

BRINGING THE LATEST IN PAEDIATRIC ENDOCRINOLOGY TO YOU

Understanding DSD

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Welcome

The range of conditions we describe as differences of sexual development (DSD) present paediatric endocrinologists, patients and parents with some immense challenges. Their diversity, combined with the associated psychological issues, physiological changes as children age and societal pressures, means we must try to align our clinical practice with the truly unique needs and circumstances of each individual.

This is easier said than done but, in this issue, we hope to bring you the latest information from the field's cutting edge. On **page 5**, Martine Cools and Olaf Hiort summarise key points from the recent consensus document on DSD. They consider issues as diverse as naming conventions, multidisciplinary management, clear communication, psychosocial support, surgery, gender well-being and research.

On **page 6**, we swoop in to look at the molecular level, as Andrew Sinclair describes his team's research into the genetics of sex reversal and the role of regulatory sequences upstream of the gene for transcription factor SOX9.

Debate surrounding surgical intervention in DSD is especially contentious. Melissa Gardner and David E Sandberg examine the issues associated with decision making on **page 7**. Ways of addressing parents' anxiety and lack of knowledge are crucial, along with psychological support and tools to aid the decision-making process.

The role of prenatal androgens in human psychosexuality is our subject on **page 8**. Rafael Loch Batista, Marlene Inacio and Berenice Bilharinho Mendonca outline their fascinating research into prenatal androgen exposure and subsequent male gender role in childhood, gynaephilic sexual orientation and male gender identity.

Finally, most important amongst the other news in this issue are the exciting details about the forthcoming ESPE Meeting in Vienna, Austria, on 19–21 September (see **page 9**). Don't miss out – make sure you register before the early bird deadline of 20 June!

Sarah Ehtisham
Editor, *ESPE News*

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Clinical Fellowship



Deadline 31 May 2019

The Clinical Fellowship funds trainee paediatric endocrinologists to develop skills and knowledge in patient care, clinical management and clinical research by undertaking training in a specialised European clinical centre. Find out more at www.eurospe.org/grants-awards/grants/clinical-fellowship and apply by 31 May 2019.



"I was able to visit Sheffield in the UK and learn from well-known experts, not only in paediatric endocrinology, but also in genetics, gynaecology, neurosurgery and urology. I learned the importance of teamwork and its benefits for decision-making and improving patient care, and made valuable contacts with whom I will continue to exchange knowledge."
Huda Elhajburrani, Libya

ESPE Council elections

An e-vote this summer will enable ESPE members to elect the next Chairs of the:

- Programme Organising Committee
- Corporate Liaison Board
- Education & Training Committee
- Clinical Practice Committee.

Details will follow by email. **Please check we have your current email address** by logging into the members' area at www.eurospe.org.

6th ASPED-ESPE Endocrine Academy

15–17 October 2019, Casablanca, Morocco



Deadline 15 June 2019

This academy in paediatric endocrinology is for trainees and junior consultants practising in the Arab countries. It includes plenary lectures and small group discussions on major topics in the field, and the faculty comprises senior ASPED (Arab Society for Paediatric Endocrinology and Diabetes) and ESPE members. Delegates are each expected to present at least one case/research project.

Successful applicants will be entitled to free registration, accommodation and meals, but not travel expenses. See www.eurospe.org/education/asped-espe-endocrine-academy for details. Applications should be sent to aspedendo@hotmail.com by 15 June 2019.

Could you host ESPE's Science Symposium?

Would you like to plan and deliver a 1.5-day symposium on an area of paediatric endocrinology, with a budget of up to €30 000?

We are welcoming applications from potential local organising committees for the 2020 ESPE Science Symposium. If you or your collaborative group would like to showcase the latest scientific knowledge, host topical discussions and provide

networking opportunities for scientists and clinicians, please apply by 17 June.

You can find guidelines, an application form and details of the successful inaugural 2018 Symposium at www.eurospe.org/education/espe-science-symposium.

The topic of your meeting should be attractive to researchers in basic or translational research, as well as ESPE

members developing experimental and clinical research within and beyond paediatric endocrinology.

We look forward to receiving your applications!



Deadline 17 June 2019



The 2018 ESPE Science Symposium

Annual Review 2018

You can find the ESPE Annual Review for 2018 at www.eurospe.org/about/annual-review (you will also receive a copy by email). It gives a round-up of the Society's activities from last year and celebrates all that ESPE continues to achieve – thanks to its members.

