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IN BRIEF

REPRODUCTIVE ENDOCRINOLOGY

Updated guidance on evaluating suspected DSDs

New recommendations for the initial evaluation of infants or adolescents with a suspected disorder of sex development (DSD) have been published by the UK Society for Endocrinology. A UK DSD taskforce consisting of a range of clinical professionals, stakeholder professional societies and members of patient support and/or advocacy groups was formed in 2009 to provide guidance to clinical professionals who encounter infants or adolescents with a DSD, and to harmonize good clinical practice. The findings, published in *Clinical Endocrinology*, emphasize the importance of supporting the affected individual and their parents, assigning a sex of rearing and excluding the possibility of other early medical problems.

Original article Ahmed, S. F. *et al.* Society for Endocrinology UK guidance on the initial evaluation of an infant or an adolescent with a suspected disorder of sex development (Revised 2015). *Clin. Endocrinol.* <u>doi:10.1111/cen.12857</u>

PCOS

Susceptibility loci identified in women of European descent

A new study has identified common genetic loci for the NIH polycystic ovary syndrome (PCOS) phenotype of hyperandrogenism and anovulation in women of European descent. In a genome-wide association study with two rounds of replication in different cohorts, three loci reached genome-wide significance. Two of the loci identified were novel: 8p32.1 in the region of *GATA4* (encoding a transcription factor that regulates gonadal development and transcription of steroidogenic genes) and *NEIL2*; and 11p14.1 in the region of *FSHB* (encoding follicle-stimulating hormone β subunit), which is strongly associated with PCOS diagnosis and luteinizing hormone levels. The third loci, 9q22.32, in the region of *AOPEP* and FANCC, was previously identified in Chinese women with PCOS. The findings, together with those from the Chinese cohort, implicate genes regulating gonadotropin action and secretion in the pathogenesis of PCOS.

Original article Hayes, M. G. et al. Genome-wide association of polycystic ovary syndrome implicates alterations in gonadotropin secretion in European ancestry populations. *Nat. Commun.* doi:10.1038/ncomms8502

DIABETES

Mechanistic insights into diabetes-associated fluid loss

New research shows that reduced expression of electrolyte transport proteins contributes to diabetic diarrhoea, a gastrointestinal complication that is common in patients with type 1 diabetes mellitus (T1DM). In mice with streptozotocininduced T1DM, the rate of fluid absorption in the small intestine (a marker of diarrhoea) was ~50% lower than that in nondiabetic control mice. Associated with this reduction, expression of Na⁺/H⁺ exchanger 3 (NHE-3) and several proteins that bind NHE-3 were reduced in the intestinal brush border membrane (BBM). Under physiological conditions, NHE-3 and its binding proteins formed complexes that facilitated trafficking of NHE-3 to the BBM, consequent NHE-3 activity and ensuing fluid absorption; however, under diabetic conditions, NHE-3 complex formation was disrupted. Treatment of diabetic mice with insulin reconstituted NHE-3 complexes and restored fluid absorption. The findings highlight the pivotal role of multiprotein complex assembly in restoring fluid absorption in T1DM.

Original article He, P. et al. Restoration of Na⁺/H⁺ exchanger NHE3-containing macrocomplexes ameliorates diabetes-associated fluid loss. J. Clin. Invest. doi:10.1172/JCI79552