

## Managing transition

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adult care  
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### Transition in chronic endocrine disease

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### Hypopituitarism during transition

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# Welcome

ESPE's 60th Annual Meeting is nearly upon us, and we can all look forward to meeting in person once again in Rome, Italy, on 15–17 September. Find out more about the meeting on page 9 or at [www.espe2022.org](http://www.espe2022.org). Register today if you haven't done so already.

In this issue of *ESPE News*, we look at the important topic of transition. This reflects a time of change in everyone's life, but for our patients it is also punctuated by the transfer from their familiar paediatric care team to an equally caring but novel team of specialists in adult endocrinology.

On page 5, Wieland Kiess appraises the factors that should be considered, and emphasises the need to look at the process from the patient's viewpoint. He reflects on the importance of treating people as young adults as they engage with their new healthcare team.

On page 6, Manuela Cerbone and Mehul Dattani look not only at the general issues that are relevant to transition, but also at those factors that are specific to individuals with hypopituitarism. They comment that, while there is no universal consensus on how to handle the transition process, it is crucial to give young people the knowledge and confidence to manage their condition, and to work together with them and their families.

Dirk Jan Stenvers and Andries Kalsbeek give us a flavour of ESPE 2022 on page 7, as they discuss the many clocks within the body that contribute to the circadian rhythm in glucose metabolism. This previews Professor Kalsbeek's talk on the topic, which you can enjoy in full at the meeting.

In exciting news, page 3 sees us welcome the Young ESPE (YES) Group. This new group of early career ESPE members will provide support for those embarking on careers in paediatric endocrinology. It will encourage the sharing of knowledge and skills, as well as stimulating collaboration, research and personal development.

On a similar note, I encourage you to read the contribution from the ESPE e-Learning team, also on page 3. Test your knowledge with the issue's clinical case highlight, and see how you score. Sign up for ESPE e-Learning at [www.espe-elearning.org](http://www.espe-elearning.org), to strengthen your skills across our field.

I look forward to seeing you in Rome!

**Sarah Ehtisham**  
Editor, *ESPE News*  
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## Follow ESPE online...

Keep an eye on the latest ESPE news and activities at [www.eurospe.org](http://www.eurospe.org)

You can also follow ESPE on Facebook and Twitter



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## ESPE 2022

15–17 September 2022, Rome, Italy

Don't miss the best update in paediatric endocrinology

Register now online



[www.espe2022.org](http://www.espe2022.org)

FIND OUT MORE ON PAGE 9



**ESPE 2022 ROME**  
The 60th Annual Meeting 15-17 September 2022

## ESPE Annual Business Meeting

The 2022 Annual Business Meeting (ABM) will be held on **16 September at 18.30–19.45**, in Session Room 1 at La Nuvola Convention Centre, Rome.

ESPE Members should have received an email with a draft agenda, minutes from the 2021 ABM, an invitation to submit questions in advance and a proxy form. We look forward to updating you on ESPE's activities and plans.

## GRANTS

## Early Career Scientific Development Grant

This ESPE grant of up to €2500 supports a short visit to an external laboratory/hospital/institute to:

- learn a new technique
- troubleshoot existing methods
- discuss new approaches in a research seminar
- compile statistics on joint research projects
- test samples in the framework of a joint research project.

It may also be used to finance the visit of an external expert to provide advice at the requester's home institute.

The grant covers travel and housing expenses only.



Apply by **30 September 2022**



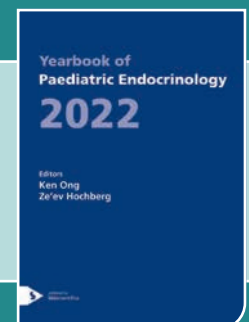
Find out more at [www.eurospe.org/grants-awards/grants/early-career-scientific-development-grant](http://www.eurospe.org/grants-awards/grants/early-career-scientific-development-grant)

## Yearbook of Paediatric Endocrinology

Read about major advances in the last year

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## YOUR SOCIETY

## YES! Let's welcome the Young ESPE Group

September's launch of the Young ESPE (YES) Group provides early career support for this important community within paediatric endocrinology.



### Who are the YES Group?

This dynamic group of early career ESPE members aims to create a space for young paediatric endocrinologists, so that they can share expertise and grow their careers through access to professional development, collaboration and research opportunities.

