

ANDROGEN EXCESS AND PCOS SOCIETY

Quarterly Review for Androgen Excess-PCOS Society
January 1st – March 31st, 2013

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Brief overviews of selected publications

Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis

Combined comment:



1. Gleeson H, Davis J, Jones J, O'Shea E, Clayton PE. The challenge of delivering endocrine care and successful transition to adult services in adolescents with congenital adrenal hyperplasia: experience in a single centre over 18 years. Clin Endocrinol (Oxf). 2013 Jan;78(1):23-8.
2. Downing J, Gleeson HK, Clayton PE, Davis JR, Wales JK, Callery P. Transition in endocrinology: the challenge of maintaining continuity. Clin Endocrinol (Oxf). 2013 Jan;78(1):29-35.
3. Krone N, Rose IT, Willis DS, Hodson J, Wild SH, Doherty EJ, Hahner S, Parajes S, Stimson RH, Han TS, Carroll PV, Conway GS, Walker BR, MacDonald F, Ross RJ, Arlt W; United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE). Genotype-phenotype correlation in 153 adult patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency: analysis of the United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE) cohort. J Clin Endocrinol Metab. 2013 Feb;98(2):E346-54..... 30

PCOS – Metabolic Dysfunction/Cardiovascular Disease/Inflammation

Bird ST, Hartzema AG, Brophy JM, Etminan M, Delaney JA. Risk of venous thromboembolism in women with polycystic ovary syndrome: a population-based matched cohort analysis. CMAJ. 2013;185(2):E115-20.
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PCOS – Ovary

Palomba S, Falbo A, La Sala GB. Effects of metformin in women with polycystic ovary syndrome treated with gonadotrophins for in vitro fertilisation and intracytoplasmic sperm injection cycles: a systematic review and meta-analysis of randomised controlled trials. BJOG. 2013 Feb;120(3):267-76..... 31

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List of Publications

Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis

Abbaszadegan MR, Hassani S, Vakili R, Saberi MR, Baradaran-Heravi A, A'rabi A, Hashemipour M, Razzaghi-Azar M, Moaven O, Baratian A, Ahadian M, Keify F, Meurice N. Two novel mutations in CYP11B1 and modeling the consequent alterations of the translated protein in classic congenital adrenal hyperplasia patients. *Endocrine*. 2013 Aug;44(1):212-9.

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Eyal O, Tenenbaum-Rakover Y, Shalitin S, Israel S, Weintrob N. Adult height of subjects with nonclassical 21-hydroxylase deficiency. *Acta Paediatr*. 2013 Apr;102(4):419-23.

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Haider S, Islam B, D'Atri V, Sgobba M, Poojari C, Sun L, Yuen T, Zaidi M, New MI. Structure-phenotype correlations of human CYP21A2 mutations in congenital adrenal hyperplasia. *Proc Natl Acad Sci U S A*. 2013 Feb 12;110(7):2605-10.

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Di Nardo G, Gilardi G. Human aromatase: perspectives in biochemistry and biotechnology. *Biotechnol Appl Biochem.* 2013 Jan-Feb;60(1):92-101.

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Polycystic ovary syndrome (PCOS)

PCOS – Adolescence

Brown M, Park AS, Shayya RF, Wolfson T, Su HI, Chang RJ. Ovarian imaging by magnetic resonance in adolescent girls with polycystic ovary syndrome and age-matched controls. *J Magn Reson Imaging*. 2013 Jan 4. [Epub ahead of print] PubMed PMID: 23292744; PubMed Central PMCID: PMC3620938.

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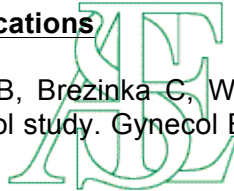
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PCOS – Dermatology and Body Hair Complications

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PCOS – Endocrine Disrupters

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PCOS – Etiology and Animal Models

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PCOS – Pregnancy Complications

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PCOS – Protocol Reviews

None.

PCOS – Psychology

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PCOS – Thyroid Complications

Artini PG, Uccelli A, Papini F, Simi G, Di Berardino OM, Ruggiero M, Cela V. Infertility and pregnancy loss in euthyroid women with thyroid autoimmunity. *Gynecol Endocrinol*. 2013 Jan;29(1):36-41. Epub 2012 Jul 27. Review. PubMed PMID: 22835333.

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Katulande P, Kariyawasam SS, Senanayake HM, Weerakkodi M. Multicystic ovaries and pituitary pseudo-adenoma associated with primary hypothyroidism. *J Obstet Gynaecol*. 2013 Jan;33(1):17-9. PubMed PMID: 23259871.

PCOS – Uterus

Vélez LM, Abruzzese GA, Motta AB. The biology of the peroxisome proliferator-activated receptor system in the female reproductive tract. *Curr Pharm Des*. 2013;19(25):4641-6. PubMed PMID: 23565653.

Premature Adrenarche

Corvalán C, Uauy R, Mericq V. Obesity is positively associated with dehydroepiandrosterone sulfate concentrations at 7 y in Chilean children of normal birth weight. *Am J Clin Nutr*. 2013 Feb;97(2):318-25.

DeSalvo DJ, Mehra R, Vaidyanathan P, Kaplowitz PB. In children with premature adrenarche, bone age advancement by 2 or more years is common and generally benign. *J Pediatr Endocrinol Metab*. 2013;26(3-4):215-21

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Lavery GG, Idkowiak J, Sherlock M, Bujalska I, Ride JP, Saqib K, Hartmann MF, Hughes B, Wudy SA, De Schepper J, Arlt W, Krone N, Shackleton CH, Walker EA, Stewart PM. Novel H6PDH mutations in two girls with premature adrenarche: 'apparent' and 'true' CRD can be differentiated by urinary steroid profiling. *Eur J Endocrinol.* 2013 Feb 1;168(2):K19-26.

