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ESE News

The newsletter of the European Society of Endocrinology

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ECE in Lyon:

A world of endocrinology awaits you
.....

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ESE Presidents on passing the baton



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

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Editorial



Once again, we find ourselves looking forward to spring, and to the chance to meet and discuss our fascinating field, with the many developments of the past year. This year's European Congress of Endocrinology takes us to Lyon, France's third largest city. Alongside Lyon's many links with science and medicine, you will enjoy its unique gastronomy and history.

Preparations are well in hand and, on pages 8–9, the Chairs of the Programme Organising Committee reveal the exciting sessions they have planned. These are sure to provoke interactive discussion and debate. We welcome contributions from our award winners, who give you previews of their presentations.

Of course, the Congress would be incomplete without your contributions. We urge you to send us your abstracts by 4 February 2019, to ensure that we cover all corners of endocrinology and, most importantly, that the voices of all endocrinologists are heard. You can submit your abstracts and find registration details at www.ece2019.org.

This issue of *ESE News* has a French theme, following the flavour of ECE 2019, with articles from leading French colleagues.

On page 10, Philippe Bouchard and Régine Sitruk-Ware bring us up to date with the latest insights into contraception. Meanwhile, on page 12, Gérald Raverot and Philippe Bertolino discuss their approach to understanding the genetics of pituitary tumours, which benefits from an integrated team of clinicians and basic scientists.

Philippe Chanson guides us through his very busy day as a Professor of Endocrinology with clinical, teaching and research commitments on page 15. On page 14, Wouter de Herder travels back in his time machine to consider the founders of French endocrinology.

Sadly, this is Wouter's last issue of *ESE News* as Editor. I thank him for steering it with a calm and steady hand, finding topics of interest and enlightening us with intriguing stories. He has also overseen its very successful redesign and expansion. We now welcome experienced Editorial Board member Justo Castaño (Córdoba, Spain) as our new Editor.

As we talk of passing batons, soon our next President, Andrea Giustina (Milan, Italy), will take over from me, after shadowing my role for almost 2 years. Join us on page 7, as he and I discuss our Society's journey and our shared passion for ensuring that endocrinology is, and continues to be, at the centre of medicine across Europe and globally.

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

Cover image: Sculpture of a lion at the Basilica of Notre-Dame de Fourvière in Lyon, France © iStock/sharlocks



Key dates

Remember to submit your abstracts by:

4 February 2019

The early bird registration deadline is:

4 April 2019

www.ece2019.org



Time to celebrate!

The French Endocrine Society (Société Française d'Endocrinologie, SFE) invites you to help celebrate its 80th anniversary in Lyon! Now with 1400 members from several countries, the Society was founded in 1939 and held its 35th meeting in Nancy in 2018.

The SFE encompasses several groups: the Endocrine Tumour Group, the Thyroid Research Group, the Pituitary Club, the Adrenal Network (COMETE) and working groups, covering the topics of hormone biology, interventional endocrinology and endocrine disruptors.

We collaborate with other societies, and also contribute to networks, especially rare endocrine disease and endocrine cancer networks.

The SFE produces its own consensus documents; the most recent was on the endocrine complications of new anti-cancer therapies (published, in English, in *Annales d'Endocrinologie* 2018 **79** 535–596). We also partner health authorities upon request.

We support basic and clinical research through grants and the training of residents in endocrinology. These are, undoubtedly, the most rewarding tasks.

Finally, besides our involvement in our continuously growing scientific and medical field, the SFE provides a forum for everybody seeking education, exchange and collaboration in endocrinology and metabolic diseases. This is the case during our annual meeting, and through other events such as the Journées Guéritée, the Journées Internationales d'Endocrinologie Clinique Henri-Pierre Klotz, and the many other meetings we sponsor.

Our next priority? Making ECE 2019 an unequalled milestone. Let's meet this challenge in Lyon!

Nadine Binart and
Patrice Rodien
Société Française
d'Endocrinologie

Welcome to Lyon

21st European Congress of Endocrinology, 18–21 May 2019

Lying at the confluence of two rivers, the Rhône and the Saône, Lyon has the special flavour of a modern city, sprinkled with reminders of its 2000-year-long history. Designated as a UNESCO World Heritage site in 1998, it is also famous for its cultural events, which include the unique Festival of Lights, as well as the Lumière Film Festival, held in the very birthplace of cinematography. The area is of course also renowned for its vineyards and fine gastronomy.