### What do the YES Group do?

- Represent early career members within specific ESPE Committees
- Organise educational and networking events
- Collaborate with similar early career groups
- Provide mentorship opportunities for members
- Keep members up to date with the latest career opportunities

### Why say 'YES'?

- Hear from experts by joining educational webinars
- Receive updates on the latest job/research opportunities
- Access special forums for young members at a similar stage in their careers
- Have the opportunity to contribute to the running of ESPE

### How can you sign up?

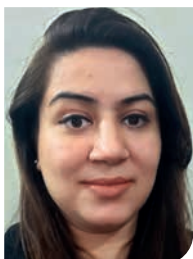


Come and meet us at ESPE 2022 on 15–17 September 2022



See [www.eurospe.org/about/yes-group](http://www.eurospe.org/about/yes-group)

### Meet the YES Group team



**Sommayya Aftab**  
Pakistan



**Hussain Alsaffar**  
Oman



**Domenico Corica**  
Italy



**Katja Dumić Kubat**  
Croatia



**Meera Shaunak**  
UK



**Rade Vukovic**  
Serbia

## RESOURCES

## New to ESPE e-Learning?



This global, educational web portal is a freely accessible, interactive environment. It provides up-to-date knowledge in paediatric endocrinology and diabetes mellitus, and currently has over 80 chapters and more than 120 problem-solving clinical cases.



For more details, see [www.eurospe.org/education/e-learning](http://www.eurospe.org/education/e-learning)



Register for free access at [www.espe-elearning.org](http://www.espe-elearning.org)

### This issue's clinical case highlight

Under 'Courses in paediatric endocrinology and diabetes>Pituitary' you will find the case of Nikola, an 8-year-old boy with spastic cerebral palsy, who is referred for obesity, metabolic syndrome and non-alcoholic fatty liver disease: thyrotrophin 4.8mIU/l (ref <4.0), free thyroxine 6.6pmol/l (ref 12.0–22.0), cortisol (at 08.00) 17.9nmol/l (0.65µg/dl) (ref >40nmol/l).

How would you interpret these laboratory findings?

- Primary hypothyroidism  
 Secondary/tertiary hypothyroidism

Would you start thyroxine treatment?

- No  
 Yes

For the answer, see **page 9**.



Nikola at the time of admission

## Patient leaflets in Dutch

ESPE's leaflets are available to support your patients with a variety of endocrine disorders. We thank the Pediatric Endocrinology Section of the Dutch Pediatric Association for supporting the recent translation of these leaflets into Dutch. You can also download the leaflets in Arabic, English, French, Spanish and Ukrainian. We welcome offers for translation into other languages.



You can find the leaflets at [www.eurospe.org/patients](http://www.eurospe.org/patients)



To help with translation see [www.eurospe.org/news/item/15324](http://www.eurospe.org/news/item/15324)

## Bringing you recent highlights from the world of research

### Burosumab versus conventional therapy in XLH

Ward *et al.* conducted a post hoc analysis of a randomised phase 3 study, comparing a combination of conventional medications (active phosphorus salts and active vitamin D; Pi/D) versus switching to burosumab in children with X-linked hypophosphataemia (XLH). The aim was to study burosumab's efficacy in comparison with conventional therapy in younger (<5 years of age) and older (5–12 years) children.

The study comprised 61 children aged 1–12 years (younger group,  $n=26$ ; older group,  $n=35$ ) from 16 different international sites. Following a 7-day washout period of Pi/D, children were randomly assigned to receive subcutaneous burosumab, starting at 0.8mg/kg every 2 weeks, or to restart Pi/D (oral phosphate 20–60 mg/kg/day and alfacalcidol 40–60ng/kg/day or calcitriol 20–30ng/kg/day). All participants received the assigned treatment for 64 days.

Burosumab appeared to have favourable outcomes in phosphate homeostasis, and greater improvement in rickets healing and lower limb deformities, as well as growth, in both age groups.



Read the full article at Ward *et al.* 2022  
*Journal of Clinical Endocrinology & Metabolism*  
doi: 10.1210/clinem/dgac296

### Sex steroids, enteric peptides and bone parameters after sleeve gastrectomy

Adolescents and young adults with severe obesity often undergo bariatric surgery, most commonly sleeve gastrectomy, and benefit from weight loss and associated metabolic improvement. This group of patients, however, also suffers from reductions in bone mineral density and alterations in bone geometry and microarchitecture following sleeve gastrectomy. Causes may include mechanical unloading from weight loss, changes in body composition, calcium and vitamin D deficiency due to decreased absorption after surgery, and alterations in hormones that impact bone health, such as sex steroids and enteric peptides. It is not clear yet if any of these factors, or a combination of them, contribute to bone loss in this scenario.

