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New identity, new ambition:

ESE looks forward

Also in this issue Researching thyroid disease in pregnancy Best-read science of 2016 ECE 2017: the highlights



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This document is available on the ESE website, **www.ese-hormones.org**

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Editor: Wouter de Herder, The Netherlands

Email: w.w.deherder@erasmusmc.nl Co-Editor:

AJ van der Lely, The Netherlands Email: ese.president@ese-hormones.org

Editorial Board: Justo Castaño, Spain Ljiljana Marina, Serbia Hans Romijn, The Netherlands Ayse Zengin, UK/Australia

Sub-Editor: Caroline Brewser

Design: Qube Design Associates

Website: www.ese-hormones.org

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Editorial



It is time, once again, to reflect on the amazing breadth and depth of our discipline, so clearly illustrated at ECE 2017 in Lisbon, Portugal. It was wonderful to see so many ESE members, including lots of new faces, during the meeting. I am sure you will agree that there was a true spirit of collaboration, and a huge amount of excellent research.

You will be reminded of many Congress highlights on page 3 of this issue and, if you were unfortunate enough not to be there, you will see that our new service 'ECE on Demand' will enable delegates and those who were ESE members at the time of the Congress to catch up with what they missed. On page 15, we celebrate the success of our many prize winners and those who were presented with awards to recognise their contributions to endocrinology. Congratulations to them all!

This issue of *ESE News* is the first to adopt ESE's exciting new visual identity, and also has an increased number of pages. Enhancing communication and amplifying the voice of endocrinologists are both key to ESE's vision for the future, as the Society revitalises itself following its recent rebranding. You can find out more about our new identity, which was formally launched at ECE 2017, on pages 8–9.

From rebirth we move to birth, to consider the topical issue of managing thyroid disease in pregnancy. When and how to provide treatment have come under close scrutiny of late and, on pages 10–11, Kristien Boelaert and Robin Peeters look at some of the challenges addressed by their groups in Birmingham, UK, and Rotterdam, The Netherlands, respectively.

In his expanded 'Editor's Selection' column on pages 12–13, Editor of *European Journal of Endocrinology* Hans Romijn indulges our passion for the latest research by looking at the most read papers in the five ESE journals in 2016. I am sure you will agree that these form a fascinating snapshot of recent areas of interest in endocrinology.

As always, the rest of the issue is full of news (make sure you look through the extended news section on pages 3–7), as well as enlightening facts and information. I do hope you enjoy your new-look newsletter. If you have any comments or suggestions please email info@euro-endo.org.

AJ van der Lely ESE President Co-Editor of *ESE News*







ECE 2017: a celebration of endocrinology

This year's Congress was a great success. With over 3600 delegates and more than 1800 abstracts, it not only set records but also encompassed the whole spectrum of endocrinology.

Throughout the 4 days of the Congress, delegates enjoyed a lively atmosphere of collaboration and cutting-edge endocrinology. ESE President AJ van der Lely opened the meeting and welcomed all the attendees, with live music providing a local flavour. There were many networking opportunities, including the Welcome Reception.

ESE's objectives include promoting endocrinology in Europe and internationally, and so the Society issued press releases to highlight the importance of endocrine research and attract public interest. The international

media were swift to respond, and over 600 articles, across 20 countries and 7 languages, featured the high quality research at the Congress.

Medscape set up a dedicated section for breaking news from ECE 2017 (www.medscape. com/viewcollection/34112). Amongst other stories, they covered the debate between Yona Greenman (Israel) and Stylianos Tsagarakis (Greece) on medical therapy for pituitary tumours. The fact that the audience's opinion was split 50/50 afterwards illustrates this issue's complexity.

A role for growth hormone (GH) in recovery of sensory function after complete spinal injury is a story of hope, captured in the research of Gulliem Cuatrecasas (Spain), who has shown that GH treatment leads to significantly increased feeling after 6 months. The topical talk by Christian Benedict (Sweden) on a link between poor sleep and obesity attracted great interest among delegates, and was widely reported in publications such as The Guardian and The Mail on Sunday.

Medscape also featured the 2nd Joint Global Symposium on Obesity at ECE 2017, where Tim Lobstein (UK), Director of Policy at the World Obesity Federation, commented, 'We have to do something at the regulatory level, at a national level ... food companies not having to pay for the cost of selling excess joules and the damage to teeth and weight gain ... justifies market intervention through regulation.'

Given the prevalence of vitamin D deficiency, research by Elisabeth Lerchbaum (Austria) into a potential link with male fertility

ECE on Demand

introduction of the ECE on Demand site and app, which enabled delegates to access ECE content easily, searchable by focus area. Webcasts of many sessions were uploaded within 24 hours, so attendees could watch lectures they were unable to attend.

Delegates and those who were ESE members at the time of ECE 2017 can access the content by logging in with their registration email address at www.eceondemand.org.

attracted attention and featured on the websites Science Daily and Medical News Today, among other publications.

Italian newspaper Giornale di Sicilia reported on the management of bone metastases from thyroid tumours, with a guote from new ESE President-Elect Andrea Giustina. French medical news website Edimark reported on ECE 2017, as did the media in Portugal, where website My Diabetes published video interviews with AJ van der Lely and Local Organising Committee Chair João Jácome de Castro, who was also interviewed for the Portuguese site Just News.

Other highlights included the extremely well-attended sessions on ESE's guidelines on Turner syndrome and aggressive pituitary tumours, and the everstrengthening component for endocrine nurses, which featured the 2016 Best Nursing Poster Award winner, Christine Yedinak (USA).

You can see photos from ECE 2017 on page 15.



A warm welcome!

Following the AGM during ECE 2017, ESE has a new President-Elect, Andrea Giustina (Italy, pictured), who will succeed current President AJ van der Lely in 2019, at the end of his term of office.

