AEPCOS NEWSLETTER

ANDROGEN EXCESS & PCOS SOCIETY

# MARCH NEWSLETTER:
## TESTOSTERONE ASSAY
### (IN CLINICAL PRACTICE AND SCIENTIFIC RESEARCH)

The March newsletter is dedicated to the problems related to testosterone assay in clinical practice and scientific research. In fact, during the month of February 2013, in Reston, VA, USA, a meeting of PATH (Partnership for Accurate Testing of Hormones) was held. Two experts of AEPCOS Society, Enrico Carmina and Frank Stanczyk, were present and represented the Society.

An editorial comment of Dr. Carmina and an interview to Frank Stanczyk are included.

Because the treated issues (note the slight difference between the opinion of the expert and the editorial comment) are often controversial, we have decided to eventually publish comments of the members. If you wish, you may send a letter to: enrico.carmina@ae-society.org

This issue of the AEPCOS newsletter also includes information about the upcoming joint scientific session of AEPCOS and American Association of Clinical Endocrinologists (AACE) that will be part of the program of 22nd AACE Annual Meeting.

Information regarding 11th Annual Meeting of AEPCOS Society is reported, too.

For any information about all AEPCOS meetings, you may contact: info@ae-society.org

**VOLUME 1, ISSUE 3**
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## FORTHCOMING AEPCOS MEETINGS

- Update on Androgen Excess Disorders, Prague, Czech Republic, June 7, 2013
- 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

# AACE-AEPCOS JOINT SCIENTIFIC SESSION AT 22ND AACE ANNUAL MEETING

PHOENIX, AZ, USA, MAY 3RD, 2013

# GONADAL DISORDERS IN WOMEN AND MEN: ANDROGEN EXCESS AND DEFICIENCY

## A Joint Symposium of AACE and Androgen Excess-PCOS Society

Co-Chairs: Walter Futterweit, MD (New York, NY, USA)

Neil F. Goodman, MD (Miami, FL, USA)

- Patricia M. Vuguin, MD (Lake Success, NY, USA)

  Diagnosis and Management of adolescent PCOS ·
- Rhoda H. Cobin, MD (New York, NY, USA)

  Cardiometabolic Risks in PCOS: Implications for Clinical Management
- Enrico Carmina, MD (Palermo, Italy)

  Newest Developments in PCOS: Genetics, Insulin Resistance and Treatment
- Ronald S. Swerdloff, MD (Torrance, CA, USA)

  Androgen Deficiency in Men

# 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.

Abstract deadline is August 2, 2013. For abstract form and preliminary program, please connect to: www.ae-society.org or contact: info@ae-society.org

Newport may be easily reached by car, by flight (25 miles from International T.F. Green/airport— PVD) or by train (18 miles from West Kingston railway station –along New York-Boston railway). A shuttle bus operates from both airport and train station to Newport hotels. For information or reservation on transportation, contact: info@ae-society.org

# REGISTRATION FORM

**11TH AEPCOS ANNUAL MEETING**

## REGISTRATION ONLY

_____AEPCOS members $260 _____Non AEPCOS members $360

## NEWPORT HYATT REGENCY RESORT

$219 for night ___October 16 ___October 17 ___October 18

Payment amount: $_____ Credit card payment: ____VISA ____MasterCard ____AMEX

Credit card number_____ Expiration date:_____/_____

Cardholder
name_____

Online payment_____ To safely pay online, connect to: www.ae-society.org

Check payment_____ Make checks payable to Androgen Excess Society

Email, mail or fax the registration form to: Androgen Excess & PCOS Society, via delle Croci 47, 1st floor, suite 10, 90139 Palermo, Italy. Fax: +39-091328997, Email: info@ae-society.org

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

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Frank Stanczyk, Ph.D.

# TESTOSTERONE ASSAY

The editor interviewed Frank Stanczyk, Ph.D., Professor of Research and Director of Reproductive Endocrine Research Laboratory at University of Southern California (Los Angeles).

1. Frank, what are the main problems in measuring total testosterone in females or children?

The measurement of serum or plasma testosterone (T) levels in children or women by RIA or chemiluminescent immunoassay without a preceding purification step (direct immunoassay), does not provide an accurate and reliable result. Guessing seems to be nearly as good, if not better, when measuring T in women or children using commercial direct immunoassay kits. Direct immunoassays can overestimate levels of T because some of the numerous T metabolites present in serum may cross-react with the antibody in the assay. Also, serum levels can be underestimated if T is not released efficiently from SHBG in the assay, which is usually achieved by an acidic reagent. In addition, T levels can be affected by matrix effects in a serum sample due to non-analyte substances that interfere with the assay, e.g., when the sample is hemolyzed or lipemic. Because of the shortcomings of direct immunoassays, it has been recommended that these assays should not be used when measuring testosterone levels in serum samples from women or children.

