ESPE 2023 in The Hague

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ESPE 2023 – read the programme online now!
Welcome

The 61st Meeting of ESPE takes place later this month in The Hague, The Netherlands. This is a great opportunity to catch up with the latest developments in paediatric endocrinology, and with all your friends and colleagues in the field. We are excited to bring you highlights from the meeting and more information in this issue of ESPE News.

In her plenary lecture at ESPE 2023, Margaret M McCarthy will talk about ‘Sex differences in the brain: intersection of the endocrine, immune and nervous systems’. You will find a fascinating preview of her talk on page 5, in which she reflects on differences which are not explained by hormones, and examines the role of non-neuronal cells. It remains to be determined whether the natural status of higher inflammatory signalling in the male brain contributes to the increased incidence of neurodevelopmental disorders in boys and men.

‘The food environment and the global childhood obesity epidemic: the role of ultra-processed food (UPF)’ is the title of Frank Hu’s topical plenary lecture. His preview on page 6 summarises our understanding of UPF’s role in the escalating levels of childhood obesity. While positive associations between higher UPF consumption and adiposity parameters in young people have been found, results are inconsistent. Some categories of UPF are important targets for health interventions, but others have shown beneficial health effects.

The theme of ESPE 2023 is ‘Global Challenges in Paediatric Endocrinology’, which includes climate change. On page 8, Chris Worth and Alice Willson tell us how some UK scientists are cycling from Manchester to The Hague, to minimise their carbon footprint while raising awareness of climate and health issues. You will find further details of ESPE 2023 on page 9; the programme and registration information are at www.eurospe.org/events-espe/espe-2023-annual-meeting.

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ESPE 2023
21–23 September 2023
The Hague, The Netherlands
Global Challenges in Paediatric Endocrinology

Find out more on page 9

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Editorial Board:
Meghna Chawla
Rakesh Kumar
Meera Shaunak
Chris Worth

Antje Garten
Editor, ESPE News
Antje.Garten@medizin.uni-leipzig.de
YES Group’s busy first year

Since our launch, the YES Group has been hard at work, representing early career members on ESPE Committees, collaborating with the JENIOUS Group of the International Society for Pediatric and Adolescent Diabetes, and creating professional development opportunities.

The ‘YES Group Webinar Series’ was launched with the highly popular lectures ‘How to publish your manuscript’ by Professor Stefano Cianfarani and the ‘ABC of how to approach DSD’ with Professor Tulay Guran.

We supported the Neonatal Diabetes Study led by the JENIOUS Group and are excited to have launched our first JENIOUS–YES collaborative survey, entitled ‘Physicians’ perspectives on type 1 diabetes and coeliac disease in children and adolescents’.

You can find the survey at https://tinyurl.com/T1DnCD

We look forward to greeting new members at the ESPE stand at the 61st Annual Meeting of ESPE in The Hague, as well as at the YES Group social event (see details sent by email).

Join the YES Group at www.eurospe.org/about/organisation/yes-group

Follow ESPE on Facebook and Twitter for YES Group activities

Meet the YES Group team

The YES Group’s six representatives sit within ESPE’s main committees, giving a voice to early career paediatric endocrinologists within ESPE.

In support of healthcare in Nagorno-Karabakh

ESPE and the European Society of Endocrinology have issued a joint statement, calling upon the international community for humanitarian aid and medical supplies to support the people of Nagorno-Karabakh (Republic of Artsakh). The population here faces a crisis, as access to the region is blocked. The joint statement also calls for the free passage of patients to specialised treatment centres outside the blocked area.


The Viva Foundation is a non-governmental organisation of doctors and volunteers which aims to provide support to those affected by means of hospital facilities, equipment, medication, materials and instruments.

Donations may be submitted via www.viva.foundation/en

EVENTS

ESPE Connect Webinars 2023
Transforming education through a global e-learning model
12 October 2023, 16.00–17.30 CEST

- Welcome and introduction Anne Rochtus (Belgium; Convener)
- Overview and introduction to e-Learning and CME accreditation for paediatric diabetes and endocrinology May Ng (UK)
- A puberty case from the ESPE e-Learning site Rasha Hamza (Egypt; Chair, ESPE Education and Training Committee)
- An e-Learning masterclass Malcolm Donaldson (UK)
- Panel Discussion and Q&A

ESPE members attend free of charge; non-members €25.