We also welcome Beata Kos-Kudła (Poland) as Publishing and Communications Committee Chair and Felix Beuschlein (Germany) as Science Committee Chair. Felix replaces Márta Korbonits, who takes the new role of Scientific Programme Chair (further details will follow). We thank retiring Executive Committee members Vera Popovic-Brkic, Jens Bollerslev and Georg Brabant.



Endo-ERN launched

The European Reference Networks (ERNs) for rare and complex diseases were officially launched on 9 March 2017 at the 3rd Conference on ERNs in Vilnius, Lithuania.

The European Reference Network for Rare Endocrine Conditions (Endo-ERN) was well represented at the event by steering committee members (all nominated by ESE and the European Society for Paediatric Endocrinology, ESPE) and a patient representative.

I was invited to give the opening plenary lecture on behalf of Endo-ERN, on the topic 'Co-ordinators' view on network management and governance'. You can find the presentations at https://ec.europa.eu/health/ ern/events/ev_2010309_en. Olaf Hiort (Paediatric Chair of Endo-ERN) and I (Adult Chair) jointly received the ERN certificate from the European Commissioner for Health and Food. Vytenis Andriukaitis.

The first General Assembly of Endo-ERN subsequently took place on 27 March in Leiden, The Netherlands. The primary aims of this meeting were:

- to update all Endo-ERN members and other stakeholders regarding the mission, structure and governance of Endo-ERN
- to obtain approval for the current application from the members, in order to be officially operational, and
- to secure the contribution by each healthcare provider of the predefined deliverables, as specified in the grant application.

European Reference Networks

At the meeting, I outlined Endo-ERN's mission, which is to reduce and ultimately abolish inequalities in care for patients with rare endocrine conditions in Europe, through facilitating knowledge-sharing and supporting related healthcare and research. Endo-ERN provides equality between paediatric and adult patients. Ultimately, Endo-ERN will result in the best possible care for every patient with a rare endocrine condition.

Opportunities, pitfalls, priorities and dissemination of expertise were discussed by Olaf Hiort, and patients' involvement, concerns and ambitions were summarised by Jette Kristensen (European Patient Advocacy Group (ePAG) representative).

The key issues discussed in ICT and e-Health were: strategic considerations, the recently submitted EU application for registries for rare endocrine conditions (Faisal Ahmed), the Endo-ERN website (www.endoern.eu) (Alberto Pereira), the EU ERN IT platform (secured patient management system) allowing the sharing of patient data and virtual consultations (Herman Brand), and FAIR (findable, accessible, interoperable and re-usable) data management (Mark Thompson). Because dissemination of expertise is of key importance to all ERNs, Jérôme Bertherat (National Co-ordinator for Rare Endocrine Diseases in France, and Endo-ERN ESE representative) presented the French experience of national networks for rare diseases, and how these allow European reference centres to connect with national and regional centres.

All members approved Endo-ERN by plenary voting, after which Endo-ERN became officially operational.

The mission of Endo-ERN is defined in its five work packages (WP) and is to be delivered throughout all eight of its main thematic groups (MTGs). You can find details of these at www.endo-ern.eu. The WP and MTG Chairs explained the goals through the predefined deliverables. Subsequent 'speed dating' sessions around the respective WP and MTG posters helped to engage the members, increase awareness, exchange ideas and make concrete plans about how to meet the deliverables in the first year.

ESE and ESPE together will continue to support this European endeavour to achieve the best care for patients with rare endocrine conditions.

Alberto Pereira Adult Chair, Endo-ERN

From the ESE Office

At the time of writing, I have just returned from ECE 2017 in Lisbon. Even if we talk purely numerically (abstract submissions, delegate numbers and so on), this meeting was an outstanding triumph, but its success goes much deeper than that. There was a feeling of real positivity and a collaborative atmosphere which was so clear to everyone that people remarked upon it almost continuously.

I thank the Programme Organising Committee for putting in place such an impressive programme that people actually attended the sessions instead of enjoying the sun! (This led to some capacity issues in the rooms, which we will address for next year...)

It was a big year for ESE, the end of an 18-month process of strategic review, which culminated in the launch of our new visual identity in Lisbon. With our priorities clearly outlined, and our identity placing us firmly at the centre of European endocrinology, we are now positioned to move forward with strength and confidence into our second decade. The key will be collaboration with our National Affiliated Societies, Specialist Societies and international partners, so we can unite in our efforts to drive research and improve clinical practice.

One main objective is sharing knowledge, and we were delighted to launch 'ECE on Demand' (www. eccondemand.org) at ECE 2017. This places most of the Congress's content online: abstracts, e-posters, webcasts and interviews. It is openly accessible to ESE members and ECE 2017 delegates. Please let me know your thoughts on this or any of ESE's activities at helen. gregson@ese-hormones.org.

Have a lovely summer!

Helen Gregson Chief Executive Officer, ESE

Free open access publishing in *Endocrine Connections*

Endocrine Connections has recently been indexed in the Web of Science, Science Citation Index Expanded database, and has just received its **first impact factor: a remarkable 2.541!**

This is testament to the high quality of the published articles and the hard work of the Editorial Board, including late Editor-in-Chief Jens Sandahl Christiansen.

To celebrate this important milestone in the journal's development, its owners, ESE and the Society for Endocrinology,

Terms and conditions

 The corresponding author must have been a member of either ESE or the Society for Endocrinology for one calendar year on the date of submission to be eligible.
 The offer is available for papers submitted between 1 January and 30 September 2017. are delighted to offer their members completely free open access publishing in *Endocrine Connections* in 2017 (subject to the terms and conditions below).

Endocrine Connections is the only society-owned, open access, endocrinology journal indexed in PubMed and Web of Science. The societies are proud to offer this unique benefit to their members and encourage them to support the journal in its aim to be the leading open access title in the field.

 All submissions are subject to peer review and the journal's usual acceptance criteria (www.endocrineconnections. com/site/misc/EC_ifora.xhtml).
 The offer applies to individual members and is not open to Corporate Members.