With regret

It was with great sadness that we heard of the recent passing of two ESPE members: Dr Birgit Köhler (Germany) and Dr Maria Kalina (Poland). We send our condolences to their families, friends, colleagues and patients. You can read their obituaries at www.eurospe.org/news.

ESPE e-Learning news

www.espe-elearning.org Registration is **free!**



DSD in e-Learning

Under 'General Content'/Disorders of Sex Development:

- 14 chapters concerning the initial endocrine approach, differential diagnosis, sex assignment and management of DSD, as well as psychological, social and cultural factors
- 7 case studies

Under 'Resource Limited Countries'/Disorders of Sex Development:

- the approach is divided into primary, secondary and tertiary care
- 3 case studies

New items

Under 'General Content'/Calcium and Bone:

- a case of a 9-month-old boy with hypercalcaemia (see image, right)

Under 'Resource Limited Countries', new cases in:

- Diabetes ISPAD Guidelines: Isha, a 2-year-old girl
- Puberty: Amna, a 6-year-old girl with Down syndrome
- Sodium and Water: Julie, a 10-year-old girl
- Thyroid: a 13-year-old girl with weight loss



Humeral lesions in hypercalcaemia

Bringing you recent highlights from the world of research

Is muscular fitness associated with future health?

Muscular fitness is a valuable indicator for monitoring child and adolescent health. Despite this, recent evidence shows a decline in muscular fitness in school-age youth. To support the development of health-promoting strategies, it is important to monitor fitness levels in children and to quantify associations with health parameters later in life.

García-Hermoso *et al.* performed a meta-analysis of articles that examined healthy children aged 3–18 years with muscular fitness assessed at baseline and a follow-up period of ≥ 1 year. They included 30 studies and found significant correlations with moderate–large ($P < 0.05$) effect sizes between muscular fitness at baseline and parameters for obesity (body mass index, skinfold thickness), cardio-metabolic health (homeostasis model assessment estimated insulin resistance, triglycerides, cardiovascular disease risk score) and bone mineral density at follow-up.

They conclude that a negative association exists between muscular fitness in childhood/adolescence and adiposity and cardio-metabolic parameters in later life, together with a positive association for bone health.



Read the full article in García-Hermoso *et al.* 2019 *Sports Medicine* doi: 10.1007/s40279-019-01098-6

Closing the loop on young people with type 1 diabetes

This review summarises the developmental and physiological needs of young people with type 1 diabetes, and considers how hybrid closed-loop (HCL) systems could address these issues. Perhaps the most important feature of HCL systems is their ability to automatically regulate overnight insulin infusion rates, based on changes in sensor glucose values.

Most studies of HCL technologies in young people show the superiority of closed-loop insulin delivery when compared with either conventional pump therapy or sensor-augmented pump therapy. The author considers features that could make the technology more attractive to these patients and their families as future-generation closed-loop systems are devised. Limited access to various system features may be desirable for youngsters. For paediatric patients, it is important to have alerts that are customisable, along with simplified strategies for meal announcement and managing glucose during exercise.

Integration of HCL has the potential to minimise the burden of type 1 diabetes while improving glycaemic control and ultimately allowing paediatric patients to fulfill the primary goal of childhood: to be a kid!



Read the full article in Sherr 2018 *Diabetes Care* 41 1572–1578

Colorectal cancer risk of a daily slice of bacon

In 2015, the World Health Organization classified processed meat as carcinogenic and red meat as probably carcinogenic to humans. The latest research by Bradbury *et al.* in a large contemporary prospective study of half a million men and women from the UK (including 2609 cases of incidental colorectal cancer) supports this statement.

It indicates that consumption of red and processed meat at an average level of 76g/day (which meets the current UK Government's recommendation of <90g/day) was associated with an increased risk of colorectal cancer. The risk was higher with consumption of processed meat than with red meat.

Colorectal cancer increased by 19% with every 25g processed meat (equivalent to one rasher of bacon or one slice of ham), and by 18% with every 50g red meat (equivalent to one thick slice of roast beef or the edible portion of one lamb cutlet), that people ate per day.



