



ESE News

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THE EUROPEAN HORMONE SOCIETY

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Leading endocrine research

**Bertherat on genetics,
tumours and
successful publication**

Also in this issue:
**Endocrine disruptors:
in search of the truth**

**1st ESE Basic
Endocrinology Course**

ECE 2014:
the news from Wrocław



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This document is available on the ESE website, www.e-se-hormones.org

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Editorial

I hope you all enjoyed the European Congress of Endocrinology in Wrocław as much as I did!

As endocrinologists, we gain a great deal from meeting to share our research and one another's company. As you can see on pages 3 and 11, it was a hugely productive and lively meeting, enjoying a record number of submitted abstracts. This year, we benefitted from dedicated poster sessions, to give us plenty of time to contemplate the work of all our colleagues.

As we have reflected in past issues of *ESE News*, working together reaps huge rewards. This is never more important than when we have an intractable issue to address. Endocrine disruptors is one such topic, and we are delighted that three leading researchers in the subject, Richard Sharpe, Manuel Tena-Sempere and Jorma Toppari, have worked together on behalf of ESE to explain to us the challenges that their field is contemplating. On page 7, you will gain an understanding of why so many questions remain, and why there are no easy answers.

Another example of great teamwork comes from Paris, where Jérôme Bertherat's group recently celebrated a rare achievement in endocrine circles - publication of two articles 'back to back' in *New England Journal of Medicine*. Their work, characterising genetic alterations in endocrine tumours, is the subject of our investigation by 'The Endo Explorer' on

page 9, and you will have already seen the group on this issue's cover.

Meanwhile, ESE initiatives go from strength to strength! In this issue, we mark the highly successful first ESE Basic Endocrinology Course, in Amsterdam (page 10), and the launch of our first clinical practice guideline on hyponatraemia (page 4), which was downloaded more than 4000 times in the first 2 weeks after its publication, and has attracted much praise. Before long, ESE's guideline on adrenal incidentaloma will also be available, as Martin Faßnacht updates us on page 6. The success of the European Young Endocrine Scientists' first annual meeting in Rotterdam last year has prompted the organisation of their second, this year in Belgrade, Serbia (see page 5).

Last, but never least, Wouter de Herder has been inspired by this year's winner of the Eurovision Song Contest to review his collection of materials on the subject of 'bearded women'. On the back cover, you will learn why Conchita Wurst is the latest, but perhaps the least endocrinologically challenged, in a long line of individuals who have caught the public's attention over centuries past.

May I wish you productive studies, wherever your interests lie!

Philippe Bouchard
ESE President
Co-Editor of *ESE News*

NEW! ESE Small Meeting Grants

Next application deadline: 30 September 2014

ESE Small Meeting Grants support the organisation of endocrine-related events (e.g. symposia or courses) which have been endorsed by the Society. Applications for endorsement and the grant can be made at the same time. The maximum value of each grant is €2500, and retrospective applications will not be considered.

For more information see www.e-se-hormones.org/prizes/ESESmallMeeting.aspx.

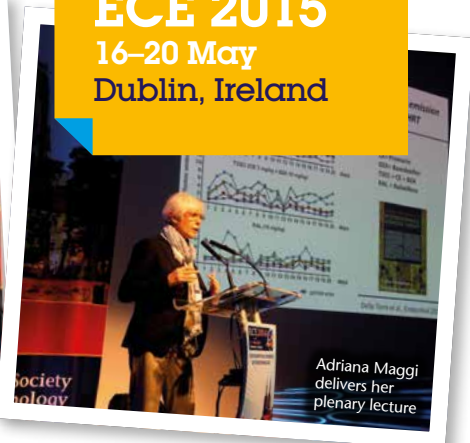
ESE is pleased to already have endorsed and awarded ESE Small Meeting Grants to:

- 7th Annual Meeting of the International Network of Young Researchers in Male Fertility (12–13 May 2014, Elsinore, Denmark)
- Renin-Angiotensin-Aldosterone System Satellite: 'Putting the A back into RAAS' (10–12 June 2014, Athens, Greece)
- 27th Congress of European Comparative Endocrinologists (25–29 August 2014, Rennes, France)

Don't forget
ECE 2015
 16–20 May
 Dublin, Ireland



Paolo Beck-Peccoz, plenary lecturer
 Chun-Xia Yi and Georg Brabant



Adriana Maggi
 delivers her
 plenary lecture

Highlights from Wrocław!

16th European Congress of Endocrinology
 3–7 May 2014, Wrocław, Poland

ECE 2014 was a lively and productive meeting, attracting 2270 delegates, in addition to the many speakers, committee members, exhibitors and staff. The number of abstract submissions saw a record high at 1234, even exceeding last year's figure.

We welcomed Ashley Grossman (UK) to deliver his Geoffrey Harris Lecture 'Did the hand, then, of the potter shake?', examining the pathogenesis of pituitary adenomas. *European Journal of Endocrinology* Prize Lecturer Martin Faßnacht (Germany) gave an excellent overview of adrenocortical carcinoma.

Double the previous number of Poster and Young Investigator Awards were made, and we are very grateful to Novartis Pharmaceuticals for their generous sponsorship.

We were pleased to welcome seven patient support groups. They played an active role in the ESE Nurses' networking event, leading to an extremely interactive session. The nurses also

enjoyed a session on craniopharyngioma and a chance to 'Meet the Nurse Expert', with discussions on hypoadrenalism and adrenal crisis, as well as thyrotoxicosis.

