ESPE NEWS

BRINGING THE LATEST IN PAEDIATRIC ENDOCRINOLOGY TO YOU

ESPE
European Society for Paediatric Endocrinology
Improving care of children with endocrine diseases by promoting knowledge and research

ISSUE 68 / *SUMMER 2025*
ISSN 2045-5003 (ONLINE)

Paediatric endocrinology and society

Special issue
P6–10 >

Keep up to date with ESPE events and deadlines!

Welcome

In this issue, we celebrate the many 2025 ESPE Award winners from May's Joint Congress in Copenhagen (see page 4). We hope you enjoyed the Congress as a chance to meet with our colleagues in adult endocrinology from the European Society of Endocrinology (ESE). It was a great opportunity to network and be updated on 'Endocrinology Across the Life Course'.

Paediatric endocrinology and society is the topical theme of the features on the following pages. The environment (social, economic and chemical) shapes all our lives, and none so much as those of young people.

On **page 6**, Gary Butler examines whether puberty is taking place at an earlier age, and the potential underlying causes. He emphasises the importance of distinguishing between pathological causes of central precocious puberty and early normal puberty.

The LIFE Child study is a large, population-based, longitudinal, childhood cohort study, aiming to monitor child development from birth to adulthood. On **page 7**, Tanja Poulain, Peggy Ober and Carolin Sobek from the study look at the interrelationship between socioeconomics and child well-being, and why socially disadvantaged children are more likely to develop an unhealthy lifestyle and consequently poorer mental and physical health.

We encounter endocrine-disrupting chemicals (EDCs) throughout our daily lives. Anne-Simone Parent examines research into their impact on hypothalamic pathways (**page 8**), particularly during conception, pregnancy and infancy. Alix Aldehoff and Kristin Schubert look at the ways in which EDCs impact metabolism other than the 'traditional' focus on their oestrogenic, androgenic, thyroid and steroidogenic actions (**page 9**). On **page 10**, Ruta Navardauskaite gives an overview of the sheer diversity of EDCs and their effects.

Elsewhere on this page, you can discover how to make use of EndoCompass, an important ESPE–ESE initiative which is set to transform the research landscape in endocrinology – with your support! The full Research Roadmap will be published as a supplement to *Hormone Research in Paediatrics* and *European Journal of Endocrinology* this summer.

As usual, you can also rely on your newsletter for all the latest ESPE news, events and deadlines. Happy reading!

Antje Garten
Editor, *ESPE News*
Antje.Garten@medizin.uni-leipzig.de

Follow ESPE online...

Keep an eye on the latest ESPE news and activities at **www.eurospe.org**

You can also follow ESPE on Facebook, X and LinkedIn

/EuroSPE

/EuroSPE

ESPE

Cover image:
Denis Tabler/Shutterstock

Welcoming EndoCompass

The EndoCompass Research Roadmap is set to transform endocrine research

Endocrine diseases affect millions of people in Europe, yet research remains underfunded and fragmented. The EndoCompass Project aims to change this by identifying research priorities to guide future studies, funding programmes and policy decisions at European and national levels.

Initiated by ESPE and the European Society of Endocrinology (ESE), the project has involved 2 years of collaboration with partner societies and over 215 experts from across Europe. Key findings were shared at the publication's official launch during the ESPE-ESE Joint Congress in Copenhagen on 10–13 May. **EndoCompass Research Roadmap – Directions for the Future of Endocrine Science** will be released shortly as a supplement to *Hormone Research in Paediatrics* and *European Journal of Endocrinology*. The Roadmap includes detailed recommendations spanning eight endocrine specialties and five overarching areas, developed by dedicated working groups.

Martine Cools and Evelien Gevers are ESPE Co-Chairs of the EndoCompass Steering Group. As Martine commented, 'The EndoCompass Project will support researchers in finding appropriate funding for their research and illustrates the need for a smooth transition from paediatric to adult endocrine care.'

Evelien added, 'EndoCompass will help ESPE's early career scientists and clinicians gain an insight into the research priorities in endocrinology for the next 5–10 years and address them jointly with colleagues seeing adult patients.'

ESPE and ESE are hugely grateful to everyone who has contributed. It has been a real team effort!

Finding your way with EndoCompass

EndoCompass is a resource for everyone in the endocrine community to cite and share. Look out for more information to help you:

- **Navigate EndoCompass** What is EndoCompass and where can you find it?
- **Explore and engage** How do the recommendations relate to your area of work?
- **Spread the word** How can you share EndoCompass with colleagues, organisations and networks to strengthen its impact?
- **Widen the impact** How can you get involved in ongoing activities to help turn recommendations into action?

The focus now shifts to putting the recommendations into practice and ensuring the findings drive real change in endocrine research.

Join the journey at **www.ese-hormones.org/endocompass**

YOUR SOCIETY

New YES leaders

Tiago Jeronimo Dos Santos (Spain) and Maja Raicevic (Montenegro) have been chosen as new leaders of the YES Group (Young ESPE). We received many excellent applications and thank everyone who applied. If you weren't selected this year, do try again for future calls.

Tiago Jeronimo Dos Santos

Active engagement in ESPE and YES activities is an important factor in scoring applications. Participation in educational events, research collaborations and community initiatives provides valuable experience and demonstrates commitment to our Society's mission.

Maja Raicevic

Congratulations to our new leaders, and thank you all for your continued support of the YES Group!

The YES Leadership Team

Find out more about the YES Group

EVENTS

Attendees at the ESPE Winter School

Winter School in Poland

The 2025 ESPE Winter School took place at Castle Baranów, near Rzeszów, Poland, on 22–27 February. Students attended from nine countries across Eastern Europe; there were over 100 applications for the 24 places.