Save the date!
Puberty
13 December 2023, 16.00–17.30 CET

See the latest details at www.eurospe.org/education/espe-connect-webinar-series
Hybrid closed-loop control in young children

None of the hybrid closed-loop systems for type 1 diabetes are currently approved by the US Food and Drug Administration (FDA) for use by children under 6 years of age. Reporting on behalf of the PEDAP Trial Study Group, Wadwa et al. studied use of the t:slim X2 insulin pump with Control-IQ Technology and a continuous glucose monitor (Dexcom G6) among 2- to 6-year-old children with type 1 diabetes mellitus.

A total of 102 children were randomised (68 to the closed-loop group and 34 to the standard care group). The mean adjusted difference in time in target glucose range in the two groups was 12.4 percentage points (i.e. approximately 3 hours/day, 95% CI 9.5−15.3, P<0.001) over the 13-week follow-up period, favouring the closed-loop group.

The results of this study could pave the way for FDA approval of hybrid closed-loop systems for children under the age of 6.

Read the full article at Wadwa et al. 2023 New England Journal of Medicine 388 991–1001

Impact of age at GH therapy initiation in SGA

Growth hormone (GH) therapy is widely used to treat short stature in children born small for gestational age (SGA), in the 10% of patients who fail to show evidence of catch-up growth. GH is licensed for the treatment of these children from 2 to 4 years in the USA or after 4 years in Europe.

Juul et al. retrospectively analysed data from two large international observational studies in order to assess the impact of patient age at the initiation of GH therapy on long term growth outcomes and safety in short children born SGA. Patients (n=3318) were split into three groups based on age at GH treatment initiation: 2 to <4 years (10.7%), 4 to <6 years (31.6%) and ≥6 years (57.7%): 31.8% were born preterm.

Following 8 years of therapy, the mean improvement in height standard deviation score from baseline was significantly greater in the 2 to <4 years group versus the groups that were 4 to <6 years (+2.5 versus +2.2, P=0.0054) or ≥6 years (+2.5 versus +1.7, P<0.0001). No unexpected safety events were reported.

The authors conclude that early initiation of GH therapy in short children born SGA may contribute to height optimisation.

Read the full article at Juul et al. 2023 Journal of Clinical Endocrinology & Metabolism 108 1043–1052

Ultra-processed food consumption and obesity

The consumption of ultra-processed food (UPF) and its association with obesity has become a truly hot topic recently. Childhood obesity has tripled since 1975, with a corresponding rise in the consumption of UPF. UPF consumption has been shown to contribute to adult obesity, but its impact on young children has not been evaluated.

González et al. conducted a longitudinal analysis of preschool children in Uruguay and Brazil to investigate whether there was an association between UPF consumption and childhood obesity. UPF consumption was positively associated with obesity (RR 1.1, 95% CI 1.02−1.18), but adjustment for confounding factors removed this significance.

The authors conclude that there is not yet conclusive evidence for UPF consumption causing obesity in young children, but that their data contribute to an increasing trend of evidence in this regard.

Read the full article at González et al. 2023 Journal of Pediatric Nursing 69 e120–e126

MC3R variants in constitutional delay in growth and puberty

MC3R is expressed in the KNDy neurones of the hypothalamic arcuate nucleus, which produce kisspeptin, a critical regulator of pubertal timing. To determine whether deleterious MC3R variants are more frequently found in patients with constitutional delay in growth and puberty (CDGP) or normosmic idiopathic hypogonadotrophic hypogonadism (nIHH), Duckett et al. studied the sequence of MC3R in 362 adolescents with a clinical diagnosis of CDGP and 657 patients with nIHH. The signalling properties of all non-synonymous variants were identified and their frequencies compared with those in 5774 controls from a population-based cohort.

The data provided evidence that deleterious mutations in MC3R are more frequently found in patients with constitutional delay in growth and puberty (CDGP) (8/362 (2.2%), OR=4.17, P=0.001), but not in those with nIHH (4/657 (0.6%), OR=1.15, P=0.779). The authors concluded that even though the damaging variants are over-represented in individuals with CDGP, they are not a common cause of it.

Read the full article at Duckett et al. 2023 Journal of Clinical Endocrinology & Metabolism doi: 10.1210/clinem/dgad373

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Sex differences in the brain

Margaret M McCarthy examines the entwinement of the endocrine, immune and nervous systems in determining differences between the male and female brain.

Anatomical sex differences in the brain were first revealed in fundamental neuroscience studies in rodent models as early as the late 1960s. By the 1990s, most neuroscience research excluded female subjects, due to erroneous perceptions of hormonally induced variability, and the notion of sex differences in the brain was relegated to a niche area of interest only in the context of reproduction.