We thank everyone involved in making the congress such a huge success, particularly Paolo Beck-Peccoz and Anna Spada, Joint Chairs of the Programme Organising Committee, and Andrzej Milewicz and Marek Bolanowski, Chair and co-Chair respectively of the Local Organising Committee.



Philippe Bouchard and the ESE Team

EYES at ECE

The European Young Endocrine Scientists (EYES) symposium included talks by leading young scientists, such as Tobias Engel (The Netherlands), winner of the best presentation at last year's EYES meeting in Rotterdam. He presented data on novel use of lipophilic statins, a potential therapeutic for aggressive human paragangliomas. Daisy Crispim (Brazil) showed that exenatide can protect pancreatic islets by increasing cell viability and decreasing inflammation in an animal model of brain death,

while Dominik Rachon (Poland) discussed use of metformin in polycystic ovary syndrome and the effects on fertility. The session showed that the next generation of endocrine scientists has a promising future.

An informal gathering organised by EYES and Klub 30 (the Polish young endocrinologists' group) allowed young endocrinologists to mingle, and began with a buffet of delicious Polish dishes. Familiar faces from last year's EYES meeting were joined by newcomers to the initiative.

For more about EYES, see page 5.

Prize winners at ECE 2014

More prizes were awarded this year than ever before, and we congratulate all the recipients.

Geoffrey Harris Prize

Ashley Grossman, UK

European Journal of Endocrinology Prize

Martin Faßnacht, Germany

Poster Prizes

Basic

Anita Kinne, Germany
 Raul M Luque, Spain
 Dániel J Tóth, Hungary
 Fang-Ju Wu, Taiwan

Clinical

Niclas Abrahamsson, Sweden
 Stine Lyngvi Fougner, Norway
 Maria Laura Monzani, Italy
 Bettina Winzeler, Switzerland

Young Investigator Prizes

Ali Abbara, UK
 Anna Aulinas, Spain
 Marcin Chrusciel, Finland
 Saswati Das, India
 Alessandra Di Franco, Italy
 Teresa Gagliano, Italy
 Pernille Holmager, Denmark
 Alejandro Ibáñez-Costa, Spain
 Aleksandra Jawiarczyk-Przybyłowska, Poland
 Max Sander, Germany
 Katharina Timper, Switzerland
 Jian-Jhong Wang, Taiwan

ESE ENDO International Endocrine Scholars Programme

Martin Blomberg Jensen, Denmark
 Stuart Morgan, UK
 Mora Murri, Spain

Special achievements

ESE is delighted to have awarded **honorary membership** to Bruno Allolio (Germany), Felipe Casanueva (Spain) and Josef Marek (Czech Republic), and also to have presented **Special Recognition Awards** to Andrzej Milewicz (Poland), Jens Sandahl-Christiansen (Denmark) and Peter Trainer (UK).

Welcome to new members

We welcome 277 new ESE members, a new Affiliated Society, the Egyptian Society of Endocrinology and Obesity, and a new Corporate Member, Immunodiagnostic Systems plc.

Great success for hyponatraemia guideline

The recent publication of ESE's first clinical practice guideline, on the subject of hyponatraemia, saw a phenomenal 4203 copies being downloaded in the first 2 weeks after its launch!

The guideline represents the best available evidence, with diagnosis and treatment strategies laid out in simple algorithms, ideal for the generalist audience that frequently encounters the condition.

Comments on Medscape have so far included:

'As a general surgeon, once in a while, I manage some case of hypernatremia [sic] associated with overhydration, vomiting or nasogastric fluid extraction. This guideline is simple and practical.'

'Was very useful. Was using vaptans previously. Now cautious.'

'Very useful and concise guidelines.'

The guideline was produced in collaboration with the European Society of Intensive Care Medicine (ESICM) and the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA). You can find a copy in *European Journal of Endocrinology* 2014 **170** G1-G47.

The review on polycystic ovary syndrome by the ESE PCOS Task Force will soon also be published in *European Journal of Endocrinology*.

New Committee members

We welcome Manuela Simoni (Italy) (Secretary), Susan Webb (Spain) and Bulent Yildiz (Turkey) to the ESE Executive Committee. Our grateful thanks are extended to retiring members Barbara Jarzab (Poland) and Justo Castaño (Spain) for their support.

1st Combo Endocrinology Course Viotia, Greece, 11-14 September 2013



Endocrinologists, gynaecologists, paediatricians and basic scientists from around the world gathered for this new course at the Conference Centre of the Evangelistria Monastery in Viotia, 120km northwest of Athens, a place of unique natural beauty and spiritual atmosphere.

We spent our days in lectures, debates and workshops focused on the ovary, and covering issues from paediatric, adolescent and adult reproductive endocrinology. The challenging tutorials were highlights: participants were divided into teams, and worked on real clinical scenarios in a stepwise approach, presenting the cases with great enthusiasm in front of the

experts in a 'virtual congress' setting. The final dinner, featuring traditional food, music and dancing at a Greek tavern, was particularly memorable.

We thank Evanthia Diamanti-Kandarakis for organising this successful course for the first time, as well as all the speakers, and especially the tutors, D Goulis, S Kalantaridou, D Macut, S Nader, E Scott and B Spiliotis.

As the participants of the first course, we all look forward to the 2nd Combo Endocrinology Course on 1-4 October 2014 at the same venue, focusing on neuroendocrine tumours. Come and join us!