A city of medicine and science

The city's first hospital, the old Lyon Hôtel Dieu, saw the writer-physician Rabelais practise medicine in the 16th century. Now, two academic hospitals, the Hospices Civils de Lyon and Claude Bernard University Lyon 1, are located at four sites in the Lyon metropolitan area. The WHO International Agency for Research in Cancer is also here, along with several large pharmaceutical companies.

Endocrinology in France

The roots of French endocrinology go back to the late 19th century. Charcot, Brissaud and Labbé in Paris deciphered the manifestations of hyperthyroidism, and Ancel and Bouin in Nancy and Strasburg established the basis of reproductive endocrinology. Courier pioneered the use of radioactive iodine in thyroid physiology and biochemistry.

The field began to be formalised in 1939 with the founding of the French Endocrine Society. After the Second World War, national research institutions – CNRS and INSERM – established laboratories in medical academic centres, encouraging the development of basic science and clinical research groups.

Now there are 30 endocrinology departments in university hospitals spread across France, with three objectives: care, teaching and research. These have enabled significant breakthroughs in neuroendocrinology and neuropeptides, genetics and genomics of adrenal hyperplasia, adrenal, pituitary and thyroid tumours, reproductive endocrinology and developmental thyroidology, not forgetting excellent research in diabetes and metabolism.

ECE 2019

The city is very proud and honoured to welcome the 21st European Congress of Endocrinology, having previously hosted the 6th Congress of the European Federation of Endocrine Societies (EFES) in 2003.

Lyon lies between the Alps and the French Riviera, and is easy to reach by plane, TGV and car. This year's event takes place at the Lyon Congress Centre, which is set in an ideal location between the magnificent Parc Tête d'Or and the River Rhône.

We look forward to an excellent meeting with endocrinologists from around the world, and hope you will enjoy everything that Lyon has to offer.

Françoise Borson-Chazot
Chair, ECE 2019 Local Organising
Committee



43rd Symposium on Hormones and Cell Regulation

Mont Sainte Odile, France, 10–13 October 2018

'The brain-gut microbiome network in metabolic regulation and dysregulation' was this year's theme. Endocrinology has experienced paradigm shifts in recent decades, such as the discovery of endocrine functions in organs not hitherto considered endocrine. A further conceptual revolution has seen an explosion of interest in the symbiosis between

animals and the microbes they host, primarily in the gut (microbiome), in metabolic regulation.

Lectures by 27 leaders in the field from Europe, the USA, Japan and Israel were complemented by short poster presentations by young investigators and students. The speakers gave enthusiastic feedback, including, 'The Symposium was a major

success. Remarkably high quality presentations were given in openness, accompanied by intense and focused informal discussions and mutual idea enrichment.' One student remarked, 'Thank you again for organising such an informative and inspiring symposium at beautiful Mont Ste Odile. I learned a lot from experts in the field, with whom I could connect through this meeting.'

Look out for details of the 2019 event at www.eese-hormones.org/events-deadlines.

Pierre De Meyts & Nathalie Delzenne
Symposium Organisers

EndoBridge 2018

Antalya, Turkey, 25–28 October 2018



The 6th annual EndoBridge meeting was co-hosted by the Society of Endocrinology and Metabolism of Turkey, ESE and the Endocrine Society. The 3-day scientific programme, which was accredited by the European Council, included 24 state of the art lectures, 16 interactive case discussion sessions and poster case presentations. It provided

a comprehensive update across hormonal disorders.

The event attracted record numbers of international delegates (578), countries represented (41) and cases discussed (90) at an EndoBridge meeting. As usual, there were great opportunities for participants to interact and participate in discussions with global leaders of endocrinology

and share their expertise. The event was conducted in English, with simultaneous translation into Russian, Arabic and Turkish.

Next year's EndoBridge meeting will take place in Antalya, Turkey, on 24–27 October 2019. Further information can be found at www.endobridge.org.

