ANDROGEN EXCESS AND PCOS SOCIETY

Quarterly Review for Androgen Excess-PCOS Society
April 1st – June 30th, 2012

Contents

AEPCOS Publications in April – June, 2012


These selected highlights from the 8th Annual Meeting of the Androgen Excess and PCOS Society Annual Meeting in Munich, Germany (AEPCOS 2010) illustrate emerging concepts in PCOS. Studies into the pathogenesis of PCOS identified androgenic, glycemic, and inflammatory contributions implicating disordered TGF-beta signaling, while suggesting an analogous mechanism in affected male kin. Novel clinical approaches diversified the therapeutic options available to treat infertility in women with PCOS, and improved amelioration of PCOS symptoms, including metabolic dysfunction and hirsutism.

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Brief overviews of selected publications

**Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis**


**PCOS - Adolescence**


**PCOS – Ovary**


**PCOS – Pregnancy Complications**

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List of April – June, 2012 Quarterly Publications

Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis


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Insulin resistance

See citations in the section “PCOS - Metabolic Dysfunction/Cardiovascular Disease/Inflammation”.

Polycystic ovary syndrome (PCOS)

PCOS – Adolescence


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PCOS – Dermatology and Body Hair Complications


PCOS – Endocrine Disrupters

None.

PCOS – Etiology and Animal Models


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**PCOS – General Health Concerns**


PCOS – Genetics


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PCOS – Immunological Considerations

None.

PCOS – After the Menopause

None.

PCOS – Metabolic Dysfunction/Cardiovascular Disease/Inflammation


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PCOS – Neuroendocrine Dysfunction


PCOS – Ovary


PCOS – Phenotypic Variation


PCOS – Pregnancy Complications


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PCOS – Protocol Reviews

None.

PCOS – Psychology


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PCOS – Thyroid Complications
None.

PCOS – Uterus


Premature Adrenarche


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Brief summaries of selected publications

**Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis**


Starting in the 1980’s, supraphysiologic glucocorticoid treatment was used to decrease the virilization of the external genitalia of affected female fetuses. More recent clinical observations, results of animal studies and greater knowledge regarding the details of human fetal adrenal physiology raise concerns about the safety of this prenatal treatment. The pathophysiology of CAH and the safety and ethical considerations of prenatal dexamethasone treatment are reviewed in this article.

**PCOS - Adolescence**


The authors performed structured interviews to assess lifestyle habits of girls with PCOS. Specifically, they obtained information regarding the level of physical activity and sedentary habits of girls with PCOS (n=35) and compared them to controls (n=46). The authors report that girls with PCOS engaged in physical activities less than controls. Indeed, frequency and intensity of exercise was decreased among the girls with PCOS. The girls in the control groups were more often involved in sporting activities. The authors concluded that the athletic and sedentary habits of adolescents with PCOS may interact with other factors leading to obesity.


This is a cross-sectional study examining insulin-glucose dynamics in 18 early adolescent, first-degree female relatives of women with PCOS and 21 healthy, age-matched control adolescents without PCOS close relatives. The adolescent girls underwent anthropometric measurements, steroid profiling and frequently sampled Intravenous Glucose Tolerance Test (IVGTT), while Homeostasis Model Assessment (HOMA) index, Glucose Disposal Index (GDI), Acute Insulin Response (AIR) and Quantitative insulin sensitivity check index (QUICKI) were derived from IVGTT results. Adolescent girls with PCOS close relatives showed higher mean HOMA and lower GDI with no differences in mean age or BMI Z-score between the adolescent groups. The higher HOMA possibly reflects lowered insulin sensitivity and lower GDI may indicate poorer beta-cell function. These results suggest the presence of multiple risk factors for type 2 diabetes in early adolescent first-degree relatives of women with PCOS prior to onset of PCOS.
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PCOS – Ovary


As more evidence is reported in the literature, understanding of the direct and stimulatory effects of PCOS-associated hyperinsulinemia on ovarian androgen secretion is becoming clearer. This interesting study from the group in Verona, Italy, supports the concept that overproduction of insulin itself may stimulate ovarian androgen excess. Subjects with PCOS were well controlled as the adrenal contribution of androgens was suppressed during the hyperinsulinemic euglycemic clamp technique. High levels of insulin were required, supporting the finding of insulin resistance in these normal weight women, with significant ovarian androgen production induced by the high insulin. The prolonged 17-hour study, producing chronic rather than acute hyperinsulinemia, is more reflective of the PCOS condition. Improvement in insulin resistance with the use of insulin-sensitizing medication, lifestyle modification or both allows these patients to take direct control of their syndrome. Lowering of ovarian androgens may enhance their reproductive outcomes by correcting hyperinsulinemia and normalizing ovarian function, or at least by improving their response to ovulation induction and assisted reproduction. These subjects were nearly all of normal weight, which underscores the importance of screening all PCOS patients for insulin resistance and impaired glucose tolerance, and to subsequently consider insulin sensitization management in their fertility care.

PCOS – Pregnancy Complications


The authors investigated whether metformin decreases the early miscarriage rate and improves the pregnancy rates (PR) and live-birth rates (LBR) in PCOS in this multicenter, randomized (1:1), double-blind, placebo-controlled study. Three hundred twenty women with PCOS and anovulatory infertility were randomized to metformin (n = 160, Diformin; obese women, 1000 mg two times daily; nonobese subjects, 500 mg + 1000 mg daily) or identical doses of placebo (n = 160). After 3 months of treatment, another appropriate infertility treatment was combined, if necessary. If pregnancy occurred, metformin/placebo was continued up to 12 weeks of gestation. Miscarriage rates were low and similar in the two groups (metformin 15.2% vs. placebo 17.9%, P = 0.8). Intent-to-treat analysis showed that metformin significantly improved PR and LBR (vs. placebo) in the whole study population (PR: 53.6 vs. 40.4%, P = 0.006; LBR: 41.9 vs. 28.8%, P = 0.014) and PR in obese women (49.0 vs. 31.4%, P = 0.04), and there was a similar trend in nonobese (PR:58.6 vs. 47.6%, P = 0.09; LBR: 46.7 vs. 34.5%, P = 0.09) and in obese women with regard to LBR (35.7 vs. 21.9%, P = 0.07). Cox regression analysis showed that metformin plus standard infertility treatment increased the chance of pregnancy 1.6 times (HR 1.6, 95% CI 1.13-2.27). They concluded that obese women with anovulatory infertility benefit from 3 months pretreatment with metformin and its combination with routine ovulation induction agents thereafter.