ESE Clinical Update 2014 Abu Dhabi, UAE, 10-11 January 2014

I write on behalf of delegates from the Philippines, who were delighted to participate in the ESE Clinical Update. The venue certainly provided the right ambience, the conference was well organised, topics for general endocrinology were really good and the pool of speakers was excellent.

The audience comprised about 50 doctors, and so the event was intimate. The speakers were articulate and animated, and you could ask questions during their presentations. Interactive sessions provided a real time assessment of the audience's knowledge base. The thyroid ultrasound workshop was a perfect opportunity for hands-on learning.



Local endocrinologists presented their cases for dissection by the audience and various specialists, which was a great chance to learn from the best in their field.

Jeremy F Robles
Cebu, Philippines

Save the date
Register and submit
your abstracts by
20 June 2014

Visit the EYES forum at
<http://eyes.forumatic.com/index.php>

All EYES on Serbia!

2nd EYES Annual Meeting
Belgrade, Serbia,
24-26 September 2014

Following the great success of the 1st EYES Annual Meeting in Rotterdam, The Netherlands in 2013, all young endocrine scientists are invited to join local endocrinologists for another exciting meeting in Belgrade in September 2014.

Over 3 days, we will hear the 30 best submitted original pieces of research from aspiring young participants. Abstracts are invited from all fields of endocrinology, focusing on basic or clinical research. Make sure you submit your results and details of your work! The opportunity to present, listen to and discuss topics offers a rich reward for all participants: a valuable chance to learn and encouragement for further efforts. Three established scientists, experts in their fields, will also honour us with invited lectures and further inspiration, setting the pace for their younger followers.

Accommodation is guaranteed for 70 applicants and a modest participation fee (€50) includes a contribution towards social events. All ESE members can apply for an ESE travel grant, and the author of the best presentation will be rewarded with an additional travel grant.

Most importantly, everyone will benefit from meeting up, discussing the various topics, forging new friendships, and strengthening and expanding the European network of endocrinology. Belgrade and the young members of the Local Organising Committee are preparing to warmly welcome all participants and ensure a memorable and successful meeting.

Register and submit your abstracts by 20 June and learn more at www.eyes2014.org or by emailing eyes2014meeting@gmail.com.

See you in Belgrade!

Local Organising Committee
EYES 2014



Bregenz Summer School 2013

As the ESE Summer School approaches on 3-7 August, Archik Das reminds us about last year's event, and why you should attend in 2014!

The ESE Summer School is not only a fantastic way to express one's interest in endocrinology, but a potentially life-changing opportunity to make new friends with students and professors alike. It is a great way to learn about cutting edge research trends in endocrine science.

You should register for the poster presentation session. ESE Summer School poster parties allow you to discuss your work in front of everyone else – so developing presentation skills and obtaining advice from multi-disciplinary experts. It's a real eye-opener, which alone makes the entire trip worthwhile!

You will enjoy themed lectures, covering basic science and clinical topics. One of the Summer School's great selling points is that the lecturers join the students during meals and leisure activities, so it is a great way to get to know people who may become future collaborators!

Combined with enjoyable group sports sessions, Bregenz's annual Summer Opera Festival and an amazing setting near the shores of Lake Constance within walking distance of the magnificent Pfänder mountain, there is so much to enjoy.

Make sure you are there in 2014!
See www.es-hormones.org/education/basicscience.aspx.

Archik Das
University of Birmingham, UK

EnGiol: Italian young endocrine scientists

EnGiol was founded in 2010 by young endocrinologists and is supported by the Italian Society of Endocrinology (SIE). Its mentor was former SIE President, Ezio Ghigo. The group's primary goal is to promote the exchange of ideas and knowledge among young physicians, biologists and biotechnologists who are interested in endocrinology. With this aim, EnGiol organises scientific meetings and symposia in conjunction with official SIE events.

Generally focusing on different endocrine disciplines, these activities are targeted towards young scientists who are 'fresh to the field'. SIE provides prizes for the most promising young researchers and for the best communications, and a friendly atmosphere encourages networking between participants. Both basic and clinical early career researchers take advantage of the opportunity to develop their communication skills and to share their professional experience.



EnGiol encourages and welcomes all young endocrinologists to participate in the symposia during the annual congresses of SIE.

A summary of EnGiol's main activities can be found on the SIE website at www.societaitalianadiendocrinologia.it. EnGiol also has an online forum (<http://engiol.forumcommunity.net>), where you can meet other participants, share their scientific activities and propose new initiatives.

From the Science Committee: Ambassadors in action

A year ago, in issue 21 of *ESE News*, I described how ESE was establishing a network of 'Science Ambassadors', to strengthen basic scientists' involvement in the Society's activities.

Each ESE member and affiliated society has been invited to nominate an individual to act as a messenger between ESE and the basic scientist community of their respective society. As such, the Science Ambassadors distribute information about ESE science activities, including basic science courses, and grants available to attend ESE events and for short term laboratory visits. A special meeting of the Science Ambassadors takes place during the annual European Congress of Endocrinology, to collect their suggestions about how best to serve the basic science community within ESE.

The table (right) shows the individuals who are currently Science Ambassadors, nominated by their respective societies. While this is already quite extensive, we still have several member societies that have not nominated their Ambassadors. If you belong to such a Society please send us the name and contact information of a potential basic scientist colleague from your group (by email to info@euro-endo.org).

We would be pleased to invite them to the growing 'Corps Diplomatique Endocrinologique'!