The realisation of a profound gender bias in relative risk of neuropsychiatric and neurological disorders that vary across the lifespan compelled researchers to rethink the importance of understanding sex differences in the brain. Similarly, the discovery that gestational or early childhood inflammation increased the risk of neurodevelopmental disorders such as schizophrenia and autism spectrum disorders drove reconsideration of the origins of dysregulation.

Programming the nervous system

Early life programming of the nervous system by gonadal steroids, in particular androgens derived from the fetal testis, is now recognised as broadly and enduringly impacting the brain and spinal cord through fundamental processes such as epigenetic programming. The process also involves sculpting the neural architecture via effects on cell birth and death, myelination, axonal growth, dendrogenesis and synaptogenesis, to name a few.

However, even in endpoints that are robustly divergent in male and female rodents, such as courting, mating and nurturing of young, there is substantial intra-sex variability which is not explained entirely by hormones. Moreover, the precise mechanisms by which steroids modulate developmental processes has proven stubbornly difficult to elucidate, leading to the conclusion that it is ‘complex’ and ‘multi-factorial’. Unravelling that complexity and identifying the multiple factors is an achievable goal.

The role of non-neuronal cells

Both the neurocentric and immune-privileged views of the brain have been challenged by a renewed appreciation for glia, the first being astroglia, also called astrocytes, and the second being microglia, which are not glia at all but, rather, modified brain-specific macrophages.

Figure. Multiple systems interact to generate lasting sex differences in the brain. Neuronal networks are the ultimate purveyors of physiology and behaviour but, rather than being a cell intrinsic property, the generation of sex differences arises from non-neuronal cells. These include astrocytes, which share a common origin with neurones, as well as immune cells which may be unique to the brain, such as microglia, or innate immune cells found throughout the body, such as mast cells. The gonadal steroids (androgens T), oestrogens (E2) and progesterones (P4) are key participants by acting both directly on neurones and also on the non-neuronal cells. In some cases they initiate cell-to-cell signalling that often involves membrane-derived signalling molecules. Deciphering the precise role of each cell type and the cellular and molecular mechanisms establishing and maintaining neural sex differences will provide needed insight into the origins of the strong male gender bias in neurodevelopmental disorders.
Ultra-processed food and the childhood obesity epidemic

Frank Hu considers the evidence linking increasing rates of childhood obesity and our food environment, in particular ultra-processed foods (UPFs).

Childhood obesity has become a significant global public health crisis. The prevalence of childhood obesity has increased dramatically from about 4% in 1975 to over 18% in 2016. Although some high income countries have seen a levelling off in childhood obesity rates, low and middle income countries, particularly those undergoing nutrition transitions, continue to witness an alarming increasing trend. In the USA, nearly 20% of children and adolescents have obesity. Childhood obesity poses significant health risks and has long term public health and societal implications.

What is the cause?
Childhood obesity is influenced by a combination of genetic, prenatal and early life factors, as well as individual behaviours such as poor diets, excessive screen time, inadequate physical activity and insufficient sleep.

In addition to these individual behavioural factors, the obesogenic food and physical activity environments also play a significant role, because individual behaviours are shaped by the environments. UPFs are a key component of the obesogenic food environment. According to the NOVA classification system, UPFs are food products that have undergone extensive processing and contain multiple added ingredients and additives. They are typically high in sodium, sugar, unhealthy fats and calories. Examples of UPFs include soft drinks, packaged savoury snacks, processed meats, fast food and pre-prepared frozen meals.

Over the past several decades, there has been a substantial increase in the types and quantities of UPFs available in the global food supply. The USA has one of the highest levels of UPF consumption among children, with more than 60% of their calorie intake coming from these foods. Furthermore, low and middle income countries have experienced a rapid increase in UPF consumption, which plays a crucial role in the nutrition transition occurring in these regions. Sugar-sweetened beverages (SSBs) are a major category of UPFs and have seen a significant rise in consumption worldwide. Latin America and the Caribbean have the highest SSB consumption among children, with more than 60% of their calorie intake coming from these foods.

Public policies play a crucial role in improving the food environment and combating childhood obesity

Frank Hu is a plenary speaker at ESPE 2023. You can hear him talk on “The food environment and the global childhood obesity epidemic: the role of ultra-processed food” on Thursday 21 September at 16:15.

A process of analysis
Several systematic reviews and meta-analyses have examined the associations between UPF consumption and childhood adiposity. Most cross-sectional and longitudinal

Continued on page 7
studies have found positive associations between higher UPF consumption and adiposity parameters during childhood and adolescence.

