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Dr Nils P Krone MD FRCPCH

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Qualifications

- Fellow of the Royal College of Paediatrics and Child Health 2010
- Sub-speciality recognition in Paediatric Endocrinology and Diabetes 2008
- Speciality recognition in General Paediatrics 2005
- MD medicine 2001
- MBChB equivalent 1999

Teaching

- Teacher on the MBChB and BMedSc course:
- Small group teaching year 1 and 2: hypothalamus-pituitary adrenal axis, adrenal, and male and female reproductive endocrinology.
- Lectures on childhood growth, sex differentiation and puberty.
- Clinical teaching of 5th year MB students

Postgraduate supervision

PhD Consortium “Translational Endocrinology/Translational Steroid Physiology”

External examiner for PhD, MSc students

Research

RESEARCH THEMES

Congenital adrenal hyperplasia, inborn errors of steroidogenesis, steroid hormone metabolomics, childhood obesity, androgen excess disorders

Inborn errors of steroidogenesis

The main focus his research is the genetics and molecular pathogenesis of different forms ofcongenital adrenal hyperplasia (CAH) and the translation of molecular results into clinical practice. Currently, his group is exploring the impact of protein stability and influences on subcellular protein localisation on the pathophysiology of adrenal pathophysiology. This project aims to establish novel treatment strategies for inborn genetic conditions. Recently, he has conducted the genetic analysis and analysis of the genoptype-phenotype correlation in a UK-wide audit study on adults with CAH. Other projects include the *in vitro* and *in silico* analysis of novel mutations and genetic variants causing CAH and adrenal/ gonadal insufficiency, including 21-hydroxylase, 17α-hydroxyalse, 11β-hydroxylase, P450 oxidoreductase, 3β-HSD type 2, and side-chain cleavage enzyme. To further enhance the understanding of molecular regulation, in particular redox-regulation, his group is establishing murine and zebrafish models to study the *in vivo* impact of knock-out and knock-down models.

Steroid hormone metabolomics

Another key interest is steroid hormone metabolomics and the translation of urine steroid metabolite analysis as diagnostic test for disorders of sex development and non-invasive monitoring of disease control in infants and children with CAH.

Childhood obesity

Nils Krone’s clinical research comprises studies into the natural history of steroid metabolism in correlation with body composition and metabolic parameters. This will allow to define the impact of steroid synthesis and metabolism on the pathophysiology of obesity. This is of key importance as modulation of mineralocorticoid, glucocorticoid and sex steroid synthesis are potential targets for future treatment of co-morbidities in obesity.

Androgen excess disorders

He is involved in and conducting studies on the identification of causes of early androgen excess in children and adolescents, who present with premature adrenache and adolescent polycystic ovarian syndrome (PCOS). Furthermore, he is developing studies into long-term metabolic consequences of such conditions to improve individualised care provision.

Other activities

- Member of the NHS Diabetes: Paediatric Diabetes Education Task & Finish Group (2010 – 2011)
- Member of Joint Society for Endocrinology/ British Society for Paediatric Endocrinology DSD taskforce and involved in the development of national guidelines for diagnosis of disorders of sex development (DSD).
- Member of the European Society for Paediatric Endocrinology (ESPE) web site editorial board and ESPE visiting scholarship committee
- Honorary Consultant in Paediatric Endocrinology & Diabetes, Birmingham Children's Hospital NHS Foundation Trust; Lead of disorders of sex development (DSD) clinic

Publications

Krone N, Reisch N, Idkowiak J, Dhir V, Ivison HE, Hughes BA, Rose IT, Holmes D, Barton T, Cole TR, Collins F, Cragun D, Dattani MT, Day R, Gottschalk M, Gregory JW, Haim M, Haskins Olney A, Hauffa BP, Hindmarsh PC, Hopkin R, Jira P, Maiter A, Nielsen S, O'Riordan SM, Roth CL, Shane K, Silink M, Sweeney E, Szarras-Czapnik M, Williamson L, Wudy SA, Hartmann M, Taylor NF, Malunowicz E, Shackleton CHL, Arlt W. Genotype-phenotype analysis in congenital adrenal hyperplasia due to P450 oxidoreductase deficiency. **J Clin Endocrinol Metab 97:E257-67** (2012)

Reisch N, Arlt W**,** Krone N. Health implications in congenital adrenal hyperplasia due to 21-hydroxylase deficiency. **Horm Res Paediatr 76:73-85** (2011)

Parajes S, Kamrath C, Rose IT, Mooij CM, Dhir V, Arlt W, Krone N. A Novel Entity of Clinically Isolated Adrenal Insufficiency Caused by a Partially Inactivating Mutation of the Gene Encoding for P450 Side Chain Cleavage Enzyme (CYP11A1). **J Clin Endocrinol Metab 96:E1798-1806** (2011)

Arlt W, Willis DS, Wild SH,Krone N, Doherty EJ, Hahner S, Han TS, Carroll PV, Conway GS, Rees DA, Stimson RH, Walker BR, Connell JMC, Ross RJ and the United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE). Health Status of Adults with Congenital Adrenal Hyperplasia: A Cohort study of 203 patients. **J Clin Endocrinol Metab 95:5110-5121** (2010)

Krone N, Hughes BA, Lavery GG, Stewart PM, Arlt A, Shackleton CHL.Gas chromatography/mass spectrometry (GC/MS) remains a pre-eminent discovery tool in clinical steroid investigations even in the era of fast tandem mass spectrometry (LC/MS/MS). **J Steroid Biochem Mol Biol 121:496-504** (2010)

Parajes S, Loidi L, Reisch N, Dhir V, Rose IT, Hampel R, Quinkler M, Conway GS, Castro-Feijóo L, Araujo-Vilar D, Pombo M, Dominguez F, Williams EL, Cole TR, Kirk JM, Kaminsky E, Rumsby G, Arlt W, Krone N. Functional Consequences of Seven Novel Mutations in the CYP11B1 Gene - Four Mutations Associated with Non-Classic and Three Mutations Causing Classic 11β-Hydroxylase Deficiency **J Clin Endocrinol Metab 95:779-788** (2010)

Dhir V, Reisch N, Bleicken CM, Lebl J, Kamrath C, Schwarz HP, Grotzinger J, Sippell WG, Riepe FG, Arlt W, Krone N**.** Steroid 17α-Hydroxylase Deficiency: Functional Characterization of Four Mutations (A174E, V178D, R440C, L465P) in the *CYP17A1* Gene. **J Clin Endocrinol Metab 94:3058-3064** (2009)

Krone N, Arlt W.Genetics of congenital adrenal hyperplasia. **Best Pract Res Clin Endocrinol Metab 23:181-192** (2009)

Bleicken C, Loidi L, Dhir V, Parajes S, Quinteiro C, Dominguez F, Grötzinger J, Sippell WG, Riepe FG, Arlt W,Krone N.Functional characterization of three CYP21A2 sequence variants (p.A265V, p.W302S, p.D322G) employing a yeast co-expression system. **Hum Mutat E443-50** (2009)

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