The packed 5 days included interactive lectures from the teaching faculty: Justin Davies (co-ordinator), Rita Bertalan, Joanne Blair, Tulay Güran, Artur Mazur, Talat Mushtaq and Jurgita Gailite (2026 convenor). Small group sessions discussed teachers' cases and students' case presentations. An introduction to clinical research saw students presenting their research proposals and projects (developed with support from the faculty). We also enjoyed a tour of the castle and the beautiful medieval city of Sandomierz. Our thanks are due to local convenor Artur Mazur.

Watch out for details of ESPE Winter School 2026 in Latvia.

***Justin Davies**, Winter School Co-ordinator*

Find out more about ESPE Winter School

RESOURCES

Test yourself with e-Learning

The ESPE–ISPAD (International Society for Adolescent and Pediatric Diabetes) e-Learning web portal is an interactive resource on paediatric endocrinology and diabetes mellitus. Use it, free of charge, to expand your knowledge of paediatric endocrinology.

Find out more **Register for free access**

This issue's clinical case highlight

A newborn with neonatal thyrotoxicosis A 25-day-old baby was admitted to the neonatal intensive care unit because of tachycardia and failure to thrive. She was born at 31 weeks of gestation with a birth weight of 1380g. Her mother was diagnosed with Graves' disease at the age of 22 years and underwent subtotal thyroidectomy at the age of 25 years. On examination, the baby was agitated with a peak heart rate of 190–220 beats/min, respiration 60/min and body temperature 37.2°C. Her eyes were prominent and oedematous, and her thyroid gland was enlarged.

Laboratory tests were as follows (reference ranges in brackets):

Free thyroxine	>200nmol/l (13–44)
Tri-iodothyronine	12nmol/l (0.3–4.1)
Thyrotrophin	<0.1mU/l (0.6–5.6)
Haemoglobin	7.3mmol/l (6–10)
Thrombin	$173x10^9$U/l ($150x10^9$–$450x10^9$)

Which treatment is initially indicated? *(Choose as many as appropriate)*

- ☐ Prednisone
- ☐ Exchange transfusion
- ☐ Iodine solution (Lugol)
- ☐ Beta-blocking agent
- ☐ Thyrostatic drug (methimazole)
- ☐ Subtotal thyroidectomy

For the answer, see **page 11**.

ESPE Award Winners 2025

We congratulate the many winners of **ESPE Awards** who received their awards at the Joint Congress of ESPE and ESE in Copenhagen on 10–13 May.

ESPE Andrea Prader Prize

Olle Söder (Stockholm, Sweden) received the ESPE Andrea Prader Prize, in recognition of his lifetime achievement in teaching and research, outstanding leadership and overall contribution to the field of paediatric endocrinology.

ESPE Outstanding Clinician Award

Marco Cappa (Basel, Switzerland) was presented with the ESPE Outstanding Clinician Award, in recognition of his outstanding clinical contribution to the practice of paediatric endocrinology.

ESPE International Outstanding Clinician Award

Paul Hofman (Auckland, New Zealand) received the ESPE International Outstanding Clinician Award, in recognition of his contribution and commitment to clinical paediatric endocrinology in a country outside Europe and the Mediterranean basin.

ESPE Research Award

John Achermann (London, UK) received the ESPE Research Award, in recognition of research achievements of outstanding quality in basic endocrine science or clinical paediatric endocrinology.

ESPE International Research Award

Thomas Carpenter (New Haven, CT, USA) received the ESPE International Research Award. This is presented to an outstanding paediatric endocrinologist from a country outside Europe and the Mediterranean basin.

Endocrinology Across the Life Course Award

Sadaf Farooqi (Cambridge, UK) received this new joint award from ESPE and ESE which recognises clinicians and basic scientists for significant contributions to endocrinology across the life course.

ESPE Young Investigator Awards

These awards for paediatricians who are still in training or who have been in a senior (principal investigator) role for no more than 5 years were presented to the following, in recognition of their scientific publications:

Alfonso Galderisi

Rebecca Moon

- **Alfonso Galderisi** (New Haven, CT, USA), whose award lecture was entitled 'Smart outcomes for smart trials: changing research to change the life trajectory of people with preclinical type 1 diabetes'
- **Rebecca Moon** (Southampton, UK), whose award lecture was entitled 'Vitamin D in pregnancy: benefits for bones and beyond'.

Poster Awards

The 2025 winners were:
Mohamed Abubaker (UK), **Merisa Abusdal** (Norway), **Corin Badiu** (Romania), **Felix Chelslin** (Sweden), **Nathalie Erpelding** (USA), **Isabel Viola Frielitz-Wagner** (Germany), **Laura Lucaccioni** (Italy), **Malene Asp Bock Mejdahl** (Denmark), **Sema Okutan** (Denmark), **Luigi Picaro** (UK), **Philippa Prentice** (UK), **Mercedes Rivera Cuello** (Spain), **Patrice Rodien** (France), **Carin Skogastierna** (Sweden), **Lorenzo Tucci** (Italy) and **Yi Wang** (China).

Henning Andersen Prizes *(supported by Novo Nordisk)*

These awards for the most highly rated abstracts were presented to:

Luís Gustavo Pérez-Rivas

Jinting Zhou

- **Luís Gustavo Pérez-Rivas** (Munich, Germany) for 'USP8 genotype is associated with recurrence risk in Cushing's disease: an international, retrospective, multicenter cohort study'
- **Jinting Zhou** (Xiangyang, China) for 'Association between premature ovarian insufficiency and biological aging: evidence from the UK Biobank and NHANES population-based surveys'.

ESPE Undergraduate Achievement Awards

These awards for scientific achievement in paediatric endocrinology were presented to **Henri Couckuyt** (Ghent, Belgium) and **Lena Van de Wynkele** (Ghent, Belgium).

People's Choice Awards

Awards for the best clinical, basic and translational abstracts as chosen by delegates and the Joint Programme Organising Committee were presented to **Anna Matveeva** (Bern, Switzerland), **María Isabel Pozo Relaño** (Córdoba, Spain) and **Mert Uçar** (Istanbul, Turkey).