Read the full article in Bradbury *et al.* 2019 *International Journal of Epidemiology* doi: 10.1093/ije/dyz064

Rotavirus vaccination and type 1 diabetes

Rotavirus infection has been reported to be a risk factor for development of type 1 diabetes in children. Perrett *et al.* undertook an observational study in Australia, where children with newly diagnosed type 1 diabetes are registered with the National Diabetes Services Scheme. Using publicly available data, they examined the incidence of newly diagnosed type 1 diabetes in children between 0 and 14 years of age, in a period extending 8 years before and 8 years after oral rotavirus vaccination was introduced in 2007. Estimated national coverage for the vaccine was 84%.

In children aged 0–4 years, the incidence decreased by 14% after introduction of the vaccine. There was no evidence of change over time in the pre-intervention and postintervention patterns of incidence. In children aged 5–9 years and 10–14 years, there was no change in the number of incident cases or temporal differences during the study period (2000–2015). Studies are ongoing to explore this association further.



Read the full article in Perrett *et al.* 2019 *JAMA Pediatrics* doi: 10.1001/jamapediatrics.2018.4578

Caring for individuals with DSD

Martine Cools and Olaf Hiort reflect on the importance of the recently published consensus statement to optimise support for patients and their families.

The 2005 Chicago Consensus Meeting laid the foundation for a revised classification and model of care for the various conditions termed 'differences of sex development' (DSD). Since then, societal changes have placed further emphasis on children's rights and autonomy, and on the demedicalisation of naturally occurring developmental variations.

This evolution has to be reconciled now with the need for medical and psychosocial support experienced by many individuals and families. To this end, the EU-funded COST (Co-operation for Science and Technology) Action 'DSDnet, a systematic elucidation of DSD', co-ordinated by Olaf Hiort, convened from 2013 to 2018. This network included experts and scientists from over 30 countries in Europe and internationally.

A working group of this COST Action reflected on the requirements for a holistic and precise phenotypic description of individuals who have a DSD, and on the standardisation of care across ages and geographical regions. This resulted in the recent consensus document: www.nature.com/articles/s41574-018-0010-8.

This aims to tailor the cornerstones of contemporary DSD management to the principles of today's society, while addressing the needs of those seeking holistic care, and to lay the foundations for multicentre, high quality, patient-centric research on outcomes of management. The main insights are highlighted below.

What's in a name?

The terms 'intersex' and 'disorders of sex development' are problematic for many individuals, due to their association with gender identity and abnormality respectively. Terms such as 'differences' or 'variations' may circumvent these problems, but most people prefer a specific name for their condition, or an umbrella term avoiding the word 'sex'.

Optimising management

Holistic management of DSD conditions is complex, and needs a multidisciplinary team (MDT). The individual conditions are very rare and require centralisation in a limited number of reference centres to guarantee sufficient expertise and optimal quality of care.



Martine Cools



Olaf Hiort

“*Intensive counselling of families in how to raise resilient, self-confident children who have a genital difference is paramount, and may require extensive psychosocial support*”

Transparency and transition

Full transparency and comprehensive age-appropriate information from early childhood onwards have been related to positive adult outcomes. Many patients experience difficulties in finding specialised teams for adults who have a DSD condition or abandon medical care while transitioning to adult clinics. The consensus document discusses management of DSD across ages, with guidance for physicians who see these patients infrequently.

Alternatives to early surgery

There is increasing awareness that early genital surgery should be avoided whenever possible. However, it is clear that simple prohibition of such surgery is inadequate in addressing the needs of patients and families. Intensive counselling of families in how to raise resilient, self-confident children who have a genital difference is paramount, and may require extensive psychosocial support. Most healthcare systems do not foresee financial support for hospitals to organise this, or reimbursement of patients who receive these treatments. This requires the urgent attention of European and national health authorities.

Assessing gender well-being

Although the incidence of gender dysphoria is only marginally increased in individuals who have a DSD, many do not conform to a strict binary interpretation of gender and may adopt atypical gender roles. Thus, assessment of gender well-being and an individual's opportunity to eventually have an atypical gender expression may be far more relevant than gender identity. From a societal point of view, a non-normative environment with regard to sex and gender may facilitate acceptance of the condition and improve well-being.

Collaborative research

The impact of recent management changes on psychosocial development and well-being is currently unknown. Systematic collection of standardised outcome data across centres in an international registry (e.g. the I-DSD registry; <https://home.i-dsd.org>) is paramount. By investing in future research to shed light on patient-centred long term outcome measures, we will improve the quality of care. This will also enhance discussions around integration of different gender expressions into our societies.