Brief summaries of selected publications

Congenital Adrenal Hyperplasia and Disorders of Steroidogenesis



Comment:

4. Gleeson H, Davis J, Jones J, O'Shea E, Clayton PE. The challenge of delivering endocrine care and successful transition to adult services in adolescents with congenital adrenal hyperplasia: experience in a single centre over 18 years. *Clin Endocrinol (Oxf).* 2013 Jan;78(1):23-8.
5. Downing J, Gleeson HK, Clayton PE, Davis JR, Wales JK, Callery P. Transition in endocrinology: the challenge of maintaining continuity. *Clin Endocrinol (Oxf).* 2013 Jan;78(1):29-35.
6. Krone N, Rose IT, Willis DS, Hodson J, Wild SH, Doherty EJ, Hahner S, Parajes S, Stimson RH, Han TS, Carroll PV, Conway GS, Walker BR, MacDonald F, Ross RJ, Arlt W; United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE). Genotype-phenotype correlation in 153 adult patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency: analysis of the United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE) cohort. *J Clin Endocrinol Metab.* 2013 Feb;98(2):E346-54.

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder that requires life-long contact with health care professionals. The challenges of organizing and ensuing successful transitions for patients from pediatric to adult care are increasingly recognized. A recent study in the UK [Arlt W, et al., [Health status of adults with congenital adrenal hyperplasia: a cohort study of 203 patients](#). United Kingdom Congenital Adrenal Hyperplasia Adult Study Executive (CaHASE). *J Clin Endocrinol Metab.* 2010;95:5110-21] suggested that most adult patients with CAH are not seeking or receiving medical services. Gleeson and colleagues [refs #1 and 2 in this section] provide information on 53 patients (57% women) with CAH from a single center in the UK. The subjects were aged 17-20 years at the time of transition. In this audit, Gleeson et al [ref #1, 2 in this section] noted that 50% of patients with CAH had poor biochemical control and/or adverse clinical consequences. Further, 50% of those transferred to an adult specialist were lost of follow-up. Glitches in the process of transferring care from pediatric to adult health care providers negatively impacts medical care, decreases quality of life, and increases risks for potentially avoidable consequences of CAH. Krone and colleagues [ref #3 in this section] concluded that the patient's genotype did not correlate well with the current health status. Rather steroid dose and health provision were the major factors influencing current health status. These papers emphasize the relevance and importance of adequate planning for transition of emerging adults with chronic health disorders to adult care.

PCOS – Metabolic Dysfunction/Cardiovascular Disease/Inflammation

Bird ST, Hartzema AG, Brophy JM, Etmnan M, Delaney JA. Risk of venous thromboembolism in women with polycystic ovary syndrome: a population-based matched cohort analysis. *CMAJ.* 2013;185(2):E115-20.

These authors questioned whether there is an additional risk among women with polycystic ovary syndrome. They thus developed a population-based cohort from the IMS LifeLink Health Plan Claims Database which includes managed care organizations in the United States. Women aged 18-46 years taking combined oral

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contraceptives and who had a diagnosis of PCOS (n = 43,506) were matched, based on a propensity score, to control women (n = 43 506) taking oral contraceptives. The definition of venous thromboembolism was based on administrative coding and use of anticoagulation and Cox proportional hazards model was used to assess the relative risk. The incidence of venous thromboembolism among women with PCOS was 23.7/10,000 person-years, while that for matched controls was 10.9/10,000 person-years. Women with PCOS taking combined oral contraceptives had an RR for venous thromboembolism of 2.14 (95% confidence interval [CI] 1.41-3.24) compared with other contraceptive users. The incidence of venous thromboembolism was 6.3/10 000 person-years among women with PCOS not taking oral contraceptives; the incidence was 4.1/10 000 person-years among matched controls. The RR of venous thromboembolism among women with PCOS not taking oral contraceptives was 1.55 (95% CI 1.10-2.19). They concluded that there was a 2-fold increased risk of venous thromboembolism among women with PCOS who were taking combined oral contraceptives and a 1.5-fold increased risk among women with PCOS not taking oral contraceptives.

PCOS – Ovary

Palomba S, Falbo A, La Sala GB. Effects of metformin in women with polycystic ovary syndrome treated with gonadotrophins for in vitro fertilisation and intracytoplasmic sperm injection cycles: a systematic review and meta-analysis of randomised controlled trials. BJOG. 2013 Feb;120(3):267-76.

This meta-analysis by Palomba et al provides more insight, and produces more questions, on the effects of metformin treatment when providing IVF care to infertile PCOS patients. The meta-analysis contained 10 RCTs, significantly more than previous meta-analyses, resulting in a total of over 900 subjects. They confirm previous findings of significantly lower OHSS rates with metformin treatment. Of greater interest, however, are higher embryo implantation rates and lower miscarriage rates when metformin is used, particularly with standard dosing and when given long-term. Live birth rates are not different with metformin administration. When the authors removed one study from the analysis, however, specifically evaluating PCOS patients with diminished ovarian reserve, metformin treatment increased the live birth rate. Clinicians are increasingly using metformin in PCOS patients undergoing IVF. This treatment certainly requires more study to confirm its benefit.