Bringing you recent highlights from the world of research

Guidelines on vosoritide in achondroplasia

The existing guidelines for managing and caring for individuals with achondroplasia were established prior to the approval of vosoritide in 2021 for use with this condition.

Savarirayan *et al.* have now developed new international consensus guidelines to supplement the earlier guidelines. These emphasise minimum requirements and practical considerations to systematically optimise patient care and assess the pragmatic outcomes of vosoritide in individuals with achondroplasia.

The guidelines were formulated by a development group comprising 14 clinical experts from 9 countries and 2 patient representatives. They are presented as 62 consensus statements, categorised into five stages: (1) before initiation of vosoritide treatment, (2) treatment initiation, (3) ongoing monitoring and evaluation, (4) stopping treatment and (5) ongoing monitoring.

Read the full article at Savarirayan *et al.* 2025
Nature Reviews Endocrinology
https://doi.org/10.1038/s41574-024-01074-9

Hydrocortisone modified-release capsules for CAH

Neumann *et al.* discuss the use of modified-release hydrocortisone capsules (Efmody®) in the treatment of children and adolescents with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency.

Traditional hydrocortisone therapy often fails to mimic physiological cortisol rhythms, particularly the early morning rise, which is crucial for controlling adrenocorticotrophin and androgen levels. Modified-release hydrocortisone offers a more physiological cortisol profile, potentially improving biochemical control and quality of life. The authors provide practical guidance on transitioning patients from conventional to modified-release hydrocortisone, including dose conversions, monitoring and expected clinical outcomes.

This treatment option may be particularly beneficial during adolescence, a period marked by hormonal fluctuations and increased risk of poor disease control. While long-term outcome data are still emerging, early clinical experience suggests improved biochemical parameters and treatment adherence. Modified-release hydrocortisone presents a promising therapeutic advancement in the management of paediatric CAH, addressing some of the limitations of standard therapy with a more physiologic approach to glucocorticoid replacement.

Read the full article at Neumann *et al.* 2025
Endocrine Connections
https://doi.org/10.1530/EC-24-0619

Somapacitan in children born small for gestational age

Among children born small for gestational age (SGA), 1 in 10 fail to catch up by 2 years of age, resulting in reduced adult height compared with their genetic potential. Although daily growth hormone (GH) injections are safe in these children, the response is found to be suboptimal, owing in part to the burden of daily injections. The long-acting GH derivative somapacitan has been approved for once-weekly treatment of GH deficiency in adults and children. Phase 3 clinical studies are underway for short stature in children born SGA.

The phase 2 REAL5 study is the first global study investigating efficacy, safety and tolerability of once-weekly somapacitan in SGA alone. Juul *et al.* have reported findings following the use of higher doses of the drug for 52 weeks.

A sustained dose-dependent growth response was demonstrated for somapacitan. Overall, somapacitan 0.24 mg/kg/week provided similar results, and comparable bioactive and total insulin-like growth factor-I responses, to daily GH (0.067 mg/kg/day) in children born SGA.

Read the full article at Juul *et al.* 2025
Journal of Clinical Endocrinology & Metabolism
https://doi.org/10.1210/clinem/dgae616

Weight loss and type 2 diabetes remission

Weight loss is routinely recommended as part of the approach to induce remission of type 2 diabetes (T2DM), but a quantitative relationship between the two is not established. Kanbour *et al.* conducted a systematic review and meta-analysis of 22 publications with an outcome of complete T2DM remission (glycated haemoglobin (HbA1c) <42mmol/mol and/or fasting glucose <5.6mmol/l) at least 12 months after weight loss intervention.

Complete remission was seen in 0.7% of those with a weight loss <10%; in 50% of those with a weight loss of 20–29%; and in 79% of those with a weight loss ≥30%. Partial remission was 48%, 69% and 90% in the same weight loss groups. Results were independent of age, sex, race, baseline body mass index, HbA1c, T2DM duration and insulin use.

A strong dose–response relationship was observed between weight loss and T2DM remission, with every 1% decrease in weight resulting in a 2.2% increased chance of T2DM remission.

Read the full article at Kanbour *et al.* 2025
Lancet Diabetes & Endocrinology
https://doi.org/10.1016/s2213-8587(24)00346-2

Insights into age at puberty

Gary Butler asks whether puberty is starting earlier and, if so, why?

Around 20 years ago, there were many reports that the age of puberty was falling. However, much has changed since the COVID-19 pandemic. How have lifestyle changes since lockdown impacted pubertal development in the last 5 years? This selection of findings may give some clues.

Secular trends

A worldwide systematic review of the onset of female puberty, as assessed by breast palpation, showed that the age at thelarche had decreased by almost 3 months per decade from 1977 to 2013.[1] A 20-year Danish cohort study of 8600 children with a diagnosis of premature sexual maturation found increases of 6-fold in girls and 15-fold in boys (greater in immigrant children).[2] In the USA, over 107 000 physician assessments showed the onset of puberty was 10.1 years in girls and 11.5 years in boys (earlier in South Asian and Pacific Islander cohorts but later in East Asians).[3] However, in Taiwan, the age of completing puberty in boys (15-ml testes) is now 12.3 years, a decline of more than a year in the last 20 years. In girls, menarche is 11.4 years, a reduction of 0.4 years per decade over the last 30 years.[4] In Israel, surveys conducted in 2003 and 2015 showed that the average age of menarche had fallen from 13.0 to 12.5 years, with younger ages in girls of Jewish origin compared with the Arab population, and younger in those of immigrant origin.[5]

