The diagnosis of PCOS in adolescent girls is not easy and is still controversial. The issue: adolescent girls can mimic the diagnostic criteria for PCOS without maturing into a PCOS phenotype. Adolescents have naturally occurring clinical signs of high androgen levels, intermittent/absent menstrual cycles and polycystic ovaries as they transition to reproductive maturity. In this paper, Roe and colleagues use AEPCOS criteria to diagnose PCOS in 148 adolescents in the USA (mostly Caucasian) and examined the incidence of metabolic syndrome (MS) in these girls compared to 57 controls (recruited adolescents who failed diagnosis for PCOS). All girls were recruited from adolescents referred to a specialty clinic, so this referral bias likely contributes to the high incidence of PCOS. Only girls with >2 years postmenarche were included as having intermittent/absent cycles (≤ 9 per year) and polycystic ovaries were identified from at least one ovary with a volume ≥ 10 cm³ and not antral follicle counts. Girls were classified with MS if they showed 3 of the following 5 modified Cook criteria: body mass index >90th percentile, serum triglycerides ≥ 150 mg/dL, serum high-density lipoprotein cholesterol (HDL-C) ≤ 40 mg/dL, blood pressure at ≥ 90th percentile for age (or taking antihypertensives), and fasting plasma glucose ≥ 100 mg/dL. Of the 205 adolescents included in the study, ~66% were diagnosed with PCOS by AEPCOS criteria, with intermittent/absent cycles as the most frequent criterion. Almost all (~64%) adolescents identified as PCOS had at least one risk factor for MS, compared to about half that incidence in controls, and ~11% of girls identified as PCOS were classified as MS compared to ~2% of controls. These data, the authors suggest, should encourage early diagnosis of PCOS during adolescence to enable timely metabolic risk assessment and early intervention to diminish onset of cardiovascular disease.

List of October – December, 2012 Quarterly Publications

AEPCOS-related publication highlight ................................................................. 1
Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis .................. 3
Insulin Resistance ............................................................................................. 4
Polycystic ovary syndrome (PCOS) ................................................................. 5
  PCOS - Adolescence .................................................................................... 5
  PCOS - Dermatology and Body Hair Complications ................................. 6
  PCOS - Endocrine Disrupters .................................................................... 7
  PCOS - Etiology and Animal Models ......................................................... 7
  PCOS - General Health Concerns .............................................................. 8
  PCOS - Genetics .......................................................................................... 8
  PCOS - Immunological Considerations ...................................................... 10
  PCOS - After the Menopause .................................................................... 10
  PCOS - Metabolic Dysfunction/Cardiovascular Disease/Inflammation ..... 10
  PCOS - Neuroendocrine Dysfunction ......................................................... 17
  PCOS - Ovary .............................................................................................. 17
  PCOS - Phenotypic Variation ..................................................................... 21
<table>
<thead>
<tr>
<th>Topic</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS - Pregnancy Complications</td>
<td>21</td>
</tr>
<tr>
<td>PCOS - Protocol Reviews</td>
<td>22</td>
</tr>
<tr>
<td>PCOS - Psychology</td>
<td>22</td>
</tr>
<tr>
<td>PCOS - Thyroid Complications</td>
<td>23</td>
</tr>
<tr>
<td>PCOS - Uterus</td>
<td>23</td>
</tr>
<tr>
<td>Premature Adrenarche</td>
<td>24</td>
</tr>
</tbody>
</table>

**Brief overviews of selected publications**

**Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis**


**Insulin resistance**

ANDROGEN EXCESS AND PCOS SOCIETY

List of Publications

**Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis**


Crocker MK, Barak S, Millo CM, Beall SA, Niyyati M, Chang R, Avila NA, Van Ryzin C, Segars J, Quezado M, Merke DP. Use of PET/CT with cosynotropin stimulation to identify and localize adrenal rest tissue following adrenalectomy in a woman with congenital adrenal hyperplasia. J Clin Endocrinol Metab. 2012 Nov;


ANDROGEN EXCESS AND PCOS SOCIETY


Sharma S, Gupta DK. Male genitoplasty for 46 XX congenital adrenal hyperplasia patients presenting late and reared as males. Indian J Endocrinol Metab. 2012 Nov;16(6):935-8


Insulin resistance


Polycystic ovary syndrome (PCOS)

PCOS – Adolescence


PCOS – Dermatology and Body Hair Complications


ANDROGEN EXCESS AND PCOS SOCIETY


PCOS – Endocrine Disrupters

None.