Bulent Yildiz
Founder & President

6th COMBO Endocrinology Course

Marathon, Greece, 28–30 September 2018



This international course on 'Drug-induced endocrinopathies' attracted over 100 participants from around the globe and featured 20 international speakers

and tutors. Participants played an active part in 'Meet the Expert' sessions and case presentations. The huge engagement of all the participants in discussions

and exchanges of opinion was very educational. We can only congratulate the organisers, led by Evanthia Diamanti-Kandarakis (Athens, Greece), and thank ESE and the Hellenic Endocrine Society for their support.

You can find videos of the lectures and other sessions at <https://comboendo.frei.gr/gallery>. The 7th COMBO Endocrinology Course will take place on 27–29 September 2019.

Dominik Rachoń
Medical University of Gdańsk,
Poland

Apply soon for the 2019 exam

The European Board Examination in Endocrinology, Diabetes and Metabolism gives clinical endocrinologists a means of gaining important universal recognition for their skills.

The exam is appropriate for newly appointed specialists in endocrinology and diabetes. ESE and UEMS (the European Union of Medical Specialists) recently developed the qualification, which was first made available in 2018, when 73 candidates from 24 countries sat the exam. The certificates are endorsed by both organisations.

The computer-based exam comprises multiple choice questions, presenting clinical scenarios which assess candidates' medical knowledge and their competency in diagnosis, investigation, management and prognosis.

You can take the exam at independently operated assessment centres across Europe. The next opportunity is on 12 June 2019. Applications to sit the 2019 exam will be accepted between 20 February and 20 March. There is a fee of €750.

You can apply online and find further information at www.ebeedm.eu. This includes:

- recommended curricula
- suggested reading
- sample questions
- answers to common questions.

Next Board exam

12 June 2019

Applications accepted

**20 February–
20 March 2019**

www.ebeedm.eu



ESE: increasingly independent

Introducing the ESE Team

ESE has undergone a great deal of change. As recently as 3 years ago, activities and management were fully outsourced to an external association management company, Bioscientifica. They were run very efficiently but, as ESE developed, it was clear that the Society was at a stage where it should be able to 'stand on its own two feet'.

In early 2016, under the excellent direction of AJ van der Lely (as President of ESE) and Richard Ross (ESE's Treasurer at that time), it was decided to change the situation. The plan was to gradually set up an experienced senior level team who could really drive the agreed strategy forward. The team would be employed directly by ESE, and so be fully motivated to deliver.

This change is now in place, with a carefully planned structure and essential leadership roles to manage strategic

implementation, scientific quality, financial sustainability and effective governance. The team currently comprises four full time roles:

- Chief Executive Officer, Helen Gregson, responsible for progressing ESE's development and delivering on its vision and objectives
- Commercial Director, Dirk De Rijdt, whose role builds a solid and sustainable financial basis that allows ESE to grow and fulfil its ambitions
- Scientific Programmes Manager,



(L-R) Dirk de Rijdt, Andrea Davis, Helen Gregson and Alex Harrison

Alex Harrison, taking care of ESE's educational and clinical activities

- Governance and Office Manager, Andrea Davis, responsible for financial management as well as governance and the ESE office. Further recruitment into the team is planned, to provide additional support in sales and marketing and administration. The team works principally out of its own ESE office in Bristol, UK, with some members working on a remote basis from different countries.

ESE continues to be supported day-to-day in its activities by Bioscientifica. However, the Society now has a solid foundation through which it operates independently. It is very much in charge of its own destiny, with a team who are extremely proud to work solely for ESE, and to dedicate their efforts to improving the wonderful world of endocrinology.

Helen Gregson
Chief Executive Officer

Concentrating on communication



As reported in *ESE News* issue 37, the ESE Council of Affiliated Societies (ECAS) recently developed Early Career Clinical Endocrinologist (ECCE) Sessions. These workshops aim to see our discipline from the perspective of younger colleagues, to best provide support.

The second ECAS ECCE Session took place on 25 October at EndoBridge 2018 in Antalya, Turkey. Representatives of 20 National Affiliated Societies and the European Young Endocrine Scientists (EYES) took part.

The session focused on communication between endocrinologists and healthcare professionals. There was an emphasis on the need for an intermediate layer between primary care and endocrine units, operating through general practitioner centres or community health centres, for treatment of prevalent chronic endocrine diseases, such as diabetes and hypothyroidism. Suggestions included organising a triage system for endocrine units to prioritise the flow of patients from primary to

secondary care, establishing an 'on-call endocrinology phoneline' to provide short term advice, and organising short courses on 'endocrinology for non-endocrinologists'.

