AEPCOS NEWSLETTER

ANDROGEN EXCESS & PCOS SOCIETY

JANUARY 2015 NEWSLETTER

AMH IN WOMEN WITH PCOS

This issue newsletter reports the program of the update meeting on AMH in ANDROGEN EXCESS DISORDERS that will be held in San Diego, March 5, 2015, during the Annual Meeting of the Endocrine Society.

Some preliminary information about the 13th Annual Meeting of AEPCOS Society that will be held in Siracusa, Sicily, Italy, October 4-6, 2015 are presented. .

For the scientific section of the newsletter, Daniel Dumesic, M.D., Professor at Department of Obstetrics and Gynecology of UCLA has interviewed Heidi Cook Andersen, M.D., Ph.D. and Kevin Maas, Ph.D. about the factors that may regulate AMH levels in women with PCOS.

VOLUME 3, ISSUE 1

JANUARY 31, 2015

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, Siracusa, Italy, October 4-6, 2015**
- **14th Annual Meeting of AEPCOS Society, Australia, November 2016**

AEPCOS UPDATE MEETING ON AMH IN ANDROGEN EXCESS DISORDERS

The AEPCOS Update Meeting on AMH in Androgen Excess Disorders will be held March 5, 2015, in San Diego, CA, USA, during the Annual Meeting of Endocrine Society.

The venue of the meeting is the beautiful boat *California Spirit* and the meeting will be held during a dinner cruise around San Diego Bay. The cruise will start at 7:30 pm and will finish around 10:30 pm.

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

Until February 28, 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 $60. From March 1, 2015, for both members and non-members, the registration fee will be $100.

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

UPDATE MEETING ON

AMH

IN ANDROGEN EXCESS DISORDERS

San Diego Bay Dinner Cruise

March 5, 2015

7:30 to 10:30 pm

California Spirit

990 North Harbor Drive

San Diego, CA 92101, USA

Time	Event/Speaker	Topic
7:00 – 7:30 pm	**Boarding to CALIFORNIA SPIRIT**	
7:30 – 10:30 pm	**CRUISE AROUND SAN DIEGO BAY**	
7:30 – 8:00 pm 8:00 –10:00 pm	**Champagne and appetizers** **Seated dinner**	
8:30 – 10:30 pm	**AEPCOS UPDATE MEETING**	
8:30 – 8:40 pm	**ANUJA DOKRAS, M.D.** *Division of Infertility and Reproductive Endocrinology, University of Pennsylvania, Philadelphia, PA, USA*	**PRESENTATION OF THE UPDATE MEETING**
8:40 – 9:00 pm	**JEFFREY CHANG, M.D.** *Division of Reproductive Endocrinology and Infertility, University of California,San Diego, CA, USA*	**AMH ROLE IN OVARIAN FOLLICULAR DEVELOPMENT AND ONTOGENY OF PCOS**
9:00 – 9:20 pm	**SELMA WITCHEL, M.D.** *Pediatric Endocrinology*, *Children's Hospital of Pittsburgh, Pittsburgh, PA, USA*	**AMH MEASUREMENT DURING INFANCY AND PUBERTY:** **CLINICAL SIGNIFICANCE**
9:20 – 9:50 pm	**ENRICO CARMINA, M.D.** *Endocrinology and Metabolism,*, *University of Palermo,*, *Palermo, Italy* **JOOP LAVEN, M.D.** *Department of Obstetrics and Gynecology, Rotterdam University, Rotterdam, The Netherlands*	**DEBATE** **AMH MEASUREMENT IN PCOS:** **USEFULNESS IN DIAGNOSIS**
9:50 – 10:30 pm	**Questions and general discussion**	

13th ANNUAL MEETING OF AEPCOS SOCIETY

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

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

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Heidi Cook-Andersen, M.D.

FACTORS INFLUENCING AMH LEVELS IN WOMEN WITH PCOS

The scientific part of the newsletter is dedicated to factors influencing AMH levels in PCOS. Daniel Dumesic, M.D. interviewed Heidi Cook-Andersen, M.D., Ph.D., and Kevin H Maas, M.D., Ph.D., in the Department of Reproductive Medicine, University of California, San Diego, La Jolla California, about their recent studies regarding the regulation of serum anti-Mullerian hormone (AMH) levels in PCOS women (J Clin Endocrinol Metab 2015;100 (1):251-7; J Clin Endocrinol Metab 2015;100 (1):293-300

1. *Heidi, your exciting research shows that elevated serum AMH levels in PCOS women positively correlate with circulating LH and androgen levels as well as negatively correlate with BMI. What are your thoughts on the biological significance of these reciprocal relationships between serum LH/androgens and BMI with circulating AMH levels?*

Our findings are consistent with those of other groups, which together confirm the existence of a strong correlation between serum AMH and LH levels. Correlations with androgens and BMI are also seen. Importantly, these findings raise the possibility of functional interactions among these factors. Unfortunately, there have been few follow-up studies to investigate these potential functional relationships and most of the studies that have been done are *in vitro* studies. We designed this study to ask if there is a functional relationship between AMH and LH levels in women with PCOS.

2. *Despite the correlation between serum AMH and endogenous LH levels in PCOS women, serum AMH levels did not increase after recombinant-human chorionic gonadotropin (r-hCG) administration in PCOS or normal women. How would you explain this discrepancy, given the complex relationships between LH, BMI and AMH?*

We were surprised by this finding. While correlations are compelling, they do not imply cause and effect. However, because of published reports demonstrating a direct effect of LH stimulation on AMH production by granulosa cells *in vitro*, we set out to test this phenomenon in women. Using an LH surrogate, we found AMH was non-responsive to hCG given intravenously at a both a modest and high dose over an interval of 48 hours. Our findings suggest that the elevated serum AMH in women with PCOS is not simply a direct effect of excess LH production. Instead, it is likely that intraovarian or other as yet unidentified mechanisms act together to regulate AMH production by granulosa cells *in vivo*.

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Kevin Maas, Ph.D.

3. *Kevin, in your complementary study, I notice that PCOS women with a high 17-hydroxyprogesterone (17-OHP) response to r-hCG administration have a low serum AMH level compared to PCOS women who are normal 17-OHP responders to r-hCG. This inverse relationship between serum AMH (as a granulosa cell marker) and 17-OHP responses to r-hCG (as a theca cell marker) is very interesting. Do you think it is mediated by metabolic factors, such as insulin or adipokines, since the high 17-OHP responders appear to have a higher BMI than the controls?*

It is possible that metabolic factors may be, at least in part, responsible for differences in the relationship of AMH levels and 17-OHP responsiveness between the two subgroups as the high responders (HR-PCOS) were somewhat, but not significantly, heavier than normal responders (NR-PCOS). We attempted to address this issue by examining hormone responses before and after using diazoxide to suppress insulin secretion in PCOS, but were unsuccessful. Therefore, we believe the role of hyperinsulinemia still needs to be explored.

Despite this, we do have some data that suggests disparate 17-OHP responses between HR-PCOS and NR-PCOS may be independent of the paracrine environment. We studied adrenal steroid production during ACTH infusion in the same women with PCOS. Preliminary analysis suggests that in HR-PCOS women adrenal steroidogenic responses appear to be elevated with ACTH administration whereas in NR-PCOS women adrenal responses are similar to normal controls. In other words, it appears that women with PCOS who have the most exaggerated response to hCG also seem to have the highest responses to adrenal stimulation. This suggests that differences in steroid producing cells among women with this disorder may be independent of location and may instead be cell intrinsic.