within the first 2 years after menarche. Menstrual intervals persistently shorter than 20 days or greater than 45 days in individuals 2 or more years after menarche are evidence of oligo-anovulation and warrant further evaluation.

Are ovarian ultrasounds useful in adolescent girls?

Ovarian ultrasounds often show a multifollicular pattern which is characterized by the presence of large follicles distributed throughout the ovary. This pattern is common in adolescent girls, has no relationship with androgen excess, and should not be considered pathological. Hence, ovarian imaging is not needed during the diagnostic evaluation of a girl with features suggestive of PCOS.

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Selma Witchel, M.D.

Can Insulin Resistance/Hyperinsulinemia be used in the Diagnosis of PCOS in Adolescents?

Insulin resistance and hyperinsulinemia are considered to be intrinsic features of PCOS in adults and adolescents. Insulin resistance and hyperinsulinemia can be detected among both lean and obese girls. Hyperinsulinemia, often compensatory to the insulin resistance, appears to exacerbate the reproductive and metabolic manifestations of PCOS. Despite the frequent finding of insulin resistance and hyperinsulinemia, these findings should not be utilized as diagnostic criteria. More importantly, insulin resistance and hyperinsulinemia warrant investigation and treatment of potential comorbidities.

What are the risks of overdiagnosing PCOS?

The diagnosis of PCOS can impact an adolescent's quality of life and generate unnecessary anxiety about future health and fertility. Thus, overdiagnosis of PCOS can lead to unfounded labelling and unwarranted interventions. Rather than prematurely labeling a girl with the diagnosis of PCOS, re-evaluation of all adolescents with features suggestive of PCOS is crucial.

Does a diagnosis of PCOS during adolescence provide a chance for meaningful interventions?

Yes, a timely diagnosis of PCOS provides an outstanding opportunity to improve awareness of the consequences and co-morbidities of PCOS (8). Testing for comorbidities can include fasting glucose, fasting insulin, lipid concentrations, and oral glucose tolerance testing followed by appropriate medical management. Signs and symptoms suggestive of depression should prompt a behavioral health evaluation. Unfortunately, most intervention trials have been limited by their short duration (less than 6 months). Research evaluating long-term interventions using high-quality randomized controlled trials and long term follow-up of girls with PCOS diagnosed during adolescence would be ideal. It is hope that such research studies could establish validated diagnostic criteria to promote timely diagnosis of PCOS while avoiding overdiagnosis.

What are the "take-home messages" of this consensus statement?

The major recommendation is that great care should be taken before diagnosing PCOS in adolescent girls with clinical features of androgen excess, i.e., hirsutism and biochemical hyperandrogenism, if oligomenorrhea has not persisted for more than 2 years. Rather, such girls can be considered to be at risk for PCOS. Frequent longitudinal re-evaluations and treatment to alleviate current symptoms are essential accompaniments to deferred diagnostic labeling. Each girl deserves individualized medical care with attention to the severity and progression of her symptoms.

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1) Witchel SF, Oberfield S, Rosenfield RL, Codner E, Bonny A, Ibáñez L, Pena A, Horikawa R, Gomez-Lobo V, Joel D, Tfayli H, Arslanian S, Dabdghao P, Garcia Rudaz C, Lee PA. The Diagnosis of Polycystic Ovary Syndrome during Adolescence. Horm Res Paediatr. 2015 Apr 1
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