Social and environmental effects

There are mixed opinions as to whether these factors contribute to central precocious puberty (CPP) or just earlier normal puberty. In California, a study of over 26 000 girls between 2003 and 2010 explored the difference in the timing of puberty in girls whose families had broken down before the age of 6 years. There was a 1.6-fold earlier onset in black girls and earlier non-race-related menarche when compared with intact families.[6] A diagnosis of autistic spectrum disorder in a USA controlled study of 10- to 13-year-olds showed that girls with this diagnosis experience earlier thelarche and menarche, but there was no such effect in boys.[7]

Environmental disruptors have long been associated with changes in sexual and reproductive development. There are a number of publications and reviews in this field that relate to puberty onset and development, but no clear picture currently emerges that can make clear associations, because of the relatively low quality evidence.[8]

Obesity

Previous publications have informed us about the link between starting and completing puberty and increasing body size. The USA Environmental Influences on Child Health Outcome programme, comprising 7500 children from 1986 to 2015, showed that boys with a faster weight gain in infancy had an earlier age at peak height velocity, notably among Hispanics. Girls with a greater weight gain in early infancy had earlier pubarche, but faster weight gain in late infancy was linked to earlier menarche.[9] A study of 1500 girls in China found those living in an urban environment experienced menarche at 12.1 years compared with rural dwellers at 13.5 years.[10] In Iran, the mean age of menarche was 9.4 years and linked with increased nutrition and body mass index.[11] In South Africa, the Birth-30 cohort showed an earlier onset of puberty with heavier weight in childhood, and this was linked to increased weight gain as adults.[12]

Gary Butler

> *"Knowing about normal puberty and population trends is crucial for us to provide appropriate counselling and reassurance"*

COVID-19 pandemic

Studies from Italy, China and the USA have reported an increase and a doubling of referrals for CPP since 2020. There are associations with increasing weight, reduced exercise time and dietary changes, but more information will come in time.[13–15]

Lessons to be learned

This information can make assessment in a clinical situation challenging, and reconfirms the importance of understanding the difference between pathological causes of CPP and early normal puberty. Healthy normal children with an early onset of puberty will have an appropriate adolescent growth spurt and end up at a height within their target height range, so no intervention is required.

It is worrying that there is still pressure to intervene. In Korea, a review of over 130 000 prescriptions for gonadotrophin-releasing hormone analogues between 2008 and 2020 for a diagnosis of CPP, as well as normal puberty, showed its incidence rose 83 times in boys and 16 times in girls.[16]

Knowing about normal puberty and population trends is crucial for us to provide appropriate counselling and reassurance for the increasing numbers of children presenting to our clinics.

Gary Butler
University College London Great Ormond Street Institute of Child Health, UK

References

1. Eckert-Lind *et al.* 2020 *JAMA Pediatrics* https://doi.org/10.1001/jamapediatrics.2019.5881.
2. Bräuner *et al.* 2020 *JAMA Network Open* https://doi.org/10.1001/jamanetworkopen.2020.15665.
3. Kubo *et al.* 2024 *JAMA Network Open* https://doi.org/10.1001/jamanetworkopen.2024.10253.
4. Chow *et al.* 2020 *Journal of the Chinese Medical Association* https://doi.org/10.1097/JCMA.0000000000000360.
5. Sinai *et al.* 2020 *Journal of Pediatric & Adolescent Gynecology* https://doi.org/10.1016/j.jpag.2020.04.005.
6. Aghaee *et al.* 2020 *BMC Pediatrics* https://doi.org/10.1186/s12887-020-02345-w.
7. Corbett *et al.* 2020 *Autism Research* https://doi.org/10.1002/aur.2406.
8. Castiello & Freire 2021 *European Journal of Endocrinology* https://doi.org/10.1530/EJE-20-1038.
9. Aris *et al.* 2022 *JAMA Network Open* https://doi.org/10.1001/jamanetworkopen.2021.46873.
10. Cheng *et al.* 2021 *European Journal of Pediatrics* https://doi.org/10.1007/s00431-020-03803-4.
11. Esfarjani *et al.* 2022 *Journal of Family Medicine & Primary Care* https://doi.org/10.4103/jfmpc.jfmpc_2170_21.
12. Nyati *et al.* 2024 *European Journal of Clinical Nutrition* https://doi.org/10.1038/s41430-023-01293-9.
13. Goffredo *et al.* 2023 *Journal of Pediatric Endocrinology & Metabolism* https://doi.org/10.1515/jpem-2022-0492.
14. Fu *et al.* 2022 *International Journal of Endocrinology* https://doi.org/10.1155/2022/9229153.
15. Trujillo *et al.* 2022 *Frontiers in Pediatrics* https://doi.org/10.3389/fped.2022.1007730.
16. Kang *et al.* 2023 *PLoS One* https://doi.org/10.1371/journal.pone.0283510.

Socioeconomics and child health

Authors from the LIFE Child study detail their findings.

Tanja Poulain

Peggy Ober

Carolin Sobek

> *Addressing psychosocial or structural factors might be more promising and sustainable than addressing behavioural factors"*

Children's health is affected by several interrelated factors: for example, genetic, social, environmental and behavioural issues. One important influence is socioeconomic status (SES). The SES represents an individual's or a family's social, economic and work-related position relative to other individuals or families. It is based on various types of characteristics:[1]

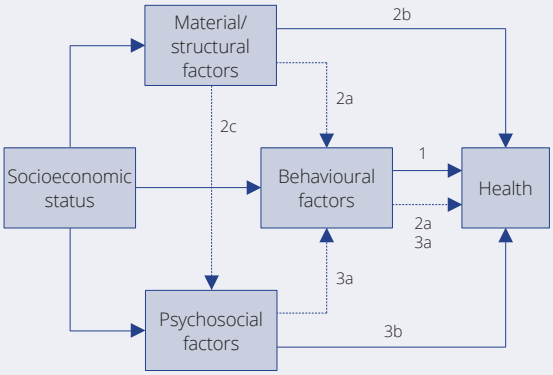
- parent- or family-based (e.g. parental school and professional education, parental occupation, parental income)
- child-based (e.g. academic performance, school-leaving certificate, type of school attended)
- area-level (e.g. poverty rates in a specific region, neighbourhood violence, air pollution, quantity of green spaces).