Martine Cools

Ghent University, Ghent, Belgium

Olaf Hiort

University of Lübeck, Lübeck, Germany

Human sex reversal linked to enhancers upstream of *SOX9*

Recent research by a team led by Andrew Sinclair provides important insights into the genetics underlying sex reversal.



Andrew Sinclair

“

*Each of the enhancers mentioned has an essential, yet distinct, role in initiating and maintaining human *SOX9* expression”*

Gonadal sex differentiation in the embryo begins with the development of the bipotential gonads into testes or ovaries. Testis determination is initiated by the Y-linked *SRY* gene. *SRY* upregulates the gene encoding the transcription factor *SOX9*, which is necessary and sufficient for testis development.

SOX9 tissue-specific expression is influenced by long-range regulatory elements within 2Mb upstream of the *SOX9* transcriptional start site. While studies have identified enhancers regulating *Sry*-mediated *Sox9* expression in mice, the human testis-specific enhancers remained to be fully elucidated.

Redefining the landscape

46,XX and 46,XY patients with disorders of sex development (DSD) had previously been identified with copy number variants which hinted at deletions or duplications within two putative *SOX9* upstream regulatory regions, denoted XYSR and RevSex. In recent work, the upstream regulatory landscape of human *SOX9* has now been redefined using bioinformatics and luciferase tiling approaches, to identify enhancers for *SOX9* expression.

From a cohort of 44 patients with DSD, two duplications were identified in the XYSR regulatory region upstream of *SOX9* in two unrelated patients. Since these duplications overlapped with each other and the XYSR region, it was anticipated that a core gonadal enhancer for *SOX9* could be found in this critical region. Within this region, DNaseI hypersensitivity data revealed strong regulatory potential in human embryonic testes, but not in ovaries.

The identified region was cloned as overlapping fragments and tested in several cell lines by luciferase assay using testicular transcription factors known to induce *SOX9* expression. The strongest regulatory response was observed with a 1514bp fragment that probably contained the core enhancer. This genomic region was named sex reversal enhancer-A (eSR-A). This fragment contains consensus binding sites for the testicular transcription factors *SRY/SOX9* and steroidogenic factor 1 (SF1). Thus, eSR-A contained a critical *SOX9* enhancer that, when deleted in mice, results in 46,XY sex reversal and, when duplicated, causes 46,XX (ovo)testicular DSD in humans.

By analysing a duplication in a 46,XX ovotesticular DSD patient within the RevSex region, a second *SOX9* enhancer was identified, which is thought to contribute to *SOX9* autoregulation. This involved an unbiased screening approach, cloning 16 overlapping fragments of a previously narrowed region within RevSex, and testing each for enhancer activity. Two of the fragments showed a significant increase in enhancer activity in response to SF1 and *SOX9*. The two fragments overlapped in a region that contained a highly conserved *SOX9*-binding motif. This region was designated sex reversal enhancer-B (eSR-B), a human-specific *SOX9* gonadal enhancer that, when disrupted, can cause sex reversal.

To locate an *SRY*-responsive enhancer of *SOX9* in humans, bioinformatics screening was used to look for conserved enhancer marks upstream of *SOX9* in publicly available databases. A locus was identified which contained a DNaseI hypersensitive site in embryonic testis, a putative *SRY*-binding site and strong active enhancer marks, and which was highly conserved between mice and humans. Since this fragment responded to the transcription factors *SRY*+SF1 and *SOX9*+SF1, but not *SOX9* alone, it is probably important for *SRY* initiation of *SOX9* expression in the developing testis. It was designated alternate long-distance initiator (eALDI) of *SOX9*.

Suggesting a model

Each of the enhancers mentioned above has an essential, yet distinct, role in initiating and maintaining human *SOX9* expression.

A model is suggested where *SRY* and SF1, which are expressed early in human testis development, bind eALDI as the primary enhancer to initiate *SOX9* expression in the embryonic male gonad. Subsequently, *SOX9* alone, or in combination with SF-1, binds sites within eSR-A, eSR-B and eALDI, to synergistically amplify testicular *SOX9* expression in humans.