Ippo Huhtaniemi
Science Committee Chair

Abbreviations used in the table:

*ENSAT, European Network for the Study of Adrenal Tumors; **EYES, European Young Endocrine Scientists; ***PPGL, pheochromocytoma/paraganglioma.

| Ambassador | Endocrine Society or Group |
|---------------------------------------|----------------------------|
| Sabina Baumgartner-Parzer | Austrian |
| Olga Cvijanovic, Ines Mrakovcic Sutic | Croatian |
| Bela Bendlova | Czech |
| Bauke Buwalda | Dutch |
| Jorma Palvimo | Finnish |
| Marc Lombes | French |
| Joerg Gromoll | German |
| Dimitrios Kiortsis | Hellenic |
| Attila Patocs | Hungarian |
| Aine McKillop | Irish |
| Stella Zannini | Italian |
| Med Jørn Sagen | Norwegian |
| Bartłomiej Budny | Polish |
| Manuel Lemos | Portuguese |
| Iwar Klimeš | Slovak |
| Milka Vrecl | Slovenian |
| Federico Mallo | Spanish |
| Karen Chapman | UK |
| Olena I Kovzun | Ukrainian |
| Enzo Lalli | ENSAT* |
| Filip Gabalec, Gefsi Mintziori | EYES** |
| Gimenez-Roqueplo | PPGL*** |
| Maria Christina Zennaro | Primary aldosteronism |

Clinical Committee Update: European Clinical Guidelines

As you can read on page 4, the first European clinical practice guideline on the diagnosis and treatment of hyponatraemia, including a significant contribution from ESE, was recently finalised. This multidisciplinary effort, involving ESE with the European Renal Association-European Dialysis and Transplant Association and the European Society of Intensive Care Medicine, has met with great success.

The development of the first guidelines initiated by ESE on adrenal incidentaloma and hypoparathyroidism is currently underway. We on the adrenal incidentaloma group had our first official meeting in Amsterdam, The Netherlands, on 16 and 17 December.

Our multinational group consists of endocrinologists (John Newell-Price, Sheffield, UK; Antoine Tabarin, Bordeaux, France; Massimo Terzolo, Turin, Italy; and Stylianos Tsagarakis, Athens, Greece), a surgeon



(Henning Dralle, Halle, Germany) and a radiologist (Anju Sahdev, London, UK). It is chaired by Olaf Dekkers (endocrinologist and methodologist from Leiden, The Netherlands) and myself (endocrinologist from Würzburg, Germany). We are advised by an external consultant and expert in guideline development, Hans de Beer. His team at CBO Utrecht, The Netherlands (the commissioned clinical research organisation for the ESE clinical guidelines) supports us in comprehensive literature searches and in grading the evidence. In addition, we collaborate with specialist

pathologists and several patient representatives.

During the first meeting and an intensive email discussion in the weeks thereafter, we determined four main topics that should be addressed by our guidelines: (1) the best diagnostic imaging procedure, (2) subclinical hypercortisolism, (3) the most adequate surgical approach, and (4) optimal follow-up. Currently, all available literature after 1995 is being reviewed before we meet again in person in September 2014 and at the beginning of 2015. We will strive to present our first draft of the guidelines at the European Congress of Endocrinology in Dublin in May 2015.

So far, for me and presumably for the other participants, this guideline process has been an interesting experience and we hope that we will come up with helpful guidelines in 2015.

Martin Faßnacht
Co-Chair, Adrenal Incidentaloma Guideline Group

Endocrine disruption: the detail behind the debate

Hormones drive the development and regulation of most important body systems. Disruption of these key processes (known as endocrine disruption; ED) can perturb whole body homeostasis, and ED is clearly important in several 'modern' Western diseases.

The big unresolved issue is whether manmade or natural endocrine-disrupting compounds (EDCs) contribute to human ED. This could occur by interfering with the development, maturation and function of specific endocrine systems, by mimicking or blocking hormone actions or by affecting hormone synthesis/metabolism. Attention has been drawn by (a) identification of numerous environmental EDCs, (b) demonstration of EDC effects in cellular and animal models, and (c) reported associations between EDC exposure and ED in wildlife and humans. Initially, the focus was on reproductive effects, but recently identification of additional 'targets' (including the thyroid, metabolic axes, the immune system and brain development/function) has provoked interest.

However, the threat posed by EDCs to human health remains controversial, with strong debate on the best strategies to handle the uncertainty, ranging from a strict precautionary approach to all potential EDCs to a traditional toxicological view, considering each on a single-compound basis with fixed threshold levels for adverse effects.

Experimental evidence: strengths and limitations

A large body of data from different mammalian and non-mammalian species has shown that EDC exposure can perturb the maturation or function of several endocrine systems, particularly during critical developmental periods, when a given EDC may induce a deleterious effect that manifests (much) later in life (e.g. reproductive studies affecting masculinisation).

While many initial studies were 'proof-of-principle', more recent refined models have tested environmentally relevant doses and routes of exposure. For example, oral oestrogenic EDCs at doses found in the environment have advanced puberty and 'feminised'

the pattern of gonadotrophin release, triggering a pre-ovulatory-like surge in male rodents. This cannot be taken as definitive proof for EDCs as a major cause of reproductive health disorders in humans or wildlife, but such data support the need for more thorough (and impassionate) research.