The third ECAS ECCE Session will be on 24 October 2019 in Antalya. It will further discuss the referral of patients from primary care to endocrinology units.

Djuo Macut
ECAS Representative,
ESE Executive Committee

Nominations open for 2020 Awards

Make your nominations for the 2020 ESE Awards by 28 February 2019.

The following awards will be presented during ECE 2020 in Prague, Czech Republic:

- Geoffrey Harris Award
- *European Journal of Endocrinology* Award
- Clinical Endocrinology Trust Award
- Jens Sandahl Christiansen Awards.

You can find details (including the criteria and nomination process) at www.e-se-hormones.org/grants-and-awards/awards.





Question of the Week

A virtual study group for the European Board Exam

A new collaboration involving EYES Ambassadors across Europe will help young endocrinologists pass the new European Board Examination in Clinical Endocrinology, Diabetes and Metabolism.

This virtual study group takes the form of a 'Question of the Week', and involves a weekly email to EYES members

containing a question, with links to additional study material which will be available at www.ese-hormones.org/eyes.

EYES Ambassadors and their colleagues are supporting this initiative by generating questions with references to literature and guidelines, based on interesting clinical cases. The format is multiple choice, with

five options. The questions are collated across the ESE Focus Areas. Each week, one question is selected from the pool and emailed to EYES members.

If you would like to be involved, please ensure you have signed up to be an EYES member at www.ese-hormones.org/eyes.

Apply for the 2019 Board Exam by 20 March

[Details on page 4](#)



Save the date

7th European Young Endocrine Scientists (EYES) Meeting

Athens, Greece, 13–15 September 2019

EYES, ESE and the Hellenic Endocrine Society invite you to enjoy this opportunity for scientific and professional interaction with other young endocrine scientists from around the world. More details will follow.

Meeting Valerie...

A young endocrinologist in France

Valerie Bernard is a young endocrine scientist based at Hôpital Saint-Antoine in Paris, France. We asked her about her experience and what she enjoys about her career in endocrinology.

Tell us about your background?

I come from the Paris region and studied medicine at the faculty of Kremlin-Bicêtre. This gave me a very early appreciation of endocrinology. I finished my medical internship in 2013. It was then that I undertook 4 years of fundamental research in a team working on prolactin and pituitary tumorigenesis, which deepened my experience and my interest in our discipline.

Where do you work now?

I am at the Department of Endocrinology and Reproductive Diseases at Hôpital Saint-Antoine, Paris. Our unit is part of a centre for rare diseases. This cares for children as well as adult with rare growth disorders. The centre was recognised by the French Ministry of Health in 2006 and is a member of the European Reference Network on Rare Endocrine Conditions (Endo-ERN). I am privileged to be able to take care of patients with a range of endocrine disorders.

What area of endocrinology most interests you?

I particularly enjoy reproductive endocrinology. My fundamental research has focused mainly on the regulation of the lactotroph axis and prolactinoma tumorigenesis. I also participate in translational research studies, for example in patients with Turner's syndrome, specifically investigating their fertility and transition from paediatric units

to adult care systems. I take part in studies exploring genetic abnormalities in patients with primary ovarian insufficiency.

How do you see your career developing?

I would like the opportunity to combine research and clinical activities in the field of reproductive endocrinology.

Will you be at ECE 2019?

As ECE 2019 is taking place in Lyon, France, I am particularly looking forward to welcoming you all to my country and meeting many young endocrine scientists. The EYES Symposium on Monday 20 May and the networking event are sure to be highlights of the Congress.

The EYES Symposium at ECE 2019 take place on Monday 20 May at 10.20–11.50. Further details will be available at www.ece2019.org.



eyes 
european young
endocrine scientists
looking forward



From one President to another

As we thank retiring President AJ van der Lely for a remarkable term of office, and warmly welcome incoming President Andrea Giustina, they each take the opportunity to reflect on ESE's continuing journey, the growth of European endocrinology and collaboration, and a future focused on inclusion.