In research on child health, most studies focus on the parent- and family-based characteristics of SES, which are usually more stable across child development than child-based and area-level characteristics.

Previous studies show strong associations between a lower SES and poorer psychological and physical health.[1] Overweight and obesity, which affect many children and adolescents in Western societies and represent a considerable health risk,[2] also show a strong association with SES. For example, overweight and obesity are more prevalent in children from families with lower SES[3] and in children growing up in regions with fewer green spaces and more fast-food restaurants.[2] It also been shown that children with obesity are more likely to achieve a lower level of education than children with normal weight.[4]

As shown in the Figure, it is argued that the association between SES and health is mediated by:

- behavioural factors (e.g. low physical activity, high sedentary behaviour, unhealthy diet and eating habits)
- psychosocial factors (e.g. parental neglect, lack of coping strategies, social support and health literacy)
- material/structural factors (e.g. built environment, inability to buy healthy food, lack of healthy school meals).[5]



1 Independent (direct) effect of behavioural factors
2a Indirect effect of material/structural factors (through behavioural factors)
2b Independent (direct) effect of material/structural factors
2c Indirect effect of material/structural factors (through psychosocial factors)
3a Indirect effect of psychosocial factors (through behavioural factors)
3b Independent (direct) effect of psychosocial factors

Conceptual model for explaining social inequalities in health with independent (direct) and indirect contributions of material/structural, psychosocial and behavioural factors. Reproduced from J Epidemiol Community Health, *Moor I, Spallek J, Richter M, 71:565–575, 2017,[5] with permission from BMJ Publishing Group Ltd.*

The LIFE Child study

In our preliminary work, conducted in the LIFE Child study at Leipzig University, several of these mediating factors were associated with children's body mass index (BMI) and the SES of a child's family. For example, children from families with a lower SES were less physically active, showed a higher media use and a less healthy diet, reported more negative life events, and lived in neighbourhoods with more streets than children from families with a higher SES.[6,7]

At the same time, these factors, especially media use, physical activity,[8] and the number of streets in the neighborhood,[7] were significantly associated with the BMI of children and adolescents.

Opportunities for improvement

The aforementioned mediating factors offer opportunities for prevention and intervention.

Regarding overweight and obesity, programmes outside or within the school context can help to promote a healthier diet and more physical activity (behavioural factors). Learning strategies to regulate emotions and strengthening social cohesion in a peer group (psychosocial factors) can also be helpful.

At the structural level, providing more green spaces, and climbing and play opportunities, as well as healthy and free school meals, could help to establish a healthier lifestyle and, therefore, to reduce weight or maintain a healthier weight.

Previous studies suggest that, overall (not specific to overweight and obesity), addressing psychosocial or structural factors might be more promising and sustainable than addressing behavioural factors.[1]

In summary

Due to social and structural reasons, socially disadvantaged children have a higher risk of developing an unhealthy lifestyle and, as a result, poorer mental and physical health. Therefore, more efforts must be made to give children from disadvantaged families or regions easier access to education and health-promoting leisure activities.

Tanja Poulain, Peggy Ober and Carolin Sobek
LIFE Leipzig Research Center for Civilization Diseases; Hospital for Children and Adolescents and Center for Pediatric Research; German Center for Child and Adolescent Health, Leipzig, Germany

References
1. Poulain *et al.* 2020 *Current Opinion in Pediatrics* https://doi.org/10.1097/mop.0000000000000876.
2. Daniels *et al.* 2021 *Preventive Medicine* https://doi.org/10.1016/j.ypmed.2021.106790.
3. Vazquez & Cubbin 2020 *Current Obesity Reports* https://doi.org/10.1007/s13679-020-00400-2.
4. Lindberg *et al.* 2021 *BMJ Open* https://doi.org/10.1136/bmjopen-2020-040432.
5. Moor *et al.* 2017 *Journal of Epidemiology & Community Health* https://doi.org/10.1136/jech-2016-207589.
6. Poulain *et al.* 2019 *International Journal of Environmental Research & Public Health* https://doi.org/10.3390/ijerph16050677.
7. Poulain *et al.* 2020 *International Journal of Environmental Research & Public Health* https://doi.org/10.3390/ijerph17176321.
8. Jungehuelsing *et al.* 2025 *Pediatric Research* https://doi.org/10.1038/s41390-025-03860-1.

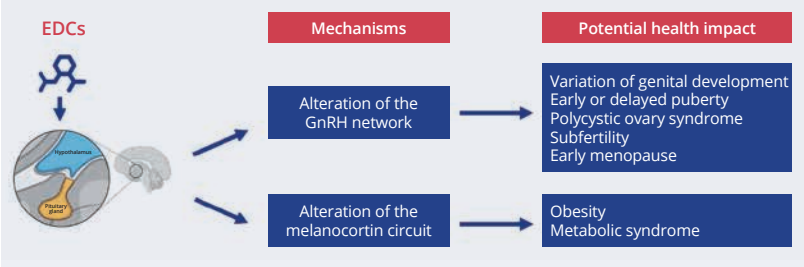
EDCs and the hypothalamus

Anne-Simone Parent examines the effect of endocrine-disrupting chemicals (EDCs) on the hypothalamic regulation of energy homeostasis and GnRH activity.

Anne-Simone Parent

> *Research tools such as spatial transcriptomics and proteomics will help identify the specific brain cells most sensitive to EDCs"*

Emerging evidence points to the significant role of EDCs in driving the increasing prevalence of obesity and reproductive disorders worldwide.[1,2] These synthetic compounds interfere with hormonal systems and can profoundly affect health when exposure occurs during critical developmental periods from conception through early childhood.