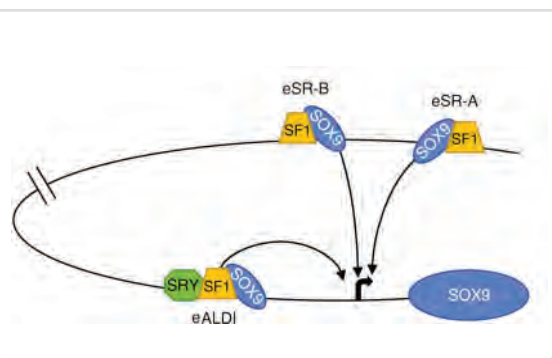
Andrew Sinclair

Deputy Director, Murdoch Children's Research Institute, and Professor, Department of Paediatrics, University of Melbourne, Melbourne, Vic, Australia

Reference

1. Croft et al. 2018 *Nature Communications* 9 5319.

Proposed model of *SOX9* activation. In XY individuals, *SRY* and SF1 are expressed early in the human XY fetal gonad, and initiate *SOX9* expression via the eALDI enhancer. *SOX9* expression is then further upregulated and maintained by SF1 and *SOX9* with all three enhancers eSR-A, eSR-B and eALDI, potentially via chromatin looping, allowing direct interaction between the enhancers and the *SOX9* promoter. Reproduced from Croft et al. 2018¹ under a Creative Commons Attribution 4.0 International Licence



Surgical intervention in DSD

Melissa Gardner and David E Sandberg examine the controversy surrounding surgery in DSD, and look for paths forward.

Disorders of sex development (DSD) encompass varied diagnoses and phenotypes, ranging from few somatic differences to those raising significant clinical management questions. Surgical procedures are particularly associated with contentious debate between and within stakeholder communities.

Controversy

All stakeholders seek what is in the best interests of the affected individual – although differences lie in how to arrive at that outcome. Additional areas of agreement include the following.

- Early surgery in DSD is largely elective. With limited exceptions, irreversible decisions could be postponed until patients can be involved in discussions and provide assent, without jeopardising physical health.
- Surgical interventions do not address several driving factors: parental anxiety, shame and desire for secrecy.¹ Parents may feel stigmatised and seek to act quickly to 'normalise' their child's genital appearance before becoming fully informed about all options, risks and benefits.²

While the intent of surgical management of the genitals and gonads is to benefit patients physically and psychosocially, these goals have not always been achieved. Grounded in reports of surgical complications and dissatisfaction among some who experienced early genitoplasty, intersex advocacy and human rights organisations condemn early DSD-related surgery, and call for a moratorium on all 'medically unnecessary' childhood genital and gonadal surgery.

As gaps exist in high quality evidence that could be used to inform decision making on both individual and healthcare policy levels, some stakeholders have pursued means outside research to address their concerns. These include courts of law, legislative bodies, ethicists and human rights organisations. Less-often considered are potential risks or comparative outcomes associated with surgery performed later in life. Fundamental differences in perspectives extend to words used by different stakeholder groups; DSD care is burdened by varied and, frequently, polarised terminology.



Melissa Gardner



David E Sandberg

“
The lack of accessible, clear information was noted as one of the most frustrating aspects of parenting a child with a DSD”

Paths forward

Current efforts to ban elective genital surgery while a patient is too young to provide informed consent leaves two possible paths forward: eliminating all elective procedures until adulthood versus continuing to leave decisions to parents, providers and patients (when mature enough to participate).

The birth of a child with a DSD, and attendant uncertainty about the child's gender and psychological and somatic sex development, is considered extraordinarily stressful for parents.³ Many decisions made during this early period have permanent and far-reaching consequences for the child.

The lack of accessible, clear information was noted as one of the most frustrating aspects of parenting a child with a DSD.^{4,5} Together with factors identified as strongly influencing the desire for surgical interventions (i.e. parental anxiety, shame, stigma and a desire to 'fix' or 'normalise' children's genital appearance and/or function), lack of knowledge needs to be resolved by the healthcare team, regardless of whether decisions about elective surgery are considered.

Indeed, advocates calling for the moratorium have also called for a robust patient- and family-centred approach to care, in which psychological services are essential. The act of ending or continuing access to elective surgical procedures during childhood is not an end itself; rather, we must address what drives the desire for these procedures.

Provided elective surgical procedures remain available, a shared decision-making process is recommended. Decision support tools are designed to help people make deliberate choices among options by:

- explicitly describing treatment choices
- providing quantitative risk and benefit estimates, when available
- tailoring information to individual patients, and
- providing a context in which patients and parents can consider treatment options in light of their own values.