Make your way to Mont Ste Odile

Alsace, France, 4–7 October 2017



The Symposium on Hormones and Cell Regulation is an annual meeting for basic research scientists to discuss the latest advances in endocrinology and related fields. Presentations by prominent international researchers cover the most recent ground-breaking data. Academic endocrinologists at all career stages benefit from the opportunity to meet and discuss their work with experts in their fields.

The Programme Organising Committee, led by Jacques Dumont, ensures the meeting is independent and stimulating, with the focal topic changing each year. This year's topic will be 'lon channels in hormonal homeostasis: transient receptor potential channels and calcium signalling'. The venue, a monastery at Mont Ste Odile in the beautiful Alsace region of France, provides the perfect environment for a focused and engaging symposium.

ESE has supported this meeting since 2012. We feel it is essential that meetings of this quality continue to be organised, and are committed to ensuring its continued success.

Reserve your place now at the 2017 symposium. For more details see www.ese-hormones.org/education/basicscience.aspx.



Further info Find out more at www.endocrineconnections.com

5th Combo Course

'Subclinical endocrinopathies and diabetes' is the topic of the 2017 Combo Endocrinology Course, which takes place on 29 September–1 October, in Athens, Greece.

Attendees will be able to enjoy lectures, 'meet the expert' sessons and case presentations. You can find out more and register at www.comboendo.gr.

Last year's topic was 'Ageing and anti-ageing endocrinology', focusing on the impact of ageing on many endocrine-related entities. Most of the lectures and part of the workshops feature in *European Journal of Endocrinology* 2017 **176** R283–R308.

We thank Evanthia Diamanti-Kandarakis (who established the series) and Christos Zouboulis (Germany), Vice President for the 2016 course, as well as everyone else who supported the event, including ESE, the Hellenic Endocrine Society and the Euroclinic of Athens.

We look forward to seeing you in 2017!

New European Examination

In response to your requests for a means of internationally recognising your level of clinical expertise, ESE has liaised with the European Union of Medical Specialists (UEMS) to hold the first Pan-European Examination in Clinical Endocrinology, Diabetes and Metabolism in 2018.

The high quality examination will lead to certification endorsed by both organisations. Tests can be taken at centres across Europe, making them widely accessible.

Further information, including a form to register your interest, can be found at www.ese-hormones.org.



Welcome Dirk!

Dirk De Rijdt is ESE's new Director of Commercial Services. With experience of the world of endocrinology and previous roles in the industry, Dirk is wellpositioned to support and shape our Society.

- His role will enable ESE to:develop new services and products
- deliver its strategic objectives
- expand relationships with members and organisations,
- andbe financially sustainable in the long term.

Dirk comments, 'I have had the honour of following ESE since its creation 10 years ago, and am happy to join its exciting journey.' We welcome Dirk to his new role.

New ESE Working Group on Endocrine Disrupting Chemicals

The Science Committee welcomes the new ESE Endocrine Disrupting Chemical (EDC) Working Group, which has recently been established, led by Josef Köhrle (Germany).

The issue of EDCs has received increasing attention within endocrine research, by regulatory authorities, and in public and political debate. In recent years, the Science Committee has discussed ESE's role in this arena. The Executive Committee has now decided to set up a working group.

At this stage, no fixed work plan or mandate has been implemented, so the group will define its priorities, extent and type of activities. Some aspects have been discussed, such as higher visibility of the field of EDCs within ESE-supported conferences, workshops, and training and education activities. The working group will also provide advice and expertise to the ESE Science and Education Committees and the ESE Executive Committee, to increase active support and lobbying for high quality science, funding and organisation for research into EDCs in Europe.

The working group could also strengthen links with groups already dealing with EDCs in related disciplines such as (embryo-)toxicology, nutrition, epidemiology and perhaps industry. As well as preparing EDC-related information for ESE and its members, the group could help raise the voice of European endocrine science related to EDCs, in order to be heard in regulatory, executive, administrative, political and public forums. Further details will follow.

I should conclude by saying how much I have enjoyed leading the Science Committee. I wish Felix Beuschlein (Germany) well as the new Chair.

Márta Korbonits Chair, Science Committee

ESE courses and grants for scientists

See www.ese-hormones.org for full details



Summer School on Endocrinology 30 July–3 August 2017, Berlin, Germany

Symposium on Hormones and Cell Regulation 4–7 October 2017, Mont Ste Odile, France

ESE Basic Course 2018 Details to be confirmed

Grants:

ESE Basic Science Meeting Grants ESE International Endocrine Scholars Programme ESE Meeting Grants ESE Poster Prizes ESE Short Term Fellowships ESE Small Meeting Grants ESE Young Investigator Awards Journal of Endocrinology Travel Grants

Improving care across Europe and beyond

The ESE Clinical Committee aims to improve the standard of care for endocrine diseases across Europe and beyond.

Among the tools we are developing or promoting are clinical guidelines and emergency cards, both of which have been identified as major ESE activities. Some address rare endocrine diseases, where the European dimension is a key factor in achieving progress. We are set to liaise with the European Reference Network for rare endocrine conditions (Endo-ERN; see page 4), to combine efforts.

Clinical guidelines on hypoparathyroidism, phaeochromocytoma and adrenal incidentaloma have all been published since 2015 in *European Journal of Endocrinology*. The result of deep analysis of evidence by recognised experts, they have become major international points of reference. Our aim was that they should be widely used, and so they needed to be available to all healthcare professionals. Consequently they can be freely downloaded from the journal website.

This year has been very productive. Two clinical guidelines were presented at ECE 2017 in Lisbon, on Turner syndrome and aggressive pituitary tumours. Both had previously been submitted for comment to all ESE members. including all ECAS (ESE Council of Affiliated Societies) members, as it is helpful to have a final text which is readily usable across Europe. We also seek the comments of scientific societies on ESE guidelines, and a representative of the Endocrine Society is invited to participate

actively in the process. In 2018, we anticipate an ESE clinical guideline devoted to adrenocortical cancer, which will be followed by another based on an endocrine work-up of obesity.