Nimmala *et al.* followed a cohort of adolescents with moderate-to-severe obesity until 12 months after sleeve gastrectomy. They found that changes in bone mineral density were positively associated with body composition, sex steroids (particularly oestrone and the free androgen index) and ghrelin, and negatively associated with sclerostin.



Read the full article at Nimmala *et al.* 2022  
*Journal of Clinical Endocrinology & Metabolism*  
doi: 10.1210/clinem/dgac361

### Corifollitropin alfa with hCG in adolescent boys with HH

Corifollitropin alfa (CFA) is a long-acting follicle-stimulating hormone (FSH) agonist. There is growing interest in the use of FSH agonists in boys with hypogonadotropic hypogonadism (HH), to stimulate Sertoli cell development during pubertal induction. Traditional protocols use testosterone or human chorionic gonadotrophin (hCG) to promote virilisation, but these methods do not induce testicular growth and may affect maturation and differentiation of the Sertoli cells.

Shankar and colleagues report a multi-centre open label study of CFA in adolescent boys with HH. A 12-week course of CFA was delivered to 17 boys as a subcutaneous injection every 2 weeks as 'priming', before a year of combination therapy with CFA every 2 weeks and hCG twice per week. Testosterone and oestradiol levels were monitored to assess dose–response, and the primary endpoint was a change in ultrasound measure of testicular volume.

After completion of treatment, the mean increase in testicular volume was 9.43ml (7.44–11.97) and there were physical and biochemical changes of puberty. The combined therapy was well tolerated. Combination therapy with CFA and hCG induced pubertal progression, a pubertal growth spurt, increase in testosterone levels and testicular growth. Longer term studies are needed to assess the potential impact on fertility.



Read the full article at Shankar *et al.* 2022 *Journal of Clinical Endocrinology & Metabolism* 107 2036–2046

### Transient congenital hypothyroidism

A number of children with congenital hypothyroidism (CH), generally with the thyroid gland *in situ*, will recover endogenous thyroid hormone production in early childhood, allowing discontinuation of levothyroxine treatment by 3 years of age. The incidence of transient CH has increased over time. However, little is known about its pathophysiology.

This review by Peters and Schoenmakers focuses on the possible causes of transient CH, including genetic mutations affecting *DUOX2* (an NADPH-oxidase enzyme) and *DUOX2A2* (its accessory protein), required for hydrogen peroxide biosynthesis in the thyroid. It also explores environmental factors, such as iodine deficiency or iodine excess during pregnancy or the neonatal period, fetal or neonatal exposure to drugs (amiodarone or maternal antithyroid drugs), maternal thyrotrophin receptor-blocking antibodies or infantile haemangiomas as possible causes of transient CH.

The authors urge further studies to evaluate the role, alone or in combination, of genetic, environmental and demographic factors in the development of transient CH.



Read the full article at Peters & Schoenmakers 2022  
*European Journal of Endocrinology* 187 R1–R16

## Transition – a crucial step

Wieland Kiess examines this vital stage in the life of children with chronic endocrine disease.

Transfer of patient care from the paediatric team to an adult service is not always easy. Numerous publications, opinion papers and reviews have touched upon medical, psychosocial, financial and societal issues in regards to how, when and with which aim transition of care should be achieved. Importantly, in many publications, the patients' view has been neglected totally. Usually, when one is to discuss care in transition, patients with chronic conditions and young adults suffering from chronic disease have to be considered.

### Timing

The time at which transfer of patient care should be initiated depends upon cultural, financial and societal issues. For example, will the state or insurance companies pay outpatient clinics involving paediatric and adult care teams at the same time? At what age does remuneration of paediatric care end?

In addition, developmental, psychological and biological issues have to be taken into account, when one is to decide upon the age of transition. Do adolescents still wish to have parents involved in their coping with a chronic condition? Are issues of confidentiality and secrecy considered? Are special aspects of diseases in adult life being taken care of by the paediatric team? Or is it time to transfer care to the adult medical team, who might be more experienced in dealing with the health issues of adults than are paediatricians?