'ESE now stands for its vision to shape the future of endocrinology, to improve science, knowledge and health'



'Some of you already know that the keyword of my term as a President will be *inclusion*'

Four wonderful and satisfying years

Close to 4 years ago we, as ESE's Executive Committee, began a fascinating project to turn ESE into an 'inside-out organisation'.

An inside-out organisation uses a corporate strategy process that relies on its core competencies to drive change, product development and innovation. This is as opposed to external influences, such as market, competition and customer preferences.

To achieve this, we needed a clear vision of who we were and are, and what our mission is. We also knew we had to construct a solid, financially sustainable, Society.

The outcome is even more impressive than we could ever have imagined. ESE now stands for its vision to shape the future of endocrinology, to improve science, knowledge and health. It is the Society's mission to advance endocrinology, and ESE actively unites, supports and represents its speciality. The Society promotes collaboration and best practice and enables its community to develop and share the best knowledge in endocrine science and medicine.

All in all, strong messages make it clear to everybody who we are and what we aim to achieve.

Another issue that the Executive Committee felt was important was the construction of a strong, independent Society. This required us to start building our own 'dream team', and I believe we were very successful in this regard as well.

By appointing Helen Gregson as our CEO, we really took off. Shortly thereafter, we were very proud and happy to bring in Dirk de Rijdt who, with his extensive experience in the pharmaceutical industry, brought us a wealth of inside knowledge in financial and commercial issues. Finally, with the appointments of Alex Harrison and Andrea Davis, we have established a strong core for ESE.

From the Society's office in Bristol, UK, they will certainly extend ESE's impact on science and endocrine care, and will increase its political influence. This dream team achieves this all with an impressive charisma that will surely attract others to join them.

I'm very happy and honoured that our President-Elect, Professor Andrea Giustina, whom I know as a visionary and inspiring leader, will take over, so that ESE can continue to prosper now, and into the future.

AJ van der Lely

Looking into the future of ESE

Working side-by-side with AJ in ESE's Executive Committee for almost 2 years has been a very instructive experience. The achievements have been impressive and effective.

My time as President-Elect has been important, as gradually learning the ropes under the guidance of a great friend and President such as AJ has been a unique opportunity. I intend to continue our work maintaining his standards of honesty, commitment and efficiency.

Some of you already know that the keyword of my term as a President will be *inclusion*. To whom will this keyword apply?

First, it applies to the 20 000 endocrinologists around the continent. I would like to see most – and ideally all – of them become members of ESE. Through ECAS (the ESE Council of Affiliated Societies) and our National Affiliated Societies we should overcome the old and new geographical, cultural, political and economic barriers between countries.

Then, it relates to the young folks, who show their love for our discipline every day. We must involve them more and more in ESE activities through EYES (the European Young Endocrine Scientists). Next, I reach out to basic researchers, who should feel that ESE is their beloved home, as the clinicians already enthusiastically do. We will do this by encouraging their valuable contribution to our Focus Areas and to the ECE Programme Organising Committee. Our Congress will continue to be a great place to learn and freely discuss endocrine research and clinical practice.

ESE will put a huge effort into embracing the European institutions, in order to put hormones in a relevant place in the European agenda for health and research. In part, this will be achieved by being physically closer to them, and therefore more present in Brussels.

Finally, we will include all the scientific societies that work for the good of endocrinology. With them, I would like to promote collaboration instead of competition, putting in place an alliance, and possibly a federation, to better fight for our beloved discipline worldwide.

You may think that this is all too much to be accomplished in a 2-year term, but do not forget that, in less than 6 months' time, ESE will have a new President-Elect, who will be the first to whom the keyword inclusion will be applied!

Andrea Giustina



ECE 2019:

for the best endocrinology

Lyon, France, 18–21 May 2019

Remember to submit your abstracts by

4 February 2019

The early bird registration deadline is

4 April 2019

www.ece2019.org



Following a solid tradition of successful and exciting Congresses organised by ESE, we look forward to the 21st European Congress of Endocrinology in 2019.

It provides an unparalleled opportunity, across Europe and internationally, to access the most relevant developments in basic and clinical endocrinology from the past year. The Congress will be a unique opportunity to gather with thousands of colleagues, including more than 100 top international speakers, to discuss the most striking progress in our area in detail.