Emergency cards are welcomed by patients and useful tools for endocrinologists. They are the successful result of collaboration between patients' associations and scientific societies. The concept is simple and efficient, with one side in the patient's national language and one side in English, enabling safe travel across Europe. The adrenal insufficiency card has been a great success in many European countries. We are now developing a hypoparathyroidism card in the same format. Just as for clinical guidelines, our aim is wide distribution, use and

THIS PATIENT NEEDS DAILY REPLACEMENT THERAPY WITH CORTISONE
In the event of serious illness, trauma, vomiting or diarrhoea, hydrocortisone 100 mg iv/im and iv saline infusion should be administered WITHOUT DELAY.
Name
Personnumber/Date of birth

recognition, at the European level and beyond, for the benefit of patients.

European Society of Endocrinology

Jérôme Bertherat Chair, Clinical Committee



5th EYES Meeting Porto, Portugal, 8-10 September 2017

Since it first took place in 2013, the annual EYES Meeting has been growing in attendees, scientific excellence and peer projection. The 5th EYES Meeting, taking place in September, has an extensive programme covering a broad range of topics in endocrinology. Lectures will be given by keynote speakers, alongside oral and poster presentations delivered by young endocrinologists.

We happily carry the endocrine torch from the east to the west of Europe for 2017. This EYES Meeting will take place in Porto, a fascinating and vibrant city on the coast in northern Portugal. The city is built along the hillsides overlooking the Douro river and port cellars. It is an ancient city steeped in history and tradition, with imposing architecture in a mixture of styles: Baroque, Neoclassical and Belle Époque. Porto and its blossoming cultural scene will provide you with an exceptional experience.



Scientific and networking events will create a unique opportunity to enhance your professional development, build your reputation, develop collaborations and shape the future of endocrinology. Your research will shape the scientific programme.

You can find out more at www.eyes2017.org.

We look forward to seeing you in Porto!

Luís Cardoso, Nuno Vicente and Adriana Lages Local Organising Committee

EYES at ECE 2017

Three outstanding early career researchers in endocrinology were invited to present their research at the EYES symposium during ECE 2017 in Lisbon, Portugal. This is what they had to say about EYES and ECE.



Vickie Braithwaite The EYES symposium at ECE is a fantastic innovation. It gives 'young' scientists the opportunity to present and chair sessions. I thank the EYES Committee for inviting me to speak at their symposium this year and for providing me with the chance to network with others in my field. I particularly enjoyed the meeting for its varied and interesting programme, excellent organisation and the superb city of Lisbon. What I especially like about ECE is the opportunity to learn about areas of endocrinology that are not 'my own'. I particularly enjoyed Matthias Tschöp's Geoffrey Harris Prize Lecture on current and novel ways of tackling obesity and metabolic disease.



Tim Korevaar I look back on an excellent ECE, which nicely brought together the wide range of basic, translational and clinical science that endocrinology has to offer. I also very much enjoyed interacting with fellow young endocrinologists through the informal setting of the EYES events. I had the pleasure of presenting on my own area of work during the EYES symposium, which led to some great discussions and interesting insights. To me, this exemplifies the value EYES adds by unifying young endocrinologists from across Europe, who have a wide range of backgrounds in different subspecialties.



Lubov Matchekhina Moscow, Russia

Receiving the award for the best presentation at the 2016 EYES Meeting in Moscow was a great honour and a nice surprise. Then, talking at the EYES symposium at ECE 2017 was a fantastic experience. I felt I was part of a huge and miraculous 'endo-world', with the chance to discuss the results of my research with colleagues, and to improve my presentation skills. The Congress itself was exciting as usual; I enjoyed the plenaries and debates and was also glad to discover the Meet the Basic Scientist sessions, which were new this year. I'm looking forward to future meetings: new cities and new plans!



A clear voice for endocrinology in Europe

ECE 2017 in Lisbon saw a celebration of ESE's new identity. Many of you had been involved in helping us to develop the Society's new visual appearance, which represents ESE's ambitions for the future.

Our new identity has allowed us to crystallise the messages that describe our organisation and its vision. It will enable ESE to stand out from the crowd and reach the individuals and organisations with which we need to work.

ESE's new logo is designed around collaboration. It captures our work uniting the endocrine community to improve patient care in Europe and around the globe. The swirling, linked colours show our belief in working together, and allow us to be bold in a crowded world. The blue tones connect us to our proud past, whilst the new design shows our drive into the future.

A big part of this development is ESE's website (www.ese-hormones. org). Its look has changed to fit the new identity, but it will be undergoing a much larger redevelopment this year, to truly meet the needs and requirements of you, our members, and the wider endocrine community.

You will also see that *ESE News*, your newsletter, has expanded, with a refreshing new page layout. This illustrates our commitment to increase collaboration and inclusivity by promoting communication with and between members. Your news is always welcome and will be included in these pages – please let us know about your events and activities.

ESE's major goals are:

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- to be at the centre of the endocrine community in Europe, acknowledged as the reference point for endocrine science, knowledge and health
- to provide continuous endocrine-related education and training provision for all career stages in clinical practice and basic research
- to foster early career basic and clinical endocrinologists, creating a dynamic community which will inspire them to become endocrinologists and remain in endocrinology
- to continue to run the leading European endocrine congress, ensuring it is kept current, attractive across the focus areas, and viewed as the 'must attend' event for endocrinologists across Europe.



Journal covers

The cover of *European Journal of Endocrinology* follows a consistent and distinctive design, making full use of ESE's logo and colour palette.

<text>

Straplines

ESE has two straplines: 'The European hormone society' and 'The voice for endocrinology'.