### Specific challenges

The transition of patients with type 1 diabetes from paediatric to adult care services is challenging, not only for patients, but also for paediatricians and the physician providing further care.<sup>1</sup> Around the time of transition,



Wieland Kiess

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*Children with chronic endocrine disease should be treated as young adults by adult endocrinologists”*

metabolic control is often unstable. Furthermore, psychiatric co-morbidities or social background should be considered. Follow up by a specialist, i.e. adult endocrinologist/diabetologist, should be guaranteed.

Typical differences between paediatric and adult healthcare services may hamper a successful transition.<sup>2,3</sup> The handing over of healthcare should be planned early and the timing should be adapted to the medical and psychosocial condition of the patient. An interdisciplinary transfer clinic seems to be the optimal setting for a successful transition.<sup>4</sup> Close co-operation between paediatricians and adult diabetologists or endocrinologists is a prerequisite.<sup>5</sup>

### Seeking the ideal solution

In this author's opinion, children with chronic endocrine disease should be treated as young adults by adult endocrinologists. To optimise the transfer from the paediatric to adult endocrinologist, a model of a common transition clinic has been developed, but this is often difficult to organise. Within such a setting, it should be possible to exchange experience and to extend the knowledge and understanding of the disease with the other party, in order to provide optimal outpatient care. This model, however, has only sporadically been put into practice to date.

To illustrate the problems of transition into adult endocrine care, one publication examined two different endocrine diseases: classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency, and childhood-onset growth hormone deficiency.<sup>5</sup> Specific problems encountered in transfer to adult care were the attachment of the patients to their paediatricians and the lack of comprehension of the need for long term, continuous therapy. The consequence was a dramatic impairment in management. Similar conclusions have been drawn from studies of the transition of patients with type 1 diabetes from paediatric to adult care.<sup>1,6</sup>

In summary, transition from paediatric to adult care is an important and crucial step in the life of people with endocrine disease and diabetes of early onset. Still, many research issues have not been solved or even addressed sufficiently.

### Wieland Kiess

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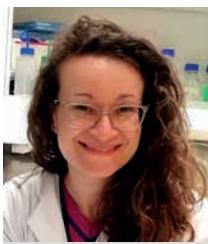
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# Management of hypopituitarism through transition

Manuela Cerbone and Mehul Dattani address the issues associated with providing optimal patient care at this stage.<sup>1</sup>



Manuela Cerbone



Mehul Dattani

Hypopituitarism is a rare, complex and heterogeneous endocrine disorder associated with significant morbidity and mortality.<sup>2,3</sup> Clinical manifestations may present at any time of life, and range from isolated pituitary deficiency to a complete loss of all pituitary hormones with or without associated extra-pituitary abnormalities.

Transition is defined as the time between the completion of puberty and the achievement of peak bone mass.<sup>4</sup> It is a time when physical, cognitive and emotional changes occur. During this challenging period, young people begin to navigate adult relationships, employment, university education, independent living and their social life.

In patients with chronic conditions, the term transition refers to the purposeful planned movement of adolescents and young adults from child- to adult-oriented healthcare systems.<sup>5</sup> The goal is to provide care that is uninterrupted, co-ordinated, developmentally appropriate, psychosocially sound, and comprehensive.<sup>5</sup>

**Table.** Barriers to successful transition

General
<ul style="list-style-type: none"> <li>• Lack of preparation/training/support</li> <li>• Lack of documentation</li> <li>• Lack of a formal transition booking system and formal point of contact during the process</li> <li>• Moving hospitals/environments</li> <li>• Lack of engagement by the young person</li> <li>• Belief that delaying transition might result in a better outcome</li> <li>• Dropping out</li> <li>• Differing needs of young adults and different perspectives of adult medical care</li> <li>• Greater independence of care in young adults under adult medical care with less parental supervision</li> <li>• Less access to educational support/social care in the adult world</li> <li>• Lack of involvement of a dedicated psychology service</li> </ul>
More specific to hypopituitarism
<ul style="list-style-type: none"> <li>• Lack of consensus with respect to optimal management</li> <li>• Lack of time/management resources among the multidisciplinary team to provide optimal care</li> <li>• Lack of consensus about the role and responsibilities of the paediatric versus adult endocrinologist</li> <li>• Lack of experience in adult services of managing some rare conditions (e.g. septo-optic dysplasia)</li> <li>• Lack of capacity among patients with severe neurobehavioural disabilities</li> <li>• Multiple medications with reduced adherence in adolescence</li> <li>• Interactions between some medications and some recreational drugs</li> <li>• Sensitive issues with respect to fertility and sexual development</li> <li>• Reduced final height affecting self-esteem</li> <li>• Clustering of co-morbidities compromising quality of life, self-esteem and independence</li> </ul>

“Expert care across the life span is required... It is important to give young people the knowledge and confidence to manage their condition and support them through the process”

This is not easy to achieve. Some of the barriers to successful transition are summarised in the Table. Factors in the successful transition of patients with hypopituitarism are considered below.