PCOS – Etiology and Animal Models


ANDROGEN EXCESS AND PCOS SOCIETY


**PCOS – General Health Concerns**


**PCOS – Genetics**


ANDROGEN EXCESS AND PCOS SOCIETY


ANDROGEN EXCESS AND PCOS SOCIETY


PCOS – Immunological Considerations


PCOS – After the Menopause


PCOS – Metabolic Dysfunction/Cardiovascular Disease/Inflammation

ANDROGEN EXCESS AND PCOS SOCIETY


ANDROGEN EXCESS AND PCOS SOCIETY


ANDROGEN EXCESS AND PCOS SOCIETY


ANDROGEN EXCESS AND PCOS SOCIETY


ANDROGEN EXCESS AND PCOS SOCIETY


PCOS – Neuroendocrine Dysfunction


PCOS – Ovary


ANDROGEN EXCESS AND
PCOS SOCIETY


PCOS – Phenotypic Variation


PCOS – Pregnancy Complications


Capalbo A, Bono S, Spizzichino L, Biricik A, Baldi M, Colamaria S, Ubaldi FM, Rienzi L, Fiorentino F. Sequential comprehensive chromosome analysis on polar bodies, blastomeres and trophoblast: insights into


**PCOS – Protocol Reviews**

None.

**PCOS – Psychology**

ANDROGEN EXCESS AND PCOS SOCIETY


**PCOS – Thyroid Complications**


**PCOS – Uterus**


ANDROGEN EXCESS AND PCOS SOCIETY


Premature Adrenarche


Brief summaries of selected publications

**Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis**


The gene encoding 21-hydroxylase (CYP21A2) is located in a complex genetic locus on chromosome 6 at the central region of the human major histocompatibility complex. There is a highly homologous pseudogene in close physical proximity and genes that encode complement 4 (C4A and C4B). Two other genes, RP1 and TNXB, are in tandem with CYP21 and C4 gene from the telomeric to centromeric ends constituting a genetic module termed RCCX (R-P-C 4-C YP21-TN X). The RCCX modules are characterized by modular duplication or deletion events in which each duplicated or deleted module usually covers a CYP21A1P-TNXA-RP2-C4 unit. The most common haplotype is a bimodular RCCX format. The RCCX modules can be considered as copy number variants. These investigators found that the most common CYP21A2 mutation associated with the nonclassic form of CAH, V281L, was associated with high C4 copy number. A large CYP21A2 deletion leads to a complete loss of function mutation and the classic salt-losing form of CAH. The large deletion was associated with low C4 copy number. Monomodular RCCX with a short C4 gene is a risk factor for autoimmune disease and was found to be less frequent in patients with CAH compared to population estimates. The investigators concluded that CAH patients have increased C4 CNV, with mutation-specific associations that may be protective for autoimmune disease. Thus, CNV involving C4 may influence propensity to develop autoimmune disorders.

**Insulin resistance**


The cJun NH(2)-terminal kinase (JNK) signaling pathway contributes to inflammation and plays a key role in the metabolic response to obesity, including insulin resistance. This pathway participates in a cell signaling cascade that senses metabolic stress leading to activation of obesity-induced inflammatory responses. Hirosumi and colleagues (Nature 2002;420:333) generated JNK1 and JNK2 knock-out mice and reported that JNK2 knockout mice were protected from weight gain, whereas no metabolic effect was noted for the JNK1 knockout mice. In this report, Han and colleagues generated mice with selective JNK1 and JNK2 deficiencies in macrophages. They found that feeding a high-fat diet to control and JNK-deficient mice caused similar obesity. Only mice with JNK-deficient macrophages, however, remained insulin-sensitive. Despite the improved insulin sensitivity, other aspects of metabolic dysfunction such as circulating fatty acid concentrations were unaffected. The protection of mice with macrophage-specific JNK deficiency against insulin resistance was associated with reduced tissue infiltration by macrophages. It remains to be determined if myeloid JNK signaling contributes to insulin resistance and inflammatory responses to a similar extent in other obese animals, e.g. humans.