Complex reality: low dose and mixture effects

Exposure to EDCs mainly occurs as mixtures of perhaps thousands of chemicals, with different mechanisms of action. This complicates assessment of the potential impact on health. Nevertheless, elegant studies have shown that cocktails, at doses below the so-called no-observed adverse effect level for each individual chemical, can induce detectable disrupting effects in cellular systems and reproductive disorders in rodents. They challenge the present risk assessment process, calling for reasonable use of the precautionary principle if particular circumstances (e.g. pregnancy exposures) are a key issue.

Consequently, debate centres on whether EDCs should be managed on the basis of a classical toxicological view of fixed thresholds, or using a no-global-threshold approach, at least for some EDCs. The latter implies that no safe level of exposure can be set, triggered by reports of non-monotonic dose-response effects for some EDCs (e.g. adverse effects occurring at very low doses, but not at higher doses). Whilst this seems contrary to how endogenous endocrine systems are mainly regulated, non-monotonic effects have been reported for several hormones and EDCs, *in vivo* and *in vitro*. In simple terms, a compound may exhibit different modes and/or sites of action at different doses (e.g. tamoxifen). This reminds us to approach a lack of understanding of a phenomenon not with incredulity but with a drive for further (mechanistic) exploration of its basis.

EDCs and human health: challenges ahead

So despite great progress, the Gordian knot remains tied: is ED a major cause of human health problems? Whether associations between EDC exposures and various disorders reflect cause and effect is unresolved. This is unsurprising, given the complexities. Also, most association studies are cross-sectional, and thus prone to confounding and chance findings. We need more powerful prospective mother-child cohort studies, coupled to appropriate mechanistic analyses in suitable exposure models, to evaluate the potential impact of early EDC exposures on different systems.

Identification of a chemical as an EDC does not automatically mean it will cause adverse effects at sufficient exposure levels, a dilemma that causes uncertainty for researchers, regulators and policy-makers. In Europe, REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) may mandate that the label 'EDC' will lead to a chemical being banned, even though no evidence for harm may exist. In this context, whether the chemical also has human benefits is an issue that has barely been raised. The maxim that clinicians should 'do no harm' (by our decisions) might also be considered relevant here.

On the other hand, this consideration is equally applicable to a precautionary approach to EDCs. Most in the field agree that where early exposures might cause deferred effects, rational application of the precautionary principle is justified, even without compelling evidence. However, where experimental and epidemiological data are available, these should be the driving force in the evaluation process, as an evidence-based decision is more likely to stand the test of time. This, again, shows a need for more research.

Finally, we must remember to look more widely than at EDCs. ED is central to common human diseases, and its prevention can have huge benefits. There are causes of ED other than EDCs (e.g. diet), and better research must define their relative importance and interaction with EDC. Such a holistic approach is good for health preservation, and reminds us that 'no hormone is an island'.

Richard M Sharpe, Edinburgh, UK
Manuel Tena-Sempere, Córdoba, Spain
Jorma Toppari, Turku, Finland
on behalf of ESE

GLP1: effect on proANP in healthy males



Synthetic glucagon-like peptide-1 (GLP1) agonists lower blood pressure in patients with type 2 diabetes, which sets in before substantial weight loss. In mice, these anti-hypertensive effects have been linked to the release of atrial natriuretic peptide (ANP), but the existence of a GLP1-ANP axis in humans was unknown.

In this randomized, controlled, double-blinded, cross-over study in 12 healthy males, Jeppe Skov *et al.* document that a 2-h infusion of native GLP1 did not affect either proANP or proBNP levels, although GLP1 infusion increased urinary sodium excretion markedly. Apparently, the natriuretic effects of GLP1 seem unlikely to be mediated exclusively via ANP.

Read the full article in *Endocrine Connections* **3** 11–16

LGR4 serves to link circadian oscillations



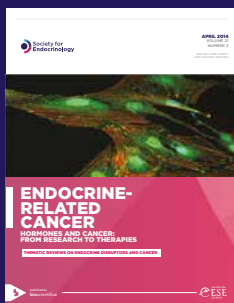
Feng Wang *et al.* report a new role for leucine-rich repeat-containing G protein-coupled receptor 4 (LGR4) linking circadian rhythms in gene expression and metabolic activity.

LGR4 homozygous mutant mice displayed an altered circadian rhythmic pattern of energy homeostasis, especially regarding lipid metabolism. In addition, LGR4 expression exhibited circadian rhythms in liver tissue. Interestingly, there were no changes in the expression levels or circadian rhythms of classic clock genes in the LGR4 homozygous mutant mice.

The data establish a molecular link between circadian physiology and plasma lipid metabolism. Since LGR4 is a G-protein coupled receptor, this study provides a potential target for regulating metabolism through circadian functions.

Read the full article in *Journal of Molecular Endocrinology* **52** 133–143

Histone deacetylation with BRAF V600E mutation



BRAF V600E mutation, the most common mutation in thyroid cancer, is associated with a more aggressive clinical course and loss of

radioiodine avidity. Unique molecular derangements caused by this mutation include decreased or lost expression of the *NIS* gene, and mislocalisation of *NIS* in the cytoplasm.

Zongjing Zhang *et al.* have revealed an epigenetic mechanism for **BRAF V600E**-promoted *NIS* silencing, involving histone deacetylation at critical regulatory regions of the *NIS* promoter. In addition, this elegant study provides further support for combination therapy targeting major signalling pathways and histone deacetylase to restore thyroid gene expression for radioiodine treatment of thyroid cancer.