Development and effective application of formalised decision support tools in the clinical context is an area in which patient advocates can hopefully collaborate with healthcare providers, rather than choosing the blunt tools of governmental legislation and lawsuits to resolve complex medical and social issues.

Melissa Gardner and David E Sandberg
Division of Pediatric Psychology and Susan B Meister Child Health Evaluation and Research Center;
Department of Pediatrics, University of Michigan,
Ann Arbor, MI, USA

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4. Crissman et al. 2011 *International Journal of Pediatric Endocrinology* doi: 10.1186/1687-9856-2011-10.
5. Boyse et al. 2014 *Journal of Pediatric Nursing* **29** 436-441.

Psychosexuality and prenatal androgens

Rafael Loch Batista, Marlene Inacio and Berenice Mendonca's studies of 46,XY individuals with DSD have shed light on the role of prenatal androgens in psychosexuality.



Rafael Loch Batista

Human sexual development is a dynamic process, regulated by genes and facilitated by endocrine mediators. This development starts in the neonatal period, after the bipotential gonads differentiate into testes in the presence of male-determining genes.¹

Usually, these gonads will produce androgens.¹ In the brain, androgens are able to virilise androgen-sensitive areas which will affect the development of a male psychosexuality. In the absence of androgens (but not in the presence of oestrogens), human psychosexuality is driven to a female pathway.²

Many factors may play a role in human psychosexuality: genes, sex steroids, culture. The specific contribution of each is hard to estimate.³

The effects of androgens on the external genitalia (at 6–8 weeks of gestation) do not happen at the same time as they occur in the brain (in the second half of gestation). Consequently, virilisation of the brain and external genitalia do not occur in parallel in humans.^{4,5} It has largely been demonstrated that prenatal androgen exposure favours a male gender role and gynaephilic (female-driven) sexual orientation, but the association of that exposure with gender identity is less uniform.

Differences of sex development (DSD) in 46,XY individuals are characterised by variable degrees of undervirilisation, according to 46,XY DSD aetiology. Many factors can have an impact on their psychosexuality. However, there is a relative lack of data on psychosexual outcomes in these patients.

Assessing androgen impact

To analyse the effect of prenatal androgen exposure, we divided a cohort of 46,XY DSD patients ($n=144$) according to prenatal androgen exposure.⁶ The frequency of male gender role at childhood, gynaephilic sexual orientation and male gender identity increased in accordance with the degree of prenatal androgen exposure. Gender change from female to male was frequent (19%; $n=27$) and happened only in individuals with prenatal androgen exposure.

It is reasonable to consider that the presence of atypical external genitalia could affect the psychosexuality of both boys and girls. However, it is a questionable concept. In conditions such as cloacal exstrophy, penis ablation and 5 α -reductase type 2 deficiency, there are several reports of male

gender identity, despite severe external genitalia undervirilisation.

Accordingly, our results showed that the virilisation score of external genitalia did not influence the psychosexuality of 46,XY individuals with different 46,XY DSD aetiologies. Collectively, this evidence suggests that external genitalia undervirilisation does not compromise male psychosexuality.

The remaining question is whether virilisation of external genitalia could influence female psychosexuality. To answer this, we compared 46,XY DSD women with and without atypical external genitalia. In these women, all psychosexual parameters analysed were similar, suggesting a limited effect of external genitalia appearance on the psychosexual development of girls as well.

“

A male psychosexuality is more likely to develop in a fetus exposed to androgens, regardless of the external genitalia virilisation score”

In conclusion

Our data show that androgens drive human psychosexuality. Their presence favours the development of a male psychosexuality, whereas female psychosexuality results from their absence.

The virilisation of a fetus is an orchestrated event, where virilised external genitalia do not necessarily match a virilised brain. With regard to this discrepancy, the brain is stronger: a male psychosexuality is more likely to develop in a fetus exposed to androgens, regardless of the external genitalia virilisation score.

Studies of people with 46,XY DSD reinforce the concept that prenatal androgen exposure is related to all male psychosexual outcomes, including gender identity. As 46,XY DSD is a heterogeneous condition, the aetiological diagnosis allows estimation of prenatal androgen exposure, which is helpful for counselling, management and sex assignment.