However, the evidence is not entirely consistent, and there is considerable heterogeneity among different categories of UPFs. Some foods classified as UPFs, such as whole wheat bread, yogurt and cold breakfast cereals, have demonstrated beneficial health effects. Therefore, it is important to consider the specific composition of nutritional profiles of UPFs, despite their classification. Additionally, novel plant-based meat alternatives, which are often classified as UPFs, can serve as healthier alternatives to red meat and contribute to reducing the environmental impact of the current food system. Furthermore, there is a need for longitudinal studies with repeated measures of food intake, especially in low and middle income countries, to better understand the long term effects of UPF consumption on childhood obesity.

Sugar-sweetened beverages
Among various categories of UPFs, SSBs have shown the most consistent findings. An updated meta-analysis showed that, among cohort studies, each serving/day increase in SSB intake was associated with a 0.07kg/m² higher body mass index (BMI) in children and a 0.42kg higher body weight in adults.\(^7\) Randomised clinical trials conducted in children indicated a lower BMI gain with SSB reduction interventions compared with control groups.\(^7\)

Due to strong scientific evidence linking SSB consumption and adult and childhood obesity as well as other adverse health outcomes, reducing SSBs is widely considered to be an important target for public health interventions.

A role for public policies
Public policies play a crucial role in improving the food environment and combating childhood obesity. Drawing from successful tobacco control policies, similar strategies such as increased taxation, marketing restrictions and package warning labels have been implemented to improve the food environment, with a particular focus on reducing consumption of UPFs including SSBs.

**Strong scientific evidence links consumption of sugar-sweetened beverages with adult and childhood obesity, as well as other adverse health outcomes.**

Several countries in Latin America have been at the forefront of adopting these policies and have achieved promising results.\(^8\) For instance, Mexico was the first country to implement an SSB tax. Chile implemented the first mandatory front-of-package warning labels on foods high in sugar, salt and unhealthy fats, which have been adopted in other countries in the region and beyond.

There is growing evidence that these policies, aimed at improving the food environment, are effective in reducing the purchase and consumption of SSBs and other UPFs, particularly in low income households.\(^2\) For instance, taxation on SSBs has been associated with reduced sales and consumption. The implementation of front-of-package warning labels has also shown positive effects by promoting product reformulation and encouraging consumers to opt for healthier alternatives.

Moreover, restrictions on UPF advertising during TV programming and the use of child-directed marketing on product packaging have been effective in reducing the sale and promotion of unhealthy foods to children.

By implementing such policies, we can create a supportive food environment that encourages and facilitates healthier eating habits, leading to improved overall diet quality and a reduction in childhood obesity. However, it is important to emphasise that curbing the childhood obesity epidemic requires a comprehensive and whole-of-society approach. Policies targeting the food environment should be integrated with efforts to promote nutrition education and physical activity, and to address social and economic factors that influence food choices and health outcomes.

**Plenary speakers at ESPE 2023**
You can hear all the following plenary lectures at the 61st Annual Meeting of ESPE in The Hague, The Netherlands on 21–23 September.

- **Sex differences in the brain: intersection of the endocrine, immune and nervous systems** Margaret M McCarthy
- **The food environment and the global childhood obesity epidemic: the role of ultra-processed food** Frank Hu
- **Structural and functional development of the adolescent brain** Eveline Crone
- **How AI will change medicine** Henk Marquering
- **Stem cells, organoids and single cell transcriptomics** Hugo Vankelecom
- **How the genome predicts human disease** Stylianos Antonarakis
- **Novel approaches in autoimmune endocrine disorders** Olle Kämpe
- **Real-world use of closed loop insulin delivery** Hans de Vries

Find out more on page 9
Ride For Their Lives

Chris Worth and Alice Willson from Manchester, UK, plan to travel to ESPE 2023 in The Hague on two wheels, to raise awareness of climate and health issues. Could you get involved?

Having felt increasingly guilty about flying around Europe for ESPE Meetings, but very aware of the fantastic opportunities presented by in-person attendance, we were already planning a greener alternative for The Hague. After attending an inspiring talk about Ride For Their Lives (www.ridefortheirlives.net) and the power of bicycles by Heather Lambert at the Royal College of Paediatrics and Child Health conference in Glasgow,1 we were confirmed in our ambitions.

The climate crisis, a theme for ESPE 2023, is the biggest threat to paediatric global health, with children now dying from air pollution in the UK.2 This is a rising trend and we must face the uncomfortable truth that flying to international conferences directly contributes to this crisis, no matter our intentions. Flying releases 15 times more emissions than using a ferry and up to 42 times more than a train such as the Eurostar.3 Cycling releases no emissions. It also reduces congestion, improves physical and mental health and is a joyous and communal activity accessible to almost everyone.