Read the full article in *Endocrine-Related Cancer* **21** 161–173

Testosterone metabolites in diabetic neuropathic pain



Diabetic neuropathy is a major factor, impairing patients' quality of life.

It is associated with neuropathic pain in about 50% of patients;

this is difficult to treat.

Donato Calabrese *et al.* have analysed the effects of dihydrotestosterone (DHT) and 3 α -diol on pain thresholds and molecular and functional parameters related to pain modulation in a diabetic rat model. Diabetes resulted in a decrease in DHT levels in the spinal cord. Both DHT and 3 α -diol treatments showed analgesic properties, affecting different pain parameters, possibly by different mechanisms of action.

The results indicate that testosterone metabolites are potential agents for the treatment of neuropathic pain.

Read the full article in *Journal of Endocrinology* **221** 1–13

TSH not appropriate in screening

Autonomously functioning thyroid nodules (AFTN) account for 5–10 % of palpable nodules. It is assumed that thyrotrophin (TSH) levels are always subnormal in the presence of AFTN. Guidelines agree that a thyroid scan should be performed for subnormal TSH, as AFTNs with low TSH levels do not necessitate evaluation by fine needle aspiration cytology (FNAC), because of the low risk of cancer in hyperfunctioning thyroid nodules and the risk of equivocal results (follicular neoplasm).

However, this retrospective study of 368 patients by Rayan Chami *et al.* indicates that serum TSH is not an effective screening tool to diagnose AFTN, because the diagnosis would have been missed in 71% of patients in the work up of a thyroid nodule. A thyroid scan remains the gold standard for detecting AFTN and should be considered before FNAC, as the reliability of FNAC in an unsuspected AFTN remains unclear.



Read the full article in *European Journal of Endocrinology* **170** 593–599

J A Romijn

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The Endo Explorer



Publications

1. G Assié et al. 2013 *New England Journal of Medicine* **369** 2105–2114.
2. E Louiset et al. 2013 *New England Journal of Medicine* **369** 2115–2125.

Jérôme Bertherat's group at Institut Cochin in Paris, France, recently achieved the notable success of a double publication in *New England Journal of Medicine*.^{1,2} We took the opportunity to learn more about their work.

Our research group is studying the pathophysiology of endocrine tumours. The laboratory is located in the Cochin Institute, affiliated with INSERM, CNRS and Paris Descartes University, and on the campus of the Cochin Hospital, allowing close interaction with the various hospital departments involved in the treatment of endocrine and metabolic diseases, especially endocrine tumours.

Endocrine tumours – the challenge

A patient presenting with an endocrine tumour can suffer from hormone excess and/or tumour growth, and in the case of malignant tumours, distant metastasis. The clinician has to take this into account during diagnosis and when deciding upon the therapeutic approach. The spectrum of endocrine tumours is very large. Indeed, for a single endocrine gland, different tumour types with various levels of secretory activity and growth potential, reflecting various types of cellular differentiation, can be diagnosed. This can be challenging for the clinician, especially in cases of rare tumours, and also represents a challenge for the researcher. This challenge can also be perceived as a rich cornucopia of models to aid our understanding of the physiology and pathophysiology of endocrine tissues.

Taking advantage of this diversity, our research is based on the characterisation of genetic alterations of endocrine tumours, followed by the fine analysis of correlations between these molecular alterations and the tumour phenotype. Using this approach, our goals are the development of a better molecular classification of endocrine tumours, and to improve our understanding of the mechanisms of endocrine tumorigenesis, to develop new therapies.

Identifying changes, identifying genes

One long term interest of our group has been investigation of alterations in the cAMP- and Wnt- β -catenin-signalling pathways in endocrine tumours, especially adrenocortical tumours. Since there is a broad spectrum of adrenocortical tumours, we consider them to be a good model for endocrine tumours in general. This interest developed after the identification of somatic or germline genetic alterations of key components of these signalling pathways in sporadic or familial adrenocortical tumours. *In vitro* models are developed to dissect the consequences of these signalling alterations in endocrine tumours.

Progress in the molecular genetics of endocrine tumours has been dramatically accelerated in the last decade by the

impressive development of methods in genomics. We have used these to study adrenal tumours, aiming to identify genes responsible for these tumours, to develop a better molecular classification of adrenal cancer, and to have a better understanding of adrenal tumorigenesis in order to develop new therapies. Very recently, this approach allowed the identification of new genes responsible for macronodular adrenal hyperplasia (*ARMCS*), cortisol-producing adenomas (*PRKACA*) and adrenocortical cancer (*ZNRF3*). We are currently aiming to integrate these various approaches in genomics (i.e. transcriptome, methylome, miRNome, exome, SNP (single nucleotide polymorphism) analysis etc.) to obtain a better view of the molecular biology of endocrine tumours.

Notable networks

The development of networks nationally (Cortico- and Medullo-surrenale: les Tumeurs Endocrines (COMETE) in France) and internationally (the European Network for the Study of Adrenal Tumors (ENSAT) and the Carney Complex Transatlantic Consortium) has been essential for the development of the research on rare adrenal tumours. ENSAT (www.ensat.org) is clearly an active example of how excellent and productive research in endocrinology can be stimulated by connections at the European level between countries with similar high levels of academic research, with a growing background of common sources of funding and regulations.