The disadvantage of direct T immunoassays can be eliminated by including in the assay one or more purification steps, such as organic solvent extraction and chromatography, which were used in the RIAs when these were first developed. Organic solvent extraction and chromatography on a Celite or Sephadex column, removes most, if not all, potentially interfering metabolites of testosterone and other androgens. Also, the organic solvent extraction step in the assay efficiently dissociates testosterone from SHBG. No matrix effects arise from samples that are hemolyzed or lipemic, as these purification steps produce a clean residue containing the analyte, which is then dissolved in assay buffer for analysis in the RIA. However, this assay methodology is cumbersome and time-consuming, and not suitable for routine clinical diagnostic testing.

2. In clinical practice, what methods of measuring total testosterone are more appropriate?

Major clinical diagnostic testing laboratories such as Quest Diagnostic Nichols Institute and Esoterix, who had used these assays for steroid hormone testing for many years, switched to mass spectrometry assays, specifically LC-MS/MS assays. These assays have high sensitivity and specificity, and provide accurate and precise results with high throughput. MS is used as the reference method at centers such as the National Institute of Standards and Technology, and is considered to be the "gold standard" for measurement of a variety of compounds. Several years ago, the Centers for Disease Control (CDC) initiated a project to standardize steroid hormone measurements using LC-MS/MS assay methodology, with the goal of being able to send a serum sample for a steroid measurement to any laboratory using LC-MS/MS methodology and obtain a reproducible value. The project began with measurement of testosterone in male serum. The standardization of testosterone measurements is established through method comparison and bias estimation between CDC's reference laboratory and testing laboratories. To gain CDC certification, laboratories have to demonstrate a mean bias of ± 6.4% to the CDC reference method. Initially, large inter-laboratory coefficients of variation were found in testosterone measurements. However, in the past few years, the precision of testosterone measurements using LC-MS/MS has improved and 8 laboratories have now been certified by the CDC.

3. What challenges remain?

Some challenges remain; a notable example is the establishment of female reference ranges. Due to the greater specificity of the MS assays, lower testosterone levels are expected compared to those obtained by direct immunoassays and the conventional RIA. Thus, physicians will require some education about the difference in T values generated by the different assay methods.

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# Partnership for Accurate Testing of Hormones: Good idea but few results

PATH (Partnership for Accurate Testing of Hormones) was created in 2010 to improve hormone measurements. It was not a new organization but an alliance between some important scientific societies (including Endocrine Society, American Association for Clinical Chemistry, College of American Pathologists, American Society for Bone and Mineral Research, International Society of Andrology, American Urological Association, Pediatric Endocrine Society, ASRM and AEPCOS Society), some companies interested in hormone testing (Abbott, Beckman, DiaSorin, Labcorp, Ortho, Quest, Roche, Siemens…) and the Clinical Chemistry Branch of US Center for Disease Control and Prevention. The first meeting was held in Atlanta at CDC. It was decided to concentrate the initial efforts on testosterone standardization program. Because Endocrine Society provided most funds for this program, William Rosner from Endocrine Society and Hubert Vesper from CDC were chosen to chair the partnership.

AEPCOS Society designed two top experts: Michel Pugest (INSERM, Lyon, France) and Frank Stanczyk (University of Southern California at Los Angeles, LA, CA, USA) to represent the Society and participate to the efforts for improving and standardizing testosterone assay.

All this effort has produced few results. On the basis of the experience of CDC laboratory, mass spectrometry after liquid chromatography (LC/MS) was suggested as the gold standard for measuring testosterone and several companies have actively published this method. However, only results in men have been produced while the accuracy of the method in subjects with low testosterone levels as women or children is not available, yet. A collaborative study of several academic centers did not show any advantage in using LC/MS compared to a classic RIA in women with Polycystic Ovary Syndrome (Legro et al. JCEM 2010; 95:5305-13). Data in children and menopausal women are still missing.

February 12-13, 2013 a new PATH meeting was held in Reston, VA, USA. The plan was to discuss the leadership and the future programs of the alliance. Endocrine Society informed the participants about its decision to give a large quantity of money (almost $200,000) to PATH in 2013 for continuing the program. However, no agreement on future plans (testosterone assay in children? standardization of estradiol assay?) was reached and it was determined to delay decisions until a new leadership was formed. Several participants (including E.C.) criticized the lack of information to members of alliance about scientific results and the method of utilizing funds. The participation of commercial companies without their involvement in financing the alliance was questioned, too.

After the meeting, the AEPCOS Board discussed its position inside PATH. Different opinions were presented and, at the end, it was decided to remain part of PATH with the goal to play a larger role in the future plans of this alliance. Of course, AEPCOS society has no funds to put in these projects and it strongly limits its capacity to influence the decisions.

The idea of an alliance between scientific societies and companies looked very good but results have been disappointing. Probably only a strong leadership and a bigger involvement of all participants to decisions may revive the PATH and produce useful results (E.C.).