Chris Worth and Alice Willson from Manchester, UK, plan to travel to ESPE 2023 in The Hague on two wheels, to raise awareness of climate and health issues. Could you get involved?

Chris Worth

We are planning a 3-day ride from Royal Manchester Children’s Hospital to ESPE 2023 in The Hague, in order to minimise our own emissions and raise awareness of climate change, its impact on child health and our collective responsibility in tackling it.

We would love anyone to join us for as much or as little as they wish (join us in Manchester, Doncaster, Hull, Rotterdam or anywhere in between) or to find their own environmentally friendly way to ESPE 2023.

Details are available at www.ridefortheirlives.net/rides/manchester-childrens-hospital-to-the-hague-for-espe-2023-conference or by contacting Chris Worth at chris.worth@mft.nhs.uk.

See you all at ESPE (we’ll be the ones eating four portions of lunch)!

Chris Worth and Alice Willson
Royal Manchester Children’s Hospital, Manchester, UK

References
The 61st Annual ESPE Meeting is set to examine some global challenges. These include climate change, which calls for more sustainable medical care, as well as the ever-rising prevalence of obesity, with low and middle income countries quickly catching up with high income nations.

Our exhilarating programme will, as usual, include plenary lectures and symposia featuring outstanding international speakers. You will benefit from Meet the Expert and How Do I... sessions by world-leading clinicians. The Controversy and Novel Advances sessions are designed to make you re-evaluate the way we think and work. Free Communications and Posters will raise the profile of work by experienced colleagues and younger trainees alike.

You are invited to join us and enjoy the very best update in basic, translational and clinical paediatric endocrinology!

Paul van Trotsenburg ESPE 2023 Meeting Host
Sabine Hannema ESPE 2023 Vice-Meeting Host

Meet the Expert
- Management of MEN1 in children and adolescents
  Maria Luisa Brandi
- Informing children about their DSD – when and how?
  Amy Wisniewski
- Uncertainties around diagnosing growth hormone deficiency
  Jan Maarten Wilt
- Clinical management of Prader–Willi syndrome in infants, children and adolescents
  Mathé Tauber
- Management of pituitary adenomas in children
  Dominique Matter
- Approach to thyroid cancer in children
  Marek Niedziela
- Management of hyperinsulinism beyond the acute phase
  Paul Thornton
- Puberty induction in hypogonadism
  Richard Quinton

How do I...
- Manage abnormal thyroid function tests in the newborn?
  Catherine Peters
- Use anti-Müllerian hormone in paediatric practice?
  Rodolfo Rey
- Manage a child with hypercalcaemia?
  Corinna Grasemann
- Manage long term complications in type 2 diabetes in adolescents?
  Orit Pinhas-Hamiel
- Initiate and follow patients on a closed-loop system?
  Revital Nimri
- Diagnose and manage hypercholesterolaemia
  Lorenzo Iughetti

Novel advances
- Ethics of expensive treatments
  Ghislaine van Thiel
- Should we strive for normality?
  Martine Vries
- DNA methylation episignatures: defining biomarkers of rare disorders
  Bekim Sadikovic

Register online now
Remember: www.eurospe.org is the only official website where you can register to attend ESPE 2023.

For this year’s plenary lectures see page 7

See the full programme at www.eurospe.org/events-espe/espe-2023-annual-meeting
Future meetings
See www.eurospe.org for details of all future meetings

61st Annual ESPE Meeting
21–23 September 2023
The Hague, The Netherlands

62nd Annual ESPE Meeting
16–18 November 2024
Liverpool, UK

63rd Annual ESPE Meeting
Jointly with the European Society of Endocrinology
10–13 May 2025
Copenhagen, Denmark

64th Annual ESPE Meeting
2026
Marseilles, France

OTHER EVENTS
ESPE Summer School
18–20 September 2023
Rockanje, The Netherlands

ESPE Diabetes, Obesity & Metabolism School
24–26 September 2023
Rockanje, The Netherlands

ESPE Connect Webinar: ESPE e-Learning Portal
12 October 2023

ESPE Science Symposium 2023: Obesity
13–14 October 2023
Athens, Greece

ESPE Maghreb School
13–18 November 2023
Tunisia

ESPE Connect Webinar: Puberty
13 December 2023

DEADLINES
SEPTEMBER
Early Career Scientific Development Grant applications – 30 September 2023

DECEMBER
ESPE Awards 2024 nominations – 10 December 2023

To stay up to date, follow ESPE on social media (see right) and read the ESPE News Alerts.
For more information about vacancies on ESPE Committees and how to apply, see www.eurospe.org/about/vacancies

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