Jérôme Bertherat

Institut Cochin, Paris, France
Université Paris-Descartes, France

ESE Basic Endocrinology Course

ESE, together with the Dutch Endocrine Society, organised its 1st Basic Endocrinology Course in Amsterdam, The Netherlands, on 15–17 January 2014. Delegate Amy Warner and organiser Eric Fliers report on the success of this new venture.

The postdoc's view...

The Basic Endocrinology Course, at the Trippenhuis in Amsterdam, was the first of its kind for ESE, and featured some excellent speakers.

Although dealing with separate topics, two talks were by researchers from the University of Santiago de Compostela in Spain. Miguel Lopez and Clara Alvarez were both very engaging; Miguel described his work on the central effects of thyroid hormone, and Clara discussed her research on pituitary stem cells. All the key areas of neuroendocrinology were covered on the course and, although I feel some of the speakers went into a little too much detail about their own work, I thought the course offered a great overview of the area.

Likewise, the selected oral presentations were of a very high standard, with some excellent early stage researchers talking about their work, showing the appeal that this first course had within the community.

The social programme was a great way to get to know the fellow participants, and the speakers and organisers themselves were all very approachable and helpful, which created a great atmosphere for learning. The main dinner was held in de Waag, an ancient and opulent building in the square nearby, a must-see on a trip to Amsterdam.

But for me the real highlight was an interactive seminar by prominent neurobiologist Dick Swaab, whose observations and research on subjects such as the existence of a soul and sexual dimorphism created a very lively discussion among the participants.

Hopefully more people will take advantage of the next great opportunity this course provides, now that the series is up and running. As the first one, it was



an excellent start, and I look forward to discovering the details of the next one.

Amy Warner

Postdoctoral Researcher, Karolinska Institutet, Stockholm, Sweden

'The social programme was a great way to get to know the fellow participants, and the speakers and organisers themselves were all very approachable and helpful'

...and the organiser's

The course topic was 'neuroendocrinology', carefully chosen as one of the most dynamic fields in endocrinology. The purpose of the course was to provide an educational forum for early career basic and translational scientists in endocrinology, especially those in training (PhD students and junior postdocs).

With the seat of the Royal Netherlands Academy of Arts and Sciences in the old city centre of Amsterdam as its venue and low budget hotel accommodation, we anticipated being able to offer an attractive event. Important ingredients were a reasonable registration fee (€ 300 including hotel accommodation and catering), plus the possibility of applying for ESE Meeting Grants particularly aimed at young members.

We had 64 participants, of whom 22 were from The Netherlands. With 14 invited speakers we were able to create a strong interactive format, including lectures by top level faculty, poster presentations and time for discussion and networking.

Indeed, looking back from the distance of a few months, feedback from the participants (overall judgment: 8.1 out of 10) indicates that the meeting was highly successful, and the organisers feel that all the projected goals were accomplished.

Nothing to improve then?! Of course. In addition to comments such as 'Congratulations: beautiful course', we were puzzled by this one: 'Maybe add another social session where it will be only students/only postdocs'. Well, no one is perfect...

In the coming years, we anticipate that the ESE Basic Endocrinology Course will be an annual event in different European cities, centred around various topics. Joint organisational input from the ESE and the national endocrine societies will ensure an attractive balance between a continuous format and some 'couleur locale'.

Eric Fliers

Chair, Dutch Endocrine Society (Nederlandse Vereniging voor Endocrinologie)

More details to follow!
2nd ESE Basic Endocrinology Course
February 2015, Edinburgh, UK
 with the UK Society for Endocrinology

A day and a night at...

ECE 2014 in Wrocław

05.30

It is the second day at ECE 2014, and I wake just after sunrise. We are three Spanish basic/translational researchers sharing a room in the WenderEDU Business Center, and we need to carefully organise our schedules to get to the Congress on time.

07.30

We are finally ready for breakfast. The buffet requires a decision between too many options, just like the programme for ECE 2014!

08.00

It is time to grab a taxi and get to the magnificent congress venue. But, before going to the sessions, I need to put up the poster that I will soon be presenting.

08.30

First plenary lecture of the day. Jose Ordovás (Boston, USA) discusses how the gene-environment interaction triggers obesity, and demonstrates that a Mediterranean diet can help to prevent stroke.

09.30

With almost no time to digest all Dr Ordovás' dietary information, I am learning about 'Obesity beyond BMI' (Symposium 5), as Antonio Vidal-Puig (Cambridge, UK) shows crucial molecular markers determining adipose tissue expandability, which seems to be related to development of obesity. Then Javier Gómez-Ambrosi (Pamplona, Spain) demonstrates the need to use adiposity index rather than BMI to define obesity cut-offs.

11.00

Coffee break: this is a great moment to meet some of the speakers and talk with many colleagues I have not seen for a while. Coffee time proves very productive and takes longer than expected. Since I am running late for the Meet the Expert session, I decide to sit down in front of the Multimedia Fountain, open my laptop and do some work (how can there be so many urgent emails?).

13.00

After grabbing a lunch box, I start visiting the posters that look most interesting to me (after carefully selecting them previously). There are so many posters that it is almost impossible to take a look at all of them, but the discussions are truly informative.

14.30

The same thing happens during the oral sessions – too many interesting talks! So I jump from one room to another, trying to see the most exciting ones.



16.00

After being revived by a short coffee break, I decide to attend the European Young Endocrine Scientists (EYES) Symposium, in order to listen and support my young endocrinologist colleagues as they discuss a range of interesting issues about inflammation in obesity.