Early-life exposure to EDCs, even at low levels, can disrupt hypothalamic circuits that control reproduction and metabolism.

This is consistent with the developmental origins of health and disease (DOHaD) concept, which links early-life environmental exposures to long-term health outcomes. The first 1000 days of life – spanning conception, pregnancy and infancy – are now widely recognised as a critical window for lifelong health programming. During this period, the brain and endocrine systems undergo rapid development and are extremely sensitive to external influences, such as EDCs. Exposures during this time can 'reprogramme' physiological systems, setting the stage for future disease risk. This insight is at the heart of the DOHaD concept, which underscores the need to protect fetal and early childhood development from harmful environmental factors.

Besides peripheral organs, the hypothalamus, a key brain region regulating reproduction and metabolism, is highly sensitive to EDC exposure during these windows. Disruptions in its development can permanently alter hormonal systems, leading to lifelong consequences such as early or delayed puberty, infertility, obesity and metabolic disorders.

Effects on reproductive health

Puberty results from the reactivation of gonadotrophin-releasing hormone (GnRH) neurones in the hypothalamus, which depends on a delicate balance of excitatory and inhibitory inputs. Key modulators include neurotransmitters (such as GABA and glutamate) and neuropeptides (such as kisspeptin, neurokinin B and MKRN3). EDCs can interfere with this system in multiple ways. Animal studies have shown that exposure to EDCs disrupts gene expression and epigenetic programming of the GnRH pulse generator during early brain development.[1,3]

Effects on metabolic health

The hypothalamus also governs energy balance, integrating signals from hormones including leptin, insulin and ghrelin to regulate appetite and metabolism. The arcuate nucleus contains two crucial neuronal populations: pro-opiomelanocortin (POMC) neurones, which reduce appetite, and neuropeptide Y (NPY)/Agouti-related peptide (AgRP) neurones, which stimulate it. These neurones are born during fetal life and form essential projections in the early postnatal period, making them especially vulnerable to EDC exposure. Research shows that EDCs can disrupt the expression of appetite-regulating genes (e.g. POMC, NPY) and reduce hypothalamic sensitivity to leptin, an anorexigenic hormone. Exposed animals eat more, gain weight and show abnormal hypothalamic wiring.[4,5]

Conclusion

The evidence is clear: early-life exposure to EDCs, even at low levels, can disrupt hypothalamic circuits that control reproduction and metabolism (Figure), with effects that may persist across generations. These chemicals act during vulnerable developmental windows, especially within the first 1000 days, a period that shapes lifelong health trajectories. Despite this, current regulatory frameworks lack scientific understanding and fail to adequately screen or limit harmful exposures.

Evidence also supports transgenerational effects, where EDCs modify germ cells, leading to reproductive and metabolic changes in unexposed descendants. The molecular mechanisms driving these heritable changes remain under investigation.

Moving forward, research tools such as spatial transcriptomics and proteomics will help identify the specific brain cells most sensitive to EDCs, deepening our understanding of how early environmental exposures shape disease risk. Public health efforts should focus on minimising EDC exposure to prevent the long-term and generational health consequences of developmental reprogramming.

Anne-Simone Parent
GIGA Neurosciences, Neuroendocrinology Unit, University of Liège; Department of Pediatrics, University Hospital Liège, Belgium

References
1. Lopez-Rodriguez *et al.* 2021 *Nature Reviews Endocrinology* https://doi.org/10.1038/s41574-020-00436-3.
2. La Merrill *et al.* 2025 *Nature Reviews Endocrinology* https://doi.org/10.1038/s41574-024-01059-8.
3. López-Rodríguez *et al.* 2021 *Environmental Health Perspectives* https://doi.org/10.1289/ehp8795.
4. Loganathan *et al.* 2020 *Endocrinology* https://doi.org/10.1210/endocr/bqaa170.
5. MacKay *et al.* 2017 *Endocrinology* https://doi.org/10.1210/en.2016-1718.

EDCs in obesity and metabolic disorders

Alix Aldehoff and Kristin Schubert look at the emerging roles of the non-EATS modalities of endocrine-disrupting chemicals (EDCs) in obesity and metabolic disorders.

Alix S Aldehoff

Kristin Schubert

> *"Non-EATS modalities are increasingly recognised as relevant to chemical-induced adverse health effects"*

Endocrine-disrupting chemicals are compounds present in numerous products in our daily lives, such as food packaging, cosmetics, toys and even drinking water. They can interfere with the hormonal system and have been suggested as potential contributors to the development of childhood and adult obesity and associated comorbidities.[1,2] EDCs can target various organs, including adipose tissue. They alter endocrine pathways involved in metabolism, appetite and satiety regulation, lipid accumulation and fat distribution.

Traditionally, EDCs are described as exerting their endocrine-disruptive effects through mechanisms collectively known as EATS modalities: (o)estrogen, androgen, thyroid and steroidogenic properties. The underlying molecular mechanisms are well-characterised, and validated Organisation for Economic Co-operation and Development (OECD) testing guidelines have been established to assess the impact of chemical-induced hazards on endocrine systems.[3]

Non-EATS modalities

However, recent research emphasises the growing relevance of non-EATS modalities, including chemical interactions with nuclear receptors such as the liver X receptor, retinoid X receptor, peroxisome proliferator-activated receptors (PPARs), aryl hydrocarbon receptor, glucocorticoid receptor or constitutive androstane receptor. These non-EATS modalities are increasingly recognised as relevant to chemical-induced adverse health effects (Figure). Unlike EATS, validated test guidelines for non-EATS modalities are currently unavailable, highlighting a critical gap in the regulatory hazard assessment and, thus, risk management of chemicals.[4]

Plastic products or those containing plastic-associated additives

Receptors	Endpoint
EATS modalities	
ERα/ERβ	O**E**strogenic
AR	**A**ndrogenic
THRs	**T**hyroidal
SHRs	**S**teroidogenic
Non-EATS modalities	
PPARs	Energy metabolism/homeostasis Adipogenesis/insulin sensitivity
CAR	Hepatotoxicity Xenobiotic metabolism
AHR	Xenobiotic metabolism Hepato-/immunotoxicity
LXR/RXR	Lipid/glucose metabolism Inflammation

Plastic additives can exert their adverse health effects via EATS and non-EATS modalities. ER, oestrogen receptor; AR, androgen receptor; THR, thyroid hormone receptor; SHR, steroid hormone receptor; PPAR, peroxisome proliferator-activated receptor; CAR, constitutive androstane receptor; AHR, aryl hydrocarbon receptor; LXR, liver X receptor; RXR, retinoid X receptor.