Rafael Loch Batista, Marlene Inacio and Berenice Bilharinho Mendonca
School of Medicine, Universidade de São Paulo, São Paulo, Brazil

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ESPE 2019: Variety and Variation in Paediatric Endocrinology

19–21 September 2019, Vienna, Austria

“The ESPE Meeting is an important place for networking and creating new ideas”

Delegate, ESPE 2018



Register now at www.espe2019.org

- Discounted early bird fees until 20 June 2019
- Additional reductions for ESPE members

Enjoy it all at ESPE 2019

The Annual ESPE Meeting is a rare and valuable opportunity for basic scientists and clinicians to network and collaborate. Showcasing the latest developments in paediatric endocrinology, ESPE 2019 has an exciting mix of basic science, translational research and clinical care, with something of interest to you all. Seven plenary lectures will display the diversity we see in our discipline, delivered by internationally renowned speakers from around the world (see panel for details).

At ESPE 2019 you'll also discover:

- Eleven symposia focusing on advances in research, treatment and clinical endocrinology
- The return of 'How do I...?' – highly regarded sessions, where you can learn how the experts manage paediatric endocrine conditions (see panel for details)
- Novel Advances sessions, exploring cutting edge research techniques and their applications
- Special sessions covering Working Groups, Controversies, Meet the Expert, the *Yearbook of Pediatric Endocrinology* and much more.



Visit www.espe2019.org/programme for the full programme.

What you said last year

“I do appreciate the combination of excellent scientists AND super-experienced paediatricians”

Delegate, ESPE 2018

“It was an impressive conference with a big variety of information, thank you”

Delegate, ESPE 2018

ESPE accommodation service

The official ESPE accommodation service offers a range of 3- to 5-star hotels at specially negotiated rates. Options will suit all budgets, with prices starting at €50 per night. Availability is limited, so book now to avoid disappointment: click on 'Accommodation' at www.espe2019.org. Deadline for bookings: 5 August 2019.



Plenary lectures at ESPE 2019

RANKL and RANK: bone and beyond

Josef Penninger, Canada

Light, body clocks and sleep: biology to new therapeutics

Russell Foster, UK

Glucocorticoid rhythms, stress response and the brain from neonates to adult

Stafford Lightman, UK

Development of novel therapies for obesity

Matthias H Tschöp, Germany

Nutrition and the hypothalamo-pituitary-gonadal axis

Manuel Tena-Sempere, Spain

How to reduce waste and increase value in translational biomedical research

Ulrich Dirnagl, Germany

Pituitary gigantism – an update

Albert Beckers, Belgium

The return of 'How do I?'

Learn how the experts...

- Manage subclinical hypothyroidism
- Manage Prader-Willi and GH at transition
- Manage a child with insulin resistance
- Manage micropenis in a child
- Diagnose GH resistance
- Manage an asymptomatic child with T1D and transglutaminase positivity

Future meetings

See www.eurospe.org/meetings for details of all future meetings



58th Annual ESPE Meeting

19–21 September 2019
Vienna, Austria



59th Annual ESPE Meeting

10–12 September 2020
Liverpool, UK



60th Annual ESPE Meeting

May/June 2021
Copenhagen, Denmark



11th International Meeting of Pediatric Endocrinology

September 2021
Buenos Aires, Argentina



OTHER EVENTS

SEPTEMBER

ESPE Summer School
Burg Feistritz, Austria
16–18 September 2019

ESPE Diabetes, Obesity & Metabolism School
Burg Feistritz, Austria
22–24 September 2019

OCTOBER

ESPE Caucasus & Central Asia School
Astana, Kazakhstan
11–15 October 2019

6th ASPED-ESPE Endocrine Academy
Casablanca, Morocco
15–17 October 2019

NOVEMBER

ESPE Maghreb School
Sousse, Tunisia
18–22 November 2019

DEADLINES

MAY

Clinical Fellowship applications 31 May 2019
Maghreb School Steering Committee Co-ordinator vacancy applications 31 May 2019

JUNE

Diabetes, Obesity & Metabolism School applications 3 June 2019
ASPED-ESPE Endocrine Academy applications 15 June 2019
Winter School Steering Committee vacancy applications 16 June 2019
Science Symposium host applications 17 June 2019
ESPE 2019 early bird registration 20 June 2019

JULY

Maghreb School Steering Committee Member vacancy applications 14 July 2019
DOM School Steering Committee vacancy applications (x3) 14 July 2019

AUGUST

ESPE 2019 Accommodation Service bookings 5 August 2019

ESPE

European Society for
Paediatric Endocrinology

Improving care of children with
endocrine diseases by promoting
knowledge and research

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ESPE Newsletter

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