## Timing

Meeting the recommended target for the best timing of transition (starting at 14 years, according to the NICE guidelines) might not always be possible, due to the lack of sufficient expertise among adult services: patients with some rare conditions would not even have survived to adulthood a few decades ago. This is often compounded by a ‘resistance to change’ amongst both the family/patient and the healthcare teams that they know well.

## Retesting

Transition is an opportune time for re-evaluation of any endocrinopathies, considering the diagnostic difficulties of specific hormonal deficiencies in younger children, but also the possible recovery of anterior pituitary function as well as the evolution of new deficits.

Current guidelines suggest that retesting of growth hormone secretion should be performed in all patients, except those with three or more pituitary hormone deficiencies and low-serum insulin-like growth factor-1 concentrations (below -2.0 SDS), those with genetic defects affecting the hypothalamo-pituitary axis, and those with hypothalamo-pituitary structural brain defects.<sup>6</sup>

## Education on adrenal crisis and desmopressin treatment

Education of the young person on increasing oral glucocorticoids during intercurrent illness, how/when to administer emergency intramuscular hydrocortisone and how to correct hypoglycaemia is essential. If diabetes insipidus is present, the young person should also understand the importance of not stopping their desmopressin, and the importance of carrying both hydrocortisone and desmopressin with them at all times, as well as adopting appropriate strategies if they become unwell, particularly if they have co-existing adrenocorticotrophin deficiency. Transition may involve revisiting optimal steroid preparations for an individual, e.g. the use of long-acting glucocorticoid therapy.

Addressing lifestyle changes such as going out, staying away from home and staying safe if using alcohol and drugs may save lives. Recreational drugs such as MDMA (3,4-methylenedioxymethamphetamine or ‘ecstasy’) may lead to polydipsia, which could be extremely dangerous in patients treated with desmopressin. Alcohol can increase urine output, and young people should be told they will not necessarily need extra desmopressin if they drink a large amount of alcohol.

## Puberty and fertility

Delayed puberty in adolescents can be associated with significant anxiety about body image, and decreased self-esteem, with social isolation. In these circumstances, sex steroid therapy can be beneficial and should be used in a timely manner.

In girls with learning disabilities, an early onset of menstrual periods might be difficult to manage for the family/carers. Therapeutic options are available for reduction or suppression of menstruation, at the same time optimising accrual of bone mass.

Young adults should have discussions about sexual health and be advised to use contraception if they are sexually active, even if they are diagnosed with hypogonadism. Fertility issues are often only discussed after transition to adult services. Patients should have access to specialist fertility services if they request this.

### Learning disability and lack of capacity

Associated abnormalities such as visual impairment, obesity, autism and learning disabilities often simultaneously present in children with septo-optic dysplasia and in those with suprasellar brain tumours, and may add to difficulties in management. Provision for these young adults is frequently woefully inadequate.

The lack of capacity to consent to medical treatment often poses ethical challenges. Best interest meetings frequently take place, to ensure that the best treatment possible is achieved, while respecting personal choices and beliefs.

### Hypothalamic obesity

Severe hypothalamic obesity is a common finding in acquired and congenital causes of hypopituitarism. This is caused by a combination of hyperphagia and low metabolic rate. Lack of exercise might also contribute, in patients with learning disabilities and/or visual impairment.

No medical treatment is currently available for hypothalamic dysfunction.

### Conclusions

Adolescents with hypopituitarism face physical and emotional changes, as well as the prospect of a chronic condition in which lifelong hormonal treatment may be required. Expert care across the life span is required, but there is no universal consensus on how transition should be provided. It is important to give young people the knowledge and confidence to manage their condition and support them through the process. A multidisciplinary professional team should work in partnership with patients and their families to ensure a successful and smooth transition.

### Manuela Cerbone and Mehul T Dattani

*London Centre for Paediatric Endocrinology and Diabetes, Great Ormond Street Children's Hospital and University College London Hospitals, and Section of Molecular Basis of Rare Disease, Genetics and Genomic Medicine Programme, University College London Great Ormond Street Institute of Child Health, UK*

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## Circadian rhythm in glucose metabolism

Dirk Jan Stenvers and Andries Kalsbeek describe the many clocks responsible for controlling the body's diurnal functionality.