Experiments with phthlate substitutes

Related to adipose tissue dysfunction and obesity, the PPARs are an important class of receptors, with PPARγ as the master regulator of human adipogenesis. We have previously shown that the metabolites of a number of prominent phthalate substitutes, including DINCH, DINP and DPHP, showed pronounced adipogenic potential.[5] Specifically, MINCH, MHiNP and OH-MPHP bound PPARγ and initiated the differentiation of human SGBS preadipocytes, similar to the effect seen with the antihyperglycaemic agent and PPARγ agonist rosiglitazone. In this way, the accumulation of lipids was enhanced and the adipokine secretion of leptin and adipsin was promoted. In a proteomics approach, adipogenic markers and signalling pathways were found to be elevated following exposure to the substitute's metabolites.

The adverse effect of the phthalate substitutes was also evident in mature differentiated adipocytes, with the generation of oxidative stress, disturbed lipid storage and metabolic homeostasis, together with the induction of an adipokine secretion profile favouring insulin resistance and inflammation.[5]

The observed effects in SGBS cells *in vitro* were most pronounced for the DINCH metabolite MINCH. Thus, we proceeded with an assessment of the effects of dietary DINCH exposure on a model of diet-induced obesity in female and male C57BL/6N mice *in vivo*.[6] While the process of adipogenesis, in part, shows species-specificities for humans and mice, we were interested in the potential of DINCH to disrupt systemic (metabolic) health.

We confirmed that both DINCH and MINCH reached adipose tissue depots and the liver, with partial retention even after a recovery period. Overall body weight was not significantly affected by DINCH exposure, in agreement with approval studies, yet sexually dimorphic effects were observed for several metabolic parameters. A reduction in whole-body insulin sensitivity and increased triglyceride levels in female mice contrasted with elevated cholesterol and high- and low-density lipoprotein levels, together with alterations in the insulin/C-peptide ratio, in males. Proteomic profiles of serum, adipose and liver tissue indicated alterations in central energy metabolism and inflammatory processes.[6]

In summary

Through their interaction with metabolic endocrine pathways, EDCs represent a potential risk factor for adipocyte dysfunction and, hence, the development of obesity and associated comorbidities. While traditional EATS modalities remain crucial, there is an emerging emphasis on the importance of non-EATS modalities, particularly recognising that nuclear receptors, such as PPARγ, play a critical role in adipogenesis and metabolic regulation.

Our results indicate that widely used phthalates and their allegedly safe substitutes and metabolites significantly affect adipocyte differentiation and function, potentially promoting lipid accumulation and altering metabolism, thereby favouring insulin resistance. Validated test guidelines for analysing chemical-induced effects through non-EATS modalities are urgently needed for current regulatory hazard assessment.

Our *in vivo* study suggests a sexually dimorphic effect on several metabolic parameters following EDC exposure, emphasising the need for future comprehensive,

Continued on page 10

Continued from page 9

sex-differentiated assessments. This would allow a thorough, mechanistic understanding of chemical-induced effects on adipose tissue integrity, effectively mitigating the adverse health effects of EDCs.

Alix S Aldehoff and Kristin Schubert
Helmholtz Centre for Environmental Research GmbH – UFZ, Leipzig, Germany

References

1. Braun 2017 *Nature Reviews Endocrinology* https://doi.org/10.1038/nrendo.2016.186.
2. Franks & McCarthy 2016 *Science* https://doi.org/10.1126/science.aaf5094.
3. OECD 2018 *OECD Series on Testing and Assessment* No. 150 https://doi.org/10.1787/9789264304741-en.
4. Martyniuk *et al.* 2022 *Environmental Research* https://doi.org/10.1016/j.envres.2021.111904.
5. Schaffert *et al.* 2022 *Environment International* https://doi.org/10.1016/j.envint.2022.107279.
6. Krupka *et al.* 2025 *Environment International* https://doi.org/10.1016/j.envint.2025.109306.

The diversity of endocrine disruptors

Ruta Navardauskaite provides a broad overview of these chemicals, their sources and their effects.

Ruta Navardauskaite

Endocrine-disrupting chemicals (EDCs) interfere with hormone signalling, affecting growth, metabolism, reproduction and development. Exposure to these substances has been linked to hormonal imbalances, reproductive disorders, neurodevelopmental delays, metabolic dysfunction and cancer risk.

They are widespread in everyday products and the environment. Common sources include bisphenol A (BPA) and phthalates in plastics, polychlorinated biphenyls (PCBs) and dioxins in industrial pollutants, and pesticides, heavy metals and flame retardants in consumer goods. These chemicals persist in ecosystems and enter the food chain, making exposure nearly unavoidable.

A key concern is that EDCs can have harmful effects even at low doses, often following non-monotonic dose responses, meaning small amounts may cause significant biological changes.

Pregnant women, infants and children are particularly vulnerable, as endocrine disruption during development can lead to long-term health issues, including developmental abnormalities and metabolic diseases.

The table below outlines common EDCs, their sources and their health effects.