17.30

It is time for the last plenary lecture of the day, delivered by Pilar Santisteban (Madrid, Spain), who gives a nice overview of the therapeutic implications of the molecular determinants associated with thyroid cancers. This is immediately followed by the Ipsen Satellite Symposium, in which clinical and basic researchers review the application of somatostatin analogues in the treatment of acromegaly and neuroendocrine tumours.

20.00

Then it's time to take a taxi back to the hotel and drop all my stuff there. I meet some colleagues and we decide to head downtown to visit Wrocław at night. We sample local Polish cuisine at one of the typical and charming restaurants located in the market square. On our way back to the hotel, we spot the 'PRL' bar. As endocrinologists, we clearly cannot say no to an opportunity to taste some of the famous original and flavoured vodkas on offer...

24.00

Back at the hotel, after a chilly but pleasant walk, I use my iPhone to say good night to the people I care about – and still have a chance to check my email inbox. Finally, while examining the programme for today and tomorrow, I realise the remarkable representation the Spanish community of endocrinologists is having at ECE 2014. Meanwhile, I fall asleep.

Manuel D Gahete

Postdoctoral Researcher
Maimónides Institute for
Biomedical Research
University of Córdoba, Spain



Conchita Wurst, and bearded women

On 10 May 2014, the controversial Austrian singer and 'bearded woman', Conchita Wurst, won the Eurovision Song Contest in Copenhagen, Denmark. In real life, the 26-year-old drag queen is better known as Thomas Neuwirth. In the German language, Wurst means 'sausage' and according to the singer-actor 'she' compares the choice of the last name to the common German expression 'Das ist mir Wurst', which translates as 'I don't care'. In an interview, Conchita Wurst stated, 'It doesn't really matter where one comes from, and what one looks like.'

The public fascination in bearded women has apparently not waned over the centuries. Endocrinologists know that many adrenal and ovarian disorders may underlie severe forms of hirsutism or virilisation in women.

The legend of the female Pope Joan first appeared in 13th century chronicles and was widely believed for centuries. It has been suggested that subsequent popes were subjected to an examination whereby, sitting on a chair containing a central hole called a 'sedia stercoraria', a cardinal had to establish that the newly elected pope had testicles, before announcing 'Duos habet et bene pendentes' ('He has two, and they dangle nicely'). In her presidential address in 1993, the former President of the US Endocrine Society, professor Maria New, discussed this case extensively.

The most famous painting of a bearded woman currently hangs in the Prado Museum in Madrid, Spain, and bears the name *La mujer barbuda* (the bearded woman). It dates from 1631 and was painted by José de Ribera (1591–1652). The woman in the painting is Magdalena Ventura from Abruzzi, Italy, who developed a beard at the age of 37. She gave birth to seven children, four of them were born after she had grown the beard. In the picture she is 52 years old and is she breastfeeding her most recently born child.



At the beginning of the 20th century, many bearded women used to earn their living by working in side shows or circuses. One of the most famous European bearded women was Clémentine Delait (1865–1939, pictured) from Thaon-les-Vosges, France. At the age of 35, she decided to stop shaving her beard and let it grow, and 4 years later she received an official permit by the French Government to wear man's clothes.

Emile C Achard (1860–1944) and Joseph Thiers (1885–1960) are recognised for their description of 'diabète des femmes à barbe' (diabetes of the bearded women) in 1921 – the combination of diabetes mellitus, deep masculine voice, hirsutism, clitoral hypertrophy and adrenal cortical hyperplasias or adenomas mostly in postmenopausal women. It has been generally agreed that their publication contains reports on patients with polycystic ovaries and Cushing's syndrome (ectopic ACTH secretion?).

Conchita Wurst is a transvestite wearing women's clothes. He did not require a permit from his government enabling him to do so. Apparently he is also generally in a good health. The other cases reported above suffered from severe forms of hyperandrogenism caused by sometimes benign, or potentially lethal, adrenal or ovarian disorders. Nowadays, these disorders are diagnosed and treated by endocrinologists and endocrine gynaecologists. For these patients and their physicians it really did matter where one came from and what one looked like.

Wouter de Herder

Save the Dates!

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

ESE Summer School on Endocrinology (Basic Postgraduate Course in Endocrinology)

3–7 August 2014
Bregenz, Austria

ESE Summit

6–7 September 2014
Curitiba, Brazil

During the 31st Brazilian Congress of Endocrinology and Metabolism (see www.cbem2014.com.br)

2nd EYES Meeting

24–26 September 2014
Belgrade, Serbia

39th Symposium on Hormones and Cell Regulation (ESE)

9–12 October 2014
Mont Ste Odile, France

EndoBridge 2014

23–26 October 2014
Antalya, Turkey

In collaboration with the Endocrine Society and the Society of Endocrinology and Metabolism of Turkey

ESE Postgraduate Course on Endocrinology, Diabetes and Metabolism

27–30 November 2014
Cluj, Romania

Supported by an unrestricted education grant from Novo Nordisk

6th ESE Clinical Update

16–17 January 2015
Abu Dhabi, UAE

17th European Congress of Endocrinology (ECE 2015)

16–20 May 2015

Dublin, Ireland

Abstract submission and online registration from 1 October 2014!

Deadlines:

20 June 2014

2nd EYES Meeting

– abstract and registration deadline

30 August 2014

39th Symposium on Hormones and Cell Regulation (ESE)

– registration deadline

15 September 2014

EndoBridge 2014 – abstract deadline

30 September 2014

ESE Small Meeting Grants

– application deadline