These succinctly summarise ESE's vision for the future and emphasise its position within the endocrine community.





Colour palette

ESE's new colour scheme expands upon our traditional blues with a core selection of purples. Three families of supporting colours (blues, oranges and greens) add variety and can colour code information.



Imagery

The main hexagonal ESE logo reflects unity, support and knowledge-sharing.

By repeating the image and building larger illustrations, we use it to show the importance of collaboration. These larger images include maps (see opposite, as used on the programme for ECE), graphs or abstract illustrations.

Icons based on the logo have been developed for use in ESE communications.





EYES and ECAS

Our branding for ECAS (ESE Council of Affiliated Societies) and EYES (European Young Endocrine Scientists) is closely visually affiliated to the core branding, using the same typeface, colours and icon. This reflects the unity of purpose of these groups and the Society.

Website

The appearance of our website incorporates the new branding, reflecting ESE's newly defined values and purpose. The website is also being restructured and will be relaunched later in 2017.



Please contact us at **info@euroendo.org** for further information or advice about using ESE's new visual identity.



The Endo Explorer **To treat or not?** <u>Thyroid disease in pregnancy</u>





Kristien Boelaert is keen that carefully designed clinical trials in thyroid disease should optimise care for pregnant women and their babies.

Over the last 15 years, I have developed a keen interest in thyroid disorders before, during and following pregnancy. 'Primum non nocere' – first do no harm, is an important ground rule to which all physicians should adhere. Our knowledge of the diagnosis and management of thyroid dysfunction is largely based on observational studies, with few randomised controlled trials guiding best practice. The evidence base regarding optimal management of thyroid disease in pregnancy is rapidly accumulating, and new findings indicate that excessive treatment of thyroid dysfunction may, in fact, cause harm.

Early research career

During my postgraduate doctoral studies, unravelling the roles of novel oncogenes in thyroid cancer, I was fortunate to work alongside colleagues studying the effects of thyroid hormone deiodinase enzymes in placental and fetal development. Through collaboration, I was able to investigate a role for human securin in fetal brain development and to lay the foundations for close relationships with scientists and clinicians with a keen interest in the links between the thyroid gland, the fetus and the mother.

The power of clinical databases

My subsequent research as a clinician scientist taught me the importance of translating findings from laboratory research to the bedside and vice versa. I have realised the value of detailed documentation of patients, building large databases which form the basis of important clinical studies.

My team's expertise in analysing large datasets led to our participation in the study of UK iodine status, which demonstrated mild to moderate iodine deficiency.¹ The long term effects of mild iodine deficiency on pregnancy outcomes and the offsprings' cognitive ability are not entirely clear, and there are currently no definite recommendations regarding iodine requirements during pregnancy in the UK.² We therefore built an economic model studying the costs and benefits of iodine supplementation in the UK, showing this to be cost-saving. This finding has implications for 1.88 billion people in 32 countries worldwide with mild iodine deficiency.³

Clinical trials: the way forward

Evidence from large and carefully conducted clinical trials is accumulating rapidly in the field of thyroid and pregnancy. Ari Coomarasamy, with whom I work closely, commented only recently that the 'thyroid emperor

has no clothes' where pregnancy is concerned.

Findings regarding outcomes relating to pregnancy and neurocognitive development in patients with mild thyroid hormone deficiency are heterogeneous.⁴ Large trials have not shown a benefit of levothyroxine replacement on either of these end points, although replacement treatment was started relatively late in pregnancy. Laboratory and clinical studies indicate that the effects of thyroid hormones on fetal brain in the offspring occur from early gestation onwards, and interventions started in mid and late second trimester may have fewer effects when the fetus has a functioning and responsive thyroid gland.

Most hypothyroidism in the western world is driven by thyroid autoimmunity, the hallmark feature of which is antibodies to thyroperoxidase (TPO). It is unclear if these antibodies have direct effects on fertility and pregnancy outcomes, or if they herald the presence of autoimmune mechanisms potentially resulting in poorer outcomes. Together with Ari Coomarasamy, we are in the process of analysing the data of the TABLET trial in which women with positive TPO antibodies and normal thyroid function were randomised to placebo or levothyroxine replacement. Further trials and studies are ongoing elsewhere across the globe, and we hope to find some clothes for the emperor in the near future.



Optimising patient management

Collaborative networks are crucial to the conduct of cutting edge laboratory, clinical and translational research. Similarly, the optimal management of pregnant patients with endocrine disorders is through a multi-disciplinary approach with endocrinologists, obstetricians, primary care physicians, midwives and other healthcare professionals. I strongly believe in the practice of evidence-based medicine,⁵ and it is likely that guidelines regarding optimal clinical practice will continue to change as research findings accumulate. I hope my ongoing involvement in making recommendations in this field will allow best practice to continue without causing harm to mothers or their unborn children.

Kristien Boelaert

Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK

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The Endo Explorer What is optimal? Thyroid function in pregnancy





Robin Peeter's group is strongly focused on unravelling thyroid (patho)physiology during pregnancy.

Adequate thyroid hormone availability is essential for normal development and optimal functioning during life, while thyroid hormone also plays a major role in ageing. It has always intrigued me how a single hormone can have so many roles: different roles at different stages of development and also in different tissues at the same time.

The impact of elevated thyroid hormone

Over the last 20 years, the research of the thyroid group at Erasmus MC has largely focused on regulation of thyroid hormone action, under the supervision of my mentor Theo Visser. In 2009, as part of a post-doctoral fellowship in Douglas Forrest's laboratory at NIH (Bethesda, MD, USA), I studied defects in thyroid hormone signalling and its consequences for brain development. We demonstrated that high levels of thyroid hormone in early development negatively affect fetal brain and auditory development. Clinical research at that time predominantly focused on negative consequences of low thyroid hormone levels on brain development, but these data suggested that high levels were equally detrimental.