Ruta Navardauskaite
Department of Endocrinology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

Endocrine disruptor	Effects on endocrine system	Common sources
Alkylphenols (e.g. nonylphenol)	Disrupts oestrogen signalling; causes reproductive and developmental effects	Detergents, cleaning products and industrial wastewater
Atrazine	Alters reproductive hormones; linked to reproductive toxicity and feminisation in amphibians	Agricultural herbicides
Bisphenol A (BPA)	Disrupts oestrogen and androgen signalling; linked to reproductive disorders, obesity and diabetes	Plastic bottles, food can linings, thermal paper receipts
Dioxins	Mimics oestrogen; associated with cancer, immune system suppression, reproductive and developmental toxicity	Industrial emissions, waste incineration, contaminated food (meat, dairy)
Glyphosate	Potential disruption of reproductive hormones and liver enzyme activity; under study for carcinogenic effects	Herbicides used in agriculture
Heavy metals (e.g. lead, cadmium, mercury)	Disrupts oestrogen and testosterone; linked to developmental delays, reproductive toxicity, neurological effects	Contaminated water, batteries, paints, industrial emissions and fish (mercury)
Organotins (e.g. tributyltin)	Disrupts androgens and thyroid hormones; linked to obesity, immune suppression and reproductive toxicity	Antifouling paints, plastics and industrial products
Parabens	Mimics oestrogen; linked to breast cancer and reproductive toxicity	Cosmetics, shampoos, lotions and preservatives
Pesticides (e.g. DDT; dichloro-diphenyl-trichloroethane)	Mimics oestrogen; linked to reproductive disorders, cancer and developmental delays	Agricultural and household pest control products
Perfluoroalkyl substances (PFAs)	Interferes with thyroid hormone signalling; causes liver damage, immune dysfunction, developmental effects	Non-stick cookware, waterproof clothing, firefighting foams
Phthalates	Reduces testosterone production; causes developmental and reproductive toxicity	Plastics, cosmetics, personal care products, vinyl flooring
Phyto-oestrogens (e.g. genistein, daidzein)	Mimics oestrogen; associated with altered reproductive development and hormone-related cancers	Soy products, legumes, flaxseeds
Polybrominated diphenyl ethers (PBDEs)	Disrupts thyroid signalling; causes neurodevelopmental issues, decreased fertility	Flame retardants in furniture, electronics, textiles
Polychlorinated biphenyls (PCBs)	Disrupts thyroid hormones; causes neurodevelopmental delays, immune dysfunction, cancer	Electrical equipment, paints, industrial chemicals (persistent in the environment)
Triclosan	Disrupts thyroid hormone activity and reproductive function; potential antimicrobial resistance	Antibacterial soaps, toothpaste and cleaning products

Future meetings

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

64th Annual ESPE Meeting
8–10 September 2026
Marseilles, France


Xantana/iStock

OTHER EVENTS

10th ASPED–ESPE Endocrine Academy
3–5 July 2025
Jeddah, Saudi Arabia

19th ESPE Connect Webinar: Diagnostics
8 July 2025
Online

ESPE–OSCAR Science Symposium
18–19 September 2025
Paris, France

20th ESPE Connect Webinar: Cushing's
2 October 2025
Online

DEADLINES

JUNE

ESPE-OSCAR Science Symposium early bird registration – 15 June 2025

SEPTEMBER

ESPE Visiting Professorship of Rare Diseases applications – 15 September 2025

ESPE Early Career Scientific Development Grant applications – 30 September 2025

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/vacancies**

ESPE NEWS ARCHIVE

You will find previous newsletters in the archive at **www.eurospe.org/newsletter**

European Society for Paediatric Endocrinology

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

President
Professor Anita Hokken-Koelega
p.a. Stichting Kind en Groei
PO Box 23068
3001 KB Rotterdam
The Netherlands

ESPE Newsletter

Editor:
Dr Antje Garten
Pediatric Research Center
Hospital for Children and Adolescents
Leipzig University, Germany
E: Antje.Garten@medizin.uni-leipzig.de

Editorial Board:
Dr Rakesh Kumar
(Chandigarh, India)
Dr Ruta Navardauskaite
(Kaunas, Lithuania)
Dr Divya Pujari
(Mumbai, India)
Dr Meera Shaunak
(London, UK)
Dr Chris Worth
(Manchester, UK)

Sub-Editor:
Caroline Brewser

Designed by:
Ian Atherton
E: corbiculadesign@gmail.com

Published by:
MCI Benelux SA
Avenue des Arts 47
1000 Brussels, Belgium
W: www.eurospe.org

ESPE Office
MCI Benelux (address above) manages the ESPE Office.

Interplan is the Professional Congress Organiser (PCO) for the Joint Congress of ESPE and ESE 2025

E: espe-ese-congress@interplan.de

ESPE Managers:
Charlotta Odlind and Teresa Cunha

For ESPE enquiries, including membership:
E: espe@mci-group.com
W: www.eurospe.org

www.facebook.com/EuroSPE
www.x.com/EuroSPE
www.linkedin.com/company/european-society-for-paediatric-endocrinology

ESPE e-Learning

Answer to the case query on **page 3**

The correct answer is iodine solution (Lugol), beta-blocking agent, and thyrostatic drug (methimazole).

The most relevant is to start with iodine solution (Lugol) and a beta-blocking agent to reduce tachycardia; antithyroid drugs are also recommended. Corticosteroid treatment may not be indicated. However, there may be a place for a brief course of glucocorticoids in severe neonatal hyperthyroidism, since it inhibits peripheral conversion of thyroxine to tri-iodothyronine.[1,2]

References

1. Polak *et al.* 2006 *Hormone Research* https://doi.org/10.1159/000092454.
2. Ogilvy-Stuart 2002 *Archives of Disease in Childhood: Fetal & Neonatal Edition* https://doi.org/10.1136/fn.87.3.f165.