Dirk Jan Stenvers

In healthy people, plasma glucose excursions depend on the time of day of glucose ingestion, with higher glucose tolerance in the morning compared with in the evening. Recent studies using a circadian misalignment protocol clearly demonstrated that the diurnal rhythm in glucose tolerance is robustly regulated by the circadian timing system, separate from behavioural and environmental changes.

The mammalian circadian timing system consists of a central brain clock and peripheral clocks in tissues throughout the body, including muscle, adipose tissue and liver. Environmental light synchronises the approximately 24-hour (i.e. circadian) rhythm of the brain clock with the exact 24-hour rhythm of the environment. The entrained timing signal from the brain clock is forwarded via neural and hormonal signals to the peripheral tissue clocks. The molecular mechanism of the central and peripheral clocks is based on transcriptional-translational feedback loops, which are present in virtually every cell of the human body. Molecular clocks in different tissues and organs are involved in the control of the



Andries Kalsbeek



Andries Kalsbeek will talk on this topic at ESPE 2022.

Register now at [www.espe2022.org](http://www.espe2022.org).

daily rhythm in glucose tolerance, insulin sensitivity and insulin secretion.

### The gut clock

Intestinal cells over the entire intestinal tract contain a molecular clock, synchronised by signals resulting from food intake. The gut clock regulates intestinal motility, nutrient absorption and the expression of membrane glucose transporters, and matches the timing of maximal uptake to the habitual feeding period.

### The muscle clock

Human skeletal muscle has an autonomous molecular clock. Rodent data showed that the skeletal muscle clock is synchronised by the central brain clock, but also by signals resulting from physical exercise and food intake. Cultured rodent myotubes show a circadian rhythm in insulin sensitivity. Consistently, human muscle tissue shows a diurnal rhythm in insulin sensitivity, with higher insulin sensitivity in the morning.

“

*It is likely that disturbance of the central and/or tissue clock rhythms contributes to the pathophysiology of insulin resistance”*

**The adipose tissue clock**

White adipose tissue (WAT) contains an autonomous circadian clock, as shown in both rodent and human *in vitro* models. The WAT clock is synchronised by the central brain clock as well as by signals resulting from food intake. Rodent adipocytes show a circadian rhythm in glucose uptake. In human WAT, ~25% of the transcriptome shows diurnal variation, including pathways involved in the regulation of glucose uptake. Subcutaneous WAT explants from human subjects show an intrinsic diurnal rhythm in insulin signalling, with peak insulin sensitivity at noon.

**The liver clock**

The liver contains an autonomous clock that is synchronised by the central brain clock via a combination of autonomic and endocrine signals. The liver clock strongly responds to signals resulting from food intake, since the liver clock can be uncoupled from the brain clock by inverting the daily feeding rhythm. The liver clock regulates several pathways involved in the control of glucose and lipid metabolism, as indicated by micro-array, proteomic and metabolomic studies. The liver clock is essential to maintain euglycaemia, by synchronising the diurnal rhythm in gluconeogenesis and glucose export to the habitual fasting period.

**The pancreatic clock**

The presence of an autonomous circadian pancreatic clock has been demonstrated in rodent as well as in



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human islet cells. The pancreatic clock is synchronised by the light/darkness cycle via signals from the brain clock, including autonomic neuronal signals, melatonin, glucocorticoids and body temperature. The amplitude of clock gene oscillations in cultured rat islets is dependent on the glucose concentration in the medium. Isolated rat pancreatic islets show a circadian rhythm in insulin secretion. Clock genes activate the transcription of genes involved in insulin biosynthesis, insulin transport and glucose-stimulated insulin secretion. Disruption of the pancreatic clock causes defective insulin secretion.

**Circadian disruption**

The first clue that the circadian timing system may be involved in the pathophysiology of insulin resistance was the observation, in the 1960s, of an altered daily rhythm in glucose tolerance in patients with diabetes mellitus. Later observations, including the development of metabolic syndrome in the *Clock* mutant mouse, food intake at the wrong circadian phase causing obesity in mice, and circadian misalignment resulting in decreased glucose tolerance in humans, led to the circadian disruption hypothesis. Sophisticated tissue-specific pancreatic, hepatic, muscle and adipose transgenic and knockout models gave further support to this hypothesis.

**Conclusion**

Taken together, it is likely that disturbance of the central and/or tissue clock rhythms contributes to the pathophysiology of insulin resistance. Circadian disruption may also cause misalignment of nutrient fluxes, both between and within tissues. For instance, a mismatch between hepatic glucose production, muscle glucose uptake and carbohydrate intake may contribute to elevated glucose levels, and metabolic inflexibility in muscle tissue may result in insulin resistance.

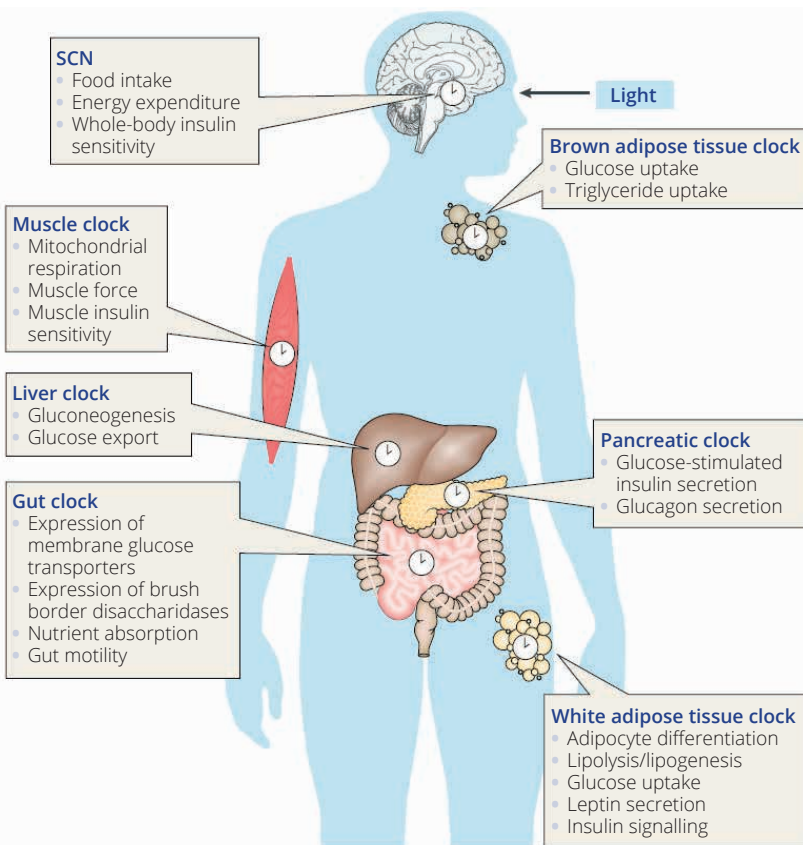
Randomised clinical trials are needed, investigating the effects of natural light/darkness exposure, sleep improvement, time-restricted feeding and the daily timing of exercise in preventing these metabolic complications.

**Dirk Jan Stenvers and Andries Kalsbeek**

*Department of Endocrinology and Metabolism, Amsterdam UMC, The Netherlands*

**Further reading**

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**Figure.** Circadian clocks regulate glucose metabolism, insulin sensitivity and insulin secretion. The molecular clocks consist of a transcriptional translational feedback loop involving the clock proteins *CLOCK*, *ARNTL*, *PER* and *CRY* and the nuclear receptors *NR1D1*, *NR1D2* and *ROR*. The central and peripheral clocks are responsible for a variety of functions. SCN, suprachiasmatic nucleus.



## ESPE 2022: marking 60 meetings

Rome, Italy

15–17 September 2022

**Personalised medicine in paediatric endocrinology** is the theme of the 60th ESPE Annual Meeting, which is the first ESPE Annual Meeting to take place in person since 2019.

The exciting and diverse programme covers basic science, translational research and clinical care, offering you **the best global update in paediatric endocrinology**.



You will have the chance to **meet with our most experienced international colleagues**. As well as topical and engaging plenary lectures, symposia, Meet the Expert and 'How do I...?' sessions, you can enjoy Controversy and Novel Advances sessions that will challenge all our ways of thinking. Oral communications and physical and electronic posters will cover the widest possible range of subjects and insights from senior and junior voices in the field alike.



If you are unable to join us in Rome, we will be running our **ESPE On Demand** service following ESPE 2022. You will be able to catch up on all the sessions for the following 6 months, using your registration details.



Find the full programme and register at [www.espe2022.org](http://www.espe2022.org)

### Avoid fraudulent websites

Remember that the ESPE website (at [www.eurospe.org](http://www.eurospe.org) or [www.espe2022.org](http://www.espe2022.org)) is the only official website where you can safely register to attend ESPE 2022.



### ESPE e-Learning

Answer to the case query on [page 3](#).

**Interpretation:** secondary/tertiary hypothyroidism

**Treatment:** I would not immediately start thyroxine treatment

Thyrotrophin is only mildly elevated, which would be inappropriately low for such a low free thyroxine value if this was due to primary hypothyroidism. This, together with the finding of significantly low morning cortisol, indicates central hypothyroidism and, most likely, central hypocortisolism. Hypothyroidism probably developed

after the age of 2 years, since Nikola has a normal IQ. Thyroxine replacement without hydrocortisone replacement can precipitate fatal adrenal crisis in patients with central hypocortisolism, so this therapy should be withheld until definite assessment of adrenal function and start of hydrocortisone replacement therapy.

## Hypothalamic dysfunction in childhood

### ESPE Science Symposium 2022

Princess Máxima Center,  
Utrecht, The Netherlands,  
7–8 October 2022

This 2-day event will discuss the aetiology of genetic and acquired hypothalamic dysfunction in childhood, its consequences and new ways of management to improve outcome.

We will also focus on building new networks and collaboration within ESPE and Europe, together with patient organisations and Endo-ERN.



Find out more at [www.eurospe.org/education/espe-science-symposium-2022-hypothalamic-dysfunction-in-childhood](http://www.eurospe.org/education/espe-science-symposium-2022-hypothalamic-dysfunction-in-childhood)



### 7th ESPE Connect Webinar

19 October 2022

16.00 CEST

The next ESPE Connect Webinar will be on the subject of **achondroplasia - newer treatment options**.



For more details see [www.eurospe.org/education/webinar-series](http://www.eurospe.org/education/webinar-series)

## Future meetings

See [www.eurospe.org/meetings](http://www.eurospe.org/meetings) for details of all future meetings



### 60th Annual ESPE Meeting

15–17 September 2022  
Rome, Italy



### 11th International Meeting of Paediatric Endocrinology

4–7 March 2023  
Buenos Aires, Argentina



### 61st Annual ESPE Meeting

21–23 September 2023  
The Hague, The Netherlands



### 62nd Annual ESPE Meeting

November 2024  
Liverpool, UK



### 63rd Annual ESPE Meeting

May 2025  
Copenhagen, Denmark



## OTHER EVENTS

### ESPE Summer School

12–14 September 2022  
Torgiano, Italy

### ESPE Diabetes, Obesity & Metabolism School

18–20 September 2022  
Torgiano, Italy

### ESPE Caucasus & Central Asia School

28 September–1 October 2022  
Yerevan, Armenia

### ESPE Science Symposium: Hypothalamic dysfunction

7–8 October 2022  
Utrecht, The Netherlands

All dates, deadlines and plans are being constantly reviewed in light of COVID-19

## DEADLINES

### SEPTEMBER

**Annual Business Meeting question and proxy form deadline – 9 September 2022**

**ASPED-ESPE Endocrine Academy Steering Committee Member application deadline – 30 September 2022**

**Early Career Scientific Development Grant application deadline – 30 September 2022**

### OCTOBER

**11th International Meeting of Paediatric Endocrinology abstract submission deadline – 3 October 2022**

**ESPE Diabetes, Obesity & Metabolism School Steering Committee Co-ordinator application deadline – 31 October 2022**

### DECEMBER

**ESPE Awards 2023 nominations – 10 December 2022**

For more information about vacancies on ESPE Committees and how to apply, see [www.eurospe.org/about/vacancies](http://www.eurospe.org/about/vacancies)

# 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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[www.corbiculadesign.co.uk](http://www.corbiculadesign.co.uk)

### Published by:

Bioscientifica Ltd  
Starling House  
1600 Bristol Parkway North  
Bristol BS34 8YU, UK  
W: [www.bioscientifica.com](http://www.bioscientifica.com)  
*Bioscientifica is a subsidiary of the Society for Endocrinology*

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Bioscientifica Ltd (address above) manages the ESPE Office.  
It is also the Professional Congress Organiser (PCO) for ESPE's Annual Meetings.

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### ESPE News archive

You will find previous newsletters in the archive at [www.eurospe.org/news/newsletters](http://www.eurospe.org/news/newsletters)