These animal studies provided the basis for work by Tim Korevaar and Marco Medici on the effects of high maternal thyroid hormone in pregnancy. While there was a consensus to treat mild forms of thyroid hormone deficiency, as it was generally believed that 'the potential benefits outweigh the potential risks', we demonstrated that high-normal levels of thyroid hormone are associated with a lower birth weight, a lower IQ and a higher risk of learning disabilities.^{1,2}

Revised guidance

This has resulted in a mindset shift in the field. While physicians often treated subclinical hypothyroidism in pregnancy with relatively high dosages (e.g. 150µg levothyroxine (LT4) in the CATS trial),³ a much lower starting dose (50µg LT4) is now advocated in the 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum,⁴ based on our recent findings. Furthermore, our studies on reference ranges have provided the basis for increasing the upper limit of thyrotrophin (TSH) during pregnancy, leading to more stringent treatment cut-offs.^{5,6}

In search of the mechanisms

Currently, we are focusing on the mechanisms by which thyroid dysfunction and autoimmunity cause a higher risk of pregnancy complications. We are very interested in the pregnancy hormone human chorionic gonadotrophin (hCG), which ensures increased production of thyroid hormone during the period of increased demand. We recently showed that thyroid peroxidase (TPO) antibody-positive women have a severely attenuated thyroidal response to hCG. While high hCG levels show a very clear positive relationship with maternal free thyroxine (FT4) levels and subsequent reciprocal relationship with maternal TSH in TPO antibody-negative women, there is no such relationship in TPO antibody-positive women.⁷ TPO antibody-positive women who have a decreased thyroidal response to hCG seem to be particularly at increased risk of premature delivery. These women are thus most likely to benefit from levothyroxine treatment in two ongoing clinical trials (TABLET, Birmingham, UK, and T4Life, Amsterdam, The Netherlands).

Consortium on Thyroid and Pregnancy

It is difficult to generalise the available evidence in this field, mainly due to large differences between study populations, methodology and clinical outcomes. In addition, several important clinical questions remain unanswered, because single studies are not adequately powered to study small subgroups.

Consequently, Tim Korevaar and I founded the Consortium on Thyroid and Pregnancy, with Peter Taylor and Colin Dayan. This provides a formal platform for co-operation between researchers and cohorts. It will facilitate high quality studies of the association of gestational thyroid function with adverse pregnancy outcomes, by performing individual participant-based meta-analyses combining data from prospective cohorts across the globe. The Consortium currently consists of 28 studies with data on more than 80 000 mother-and-child pairs.

'We demonstrated that highnormal levels of thyroid hormone are associated with a lower birth weight, a lower IQ and a higher risk of learning disabilities'

Our group will also focus on two important knowledge gaps. First, it is unclear how and to what extent maternal LT4 crosses the placenta, or how this is regulated. We therefore lack essential information on optimal LT4 dose and dose-adjustment strategies during pregnancy. Secondly, current LT4 treatment is merely guided by maternal thyroid parameters, as reliable non-invasive markers of fetal thyroid hormone status to monitor LT4 therapy are lacking. We aim to fill these gaps, since identification of accurate markers of fetal thyroid status and understanding transplacental transport will allow for more tailored treatment of pregnant women, to optimise pregnancy outcome and fetal development.

Robin Peeters

Erasmus MC, Rotterdam, The Netherlands

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- 5. Korevaar et al. 2013 Journal of Clinical Endocrinology & Metabolism 98 4382-4390.
- 6. Medici et al. 2014 Clinical Chemistry 61 704-713.
- 7. Korevaar et al. 2017 Journal of Clinical Endocrinology & Metabolism 102 69–77.

The best reads of 2016

In this special feature, Hans Romijn, Editor of European Journal of Endocrinology, reviews some of the most downloaded papers from ESE journals in 2016.





GH deficiency in young adulthood and the benefits of GH replacement

The management of children with growth hormone deficiency (GHD) has traditionally focused on the use of recombinant human GH (rhGH) therapy to normalise final adult height. However, rhGH therapy shows benefits in both children and young adults with GHD throughout each stage of their life.

This review by Ahmid et al.

summarises data showing that rhGH has less direct impact on bone density, with a greater impact on body composition and cardiovascular risk factors, including improvement in serum lipid profiles.

Even with scarce evidence, several short term studies during transition revealed that untreated GHD has a risk of alteration in somatic and metabolic consequences, although it is difficult to establish whether these mild alterations represent the early long term consequences and whether subsequent rhGH treatment improves long term health.

See Endocrine Connections **5** R1–R11



Sweetened beverage intake and latent autoimmune diabetes in adults and type 2 diabetes

Sugar-sweetened beverage intake is associated with an increased risk of type 2 diabetes. The risk increases by 13% for an increment of each serving per day in intake.

In this study, Löfvenborg *et al.* document that a daily intake of more than two servings of sweetened beverages is associated with increased risk of latent autoimmune diabetes in adults (LADA; odds ratio: 1.99, 95% Cl: 1.11–3.56), and for each 200ml daily serving, the odds ratio is 1.15 (95% Cl: 1.02–1.29).

Therefore, a high intake of sweetened beverages is also associated with an increased risk of LADA. The observed relationship resembled that with type 2 diabetes, suggesting common pathways possibly involving insulin resistance.

See European Journal of Endocrinology **175** 605–614



Novel mechanisms for DHEA action

Metabolism of dehydroepiandrosterone (DHEA) and its sulphated metabolite DHEA-S provides approximately 50% of androgens in men and about 75% of oestrogens in premenopausal women.

Early work on DHEA action focused on its metabolism to more potent sex hormones, testosterone and oestradiol, and the subsequent effect of these hormones on the activation of the androgen and oestrogen steroid receptors. However, it is now clear that DHEA and DHEA-S act directly as ligands for many nuclear receptors and various membrane receptors.

In this elegant review, Prough et al. summarise the established molecular mechanisms by which DHEA activates its biological effects in cells, including receptors and intracellular signalling pathways, with a focus on novel and physiological modes of DHEA action.

See Journal of Molecular Endocrinology **56** R139–R155

Methylated circulating tumour DNA in blood: power in cancer prognosis and response



Circulating tumour DNA (ctDNA) in the plasma of cancer patients provides an opportunity for non-invasive sampling of tumour DNA. This 'liquid biopsy' allows for analyses of DNA, including quantity, chromosomal alterations, mutations and epigenetic changes. These plasma markers may be associated with parameters such as tumour burden, aggressiveness, response to treatment, and survival. 'Liquid biopsies' can be used to guide

and improve treatment throughout the course of the disease.

This very elegant review by Warton *et al.* documents that cancer monitoring by measuring tumour DNA dynamics in blood is a new and developing area, which is expected to advance rapidly through the application of both existing and innovative technology. The benefits of this technique can be anticipated to improve management of cancer patients.



Liquid biopsy: All individuals carry circulating DNA in their blood. Upon tumour development, ctDNA carrying tumour-specific molecular alterations is released into the circulation, at levels relative to tumour burden. Throughout treatment, and upon completion, ctDNA can be used to monitor patient response and prognosis. (From Warton *et al.* 2016 *Endocrine-Related Cancer* **23** R157–R171.)

See Endocrine-Related Cancer 23 R157-R171



Microvesicles and exosomes: new players in metabolic and cardiovascular disease

Extracellular vesicles (EVs) are small (50nm to 2µm) vesicles released from the surface of a wide range of cell types into different bodily fluids. Both exosomes and microvesicles (MVs) are able to deliver to cells in remote locations.

The cargo includes genetic material such as mRNA, microRNA (miRNA) or even small amounts of DNA and proteins, including transcription factors, cytokines, and growth factors. MVs also carry cellular receptors and transmembrane proteins on their surface, which are characteristic of the cells from which they were released.

This review by Lawson *et al.* focuses on the role that MVs and exosomes have in diabetes, cardiovascular disease, endothelial dysfunction, coagulopathies and polycystic ovary syndrome. The authors speculate on the potential that the protein or RNA cargo of EVs offers, not only as biomarkers but also as vehicles for delivering bioactives.

See Journal of Endocrinology **228** R57–R71

Schematic representation of the mechanisms of formation of microvesicles, exosomes and apoptotic bodies. Microvesicles (0.2-2.0µm) originate via budding and shedding from the plasma membrane of cells and therefore may contain specific surface markers from the cell of origin. Exosomes (50-100nm), on the other hand, originate intracellularly through a sorting pathway involving intermediate organelles such as the early endosome and a late multivesicular body, which fuses with the plasma membrane to release exosomes via exocytosis. Apoptotic bodies (1-2µm) originate via blebbing of the plasma membrane. (From Lawson et al. 2016 Journal of Endocrinology 228 R57-R71.)





How to stay young and vigorous?



'So, how can one retain one's vigour? Are there any endocrine options here that might be helpful?' ESE recently celebrated its tenth anniversary, and has just launched its new visual identity. The organisation's ambition is to be increasingly active and extensively involved in the field of endocrinology in Europe and beyond. Redefining the Society's brand and its aims is sure to provide vigour and enthusiasm to address future challenges.

So, how can one retain one's vigour? Are there any endocrine options here that might be helpful?

We have to go back a long time in European medical history for a potential answer to this question. It starts with Charles-Édouard Brown-Séguard, a French physician and physiologist, who lived from 1817 to 1894. Some call him the 'father of endocrinology', since he played an important role in studies on internal secretions. These led to the further development of the concept of hormonal secretion, which was also based on theories developed by Théophile de Bordeu and Claude Bernard. But here we will mainly focus on Brown-Séquard's introduction of 'organotherapy'.

On 1 June 1889, Brown-Séquard presented a sensational report to the Société de Biologie in Paris. He had repeatedly injected himself with 1ml of a watery mixture of blood from the spermatic vein, semen and the extracted testicles of freshly killed healthy young guinea pigs and dogs. At the age of 72, he stated that he had 'rejuvenated' himself. He claimed that this therapy increased his physical strength and mental abilities, relieved his constipation, and lengthened the arc of his urine!

By the way, this was not the first time he had used himself as a test subject in one of his clinical experiments. In 1854 in Mauritius, he ingested material vomited by cholera victims to test the efficacy of opium (laudanum) as a remedy. The story goes that he took such a large dose of laudanum that he almost died.

Nowadays, one wonders if the results of his rejuvenation experiment were more a placebo effect than caused by the injected mixture, since we now know that steroids cannot be extracted with water, nor dissolved in it.

Brown-Séquard's claim prompted many researchers around the world to pursue this new field of 'organotherapy'. Brown-Séquard's fluid (advertised as the 'elixir of life'), testicular derivatives and human or animal testicle transplants were used to treat tuberculosis, diabetes mellitus, epilepsy, gangrene, anaemia, atherosclerosis, 'flu, adrenal insufficiency, hysteria and migraine. It was the best-selling prescription for many years.

In 1855, the same year that Thomas Addison published his famous monograph, 'On the constitutional and local effects of disease of the suprarenal capsule', Brown-Séquard published on his most important endocrine discovery: that the adrenal glands are essential for life. However, the belief that Brown-Séquard's fluid was really the elixir of life slowly evaporated.

So, a recommendation, which is still current, applies here. Don't try this (Brown-Séquard's fluid) at home – or in your laboratory! Meanwhile, I think we can all agree that ESE's invigorating approach is set for far greater future success.

Wouter de Herder Editor, *ESE News* Erasmus MC, Rotterdam, The Netherlands

FURTHER READING

Brown-Séquard C 1889 Comptes Rendus de la Société de Biologie **41** 415–422. Brown-Séquard C 1889 Lancet **2** 105–107.

Recognising success at ECE 2017



Honorary Membership of ESE was awarded to former President, **Philippe Bouchard** (France)



George Mastorakos (Greece) and **Anna Spada** (Italy) received Special Recognition Awards from ESE President AJ van der Lely



Medal

Lecturers



Matthias Tschöp (Germany) Geoffrey Harris Prize



Miguel López (Spain) European Journal of Endocrinology Prize



Evanthia Diamanti-Kandarakis (Greece) European Hormone Medal (ECAS)



Renato Pasquali (Italy) Clinical Endocrinology Trust Award (CET)



Bruce McEwen (USA) Fondation Ipsen Endocrine Regulations Prize



Young Investigator Award winners

Taís Silveira Assmann (Brazil), Elizabeth Baranowski (UK), Leticia Brondani (Brazil), Sabrina Chiloiro (Italy), Carla Di Dato (Italy), Milena Doroszko (Finland), Andreas Ebbehøj (Denmark), Camilla Maria Falch (Norway), Nazarii Kobyliak (Ukraine), Konrad Patyra (Finland), Anna Shalimova (Ukraine), Sandrine Urwyler (Switzerland), with the Co-Chairs and Chair of the Programme Organising Committee (POC): Guillaume Assié, Riccarda Granata and Bulent Yildiz



Poster Prize winners

Anastasia Arvaniti (UK), Kerstin Bathon (Germany), Sabrina Corbetta (Italy), Patricia Crock (Australia), Yolanda Diz-Chaves (Spain), Sang Yong Kim (Republic of Korea), Sinem Kiyici (Turkey), Natascha Schweighofer (Austria), seen here with POC Co-Chairs and Chair: Guillaume Assié, Riccarda Granata and Bulent Yildiz

New ESE prizes for ECE 2018



Two new awards in honour of the late Jens Sandahl Christiansen will be awarded at **ECE 2018** for the first time.

- They will recognise studies of metabolism 'at large'
- The recipient should be under 45 years of age
- One clinical and one basic science award will be made

Further details, including nomination information, will be available later this year.

The Endo Crossword

and the second s

Congraulations

Our winners from issue 32

were Luigi Cerri (Italy) and Yong Yong Tew (Malaysia).

Answers to the puzzle

11. Morula, 13. Stoma,

18. Nesidiectomy

14. L-Dopa, 16. 25 April,

Down 1. Vasco da Gama,

2. Exon, 3. Lagomorpha,

Glycine, 7. Homo,
 IPPSD, 12. Rooster,

14. Limbic, 15. Foam,

Across 1. Visceral, 5. Tagus, 6. WHO, 8. Parotin, 9. Iso,

in issue 32

Send us your solutions to this topical puzzle for your chance to win one of three ≤ 20 Amazon vouchers! Let us have your answers, along with your name and email address, by emailing them to **info@euro-endo.org** or faxing them to 0044 1454 642222.



Endo Prize Puzzle

Across

- Fasting-induced glucogenic hormone from white adipose tissue, identified 2016 (8)
- 5 Syndrome of pituitary tumour enlargement and excess ACTH secretion after adrenalectomy (7)
- **6** Carbohydrate literally meaning 'sweet wine' (7)
- 8 See 15 across
- **12** Small intestine hormone; reduces appetite and limits food intake (abbrev.) (3)
- **13** Blocker of vesicular monoamine transporter, derived from *Rauwolfia* spp. (9)
- **15,8** Swedish pharmacologist; Nobel laureate for research into dopamine (5,8)
- **16** Group of hormones important in insect moulting (12)

Down

- **1,9** Lab test animal probably responsible for global spread of chytridiomycosis (7,6)
- **3** Gland described by Descartes as 'the seat of the rational soul' (6)

17. Fry

- 4 'New' organ, according to press interpretation of research published in 2016 (9)
- 6, 10 'Father' of neuroendocrinology, after whom an ESE Prize Lecture is named (8,6)
- 7 Hormone the name of which literally means 'move the bile sac' (abbrev.) (3)
- 9 See 1 down
- 10 See 6 down
- 11 Most common nutritional deficiency worldwide, affecting >40% of those over 50 in Europe and the USA (7,1)
- 14 Deficiency which is the biggest cause of paediatric impaired cognitive development globally (6)

Did you know?

Rhinoceros parathyroids

The parathyroid glands were first discovered in a great Indian rhinoceros (*Rhinoceros unicornis*). When London Zoo's rhino died in 1849, they gave it to Sir Richard Owen (1804–1892), Hunterian Professor and Curator at the Royal College of Surgeons (London, UK). He carried out a detailed



dissection, finally publishing his findings in 1862. He noted 'a small compact yellow glandular body attached to the thyroid at the point where the vein emerged'. However, it was Viktor Sandström (Uppsala, Sweden) who named the glands in 1880, and Eugène Gley (Paris, France) who determined their function over a decade after that. The specimen, showing parts of the larynx and trachea, is still at the Hunterian Museum.

Save the date

For more information about any ESE event see www.ese-hormones.org/ meetings.

ESE Summer School

30 July-3 August 2017 Bregenz, Austria

5th European Young Endocrine Scientists (EYES) Meeting 8–10 September 2017

Porto, Portugal

42nd Symposium on Hormones and Cell Regulation (ESE)

4–7 October 2017 Mont Ste Odile, France

21st ESE Postgraduate Course on Endocrinology, Diabetes and Metabolism 5-7 October 2017

Lviv, Ukraine

EndoBridge 2017

19–22 October 2017 Antalya, Turkey

Europit

20–23 November 2017 Annecy, France

ECE2018

20th European Congress of Endocrinology 19–22 May 2018 Barcelona, Spain

Deadlines:

28 August 2017 EndoBridge Clinical Cases Submission deadline

30 September 2017 ESE Small Meeting Grant Application deadline

30 November 2017

ESE Short-Term Fellowship Application deadline