ECE 2019 has an attractive, varied and interactive scientific programme, fully covering all of ESE's eight major Focus Areas:

- Adrenal and neuroendocrine tumours
- Calcium and bone
- Diabetes, obesity and metabolism
- Environment, society and governance
- Interdisciplinary endocrinology
- Pituitary and neuroendocrinology
- Reproductive endocrinology
- Thyroid

The Programme Organising Committee, which includes over 30 international experts from all fields of endocrinology, has devoted itself to creating a dynamic programme. This is accessible and can be tailored to the needs of all participants. It provides a welcoming environment where excellent basic science and cutting-edge clinical practice merge to provide a unique learning experience for all participants.



ECE 2019
21st European Congress
of Endocrinology

11 award and plenary lectures will exemplify excellence in basic and clinical research, covering different topics of interest to the wide audience. Amongst others, these will include diabetes, bone and pituitary disease, the neuroendocrine basis of obesity, population genetics and the impact of urban design in endocrine and metabolic health.

19 'Meet the Expert' sessions will include 16 clinical sessions on topics as diverse as diabetes, the adrenal, the pituitary and neuroendocrinology, the thyroid, and reproductive endocrinology, as well as 3 basic science sessions on positron emission tomography, animal models in translational research and the 'gravitostat'.

6 'New Scientific Approach' sessions are set to cover different aspects of cutting edge techniques relevant to today's and tomorrow's endocrinology. Topics include the application of artificial intelligence, steroidomics and functional brain imaging in preclinical models.

6 debates will provoke dynamic and participative discussion of controversial areas in basic and clinical endocrinology. For example: does food addiction exist, what are the actual roles of microRNAs as putative hormones, and how should we manage osteoporotic patients?

30 symposia form the main core of ECE 2019, as over 90 top speakers discuss all major areas of our field. Watch out for sessions for young endocrinologists and nurses, as well as late-breaking communications.

If you are curious to know how it feels to be at the true centre of endocrinology, and wish to enjoy, and taste, the unique atmosphere of the capital of gastronomy, please mark ECE 2019 in Lyon on your calendar, and join us for what promises to be the endocrine event of the year.

Manuel Tena-Sempere

ECE 2019 Programme Organising Committee Co-Chair (Basic Science)

Sebastian Neggers

ECE 2019 Programme Organising Committee Co-Chair (Clinical)



Our award lecturers



Günter Stalla
Geoffrey Harris Award

The pituitary gland has always held a special allure: so small and yet such complex pathophysiology and clinical presentation! I heard the call of its sirens in the late 1970s, just after finishing my medical examination. It was the realisation of how little we know about pituitary disorders that prompted me to specialise in endocrinology.

In 1990, I had the great opportunity to head an endocrine outpatient unit and a research laboratory, enabling me to embark on a life-long quest regarding pituitary disorders, particularly tumours,

in a truly translational manner. Over the years, we identified factors that are deregulated during pituitary tumorigenesis and established novel therapeutics. The comorbidities are as complex as the tumours that cause them, leading to deep scars that affect patient's well-being.

Almost 30 years later, we undoubtedly know a lot more about the underlying molecular events but, when it comes to patient management, we still rely on improved versions of traditional therapeutics. There remains a long way to go, and it is only with the co-operation and rigorous training of the next generation of experts that we can hope to defeat this multifaceted, devastating disease.



Mirjam Christ-Crain
European Journal of Endocrinology Award

The differential diagnosis of hypotonic polyuria is a frequent problem. Three fundamentally different types of defect must be distinguished: central diabetes insipidus (DI) characterised by a lack of the antidiuretic hormone arginine vasopressin (AVP); nephrogenic DI characterised by renal insensitivity to AVP; and primary polydipsia due to primary excess fluid intake. Differentiation is crucial as treatment differs substantially, and incorrect strategies may lead to severe complications.

For decades, the indirect water-deprivation test has been the reference

standard for differentiation. However, it is technically cumbersome and highly vulnerable to false diagnosis. A new test with high diagnostic accuracy is urgently needed.

We therefore investigated measurement of copeptin (the AVP prohormone's C-terminal segment, a stable and easily measured AVP surrogate). We found that high baseline copeptin levels unequivocally identified patients with nephrogenic DI and that stimulated copeptin levels differentiated between central DI and primary polydipsia.

Previously, our large prospective diagnostic outcome study directly compared the diagnostic performance of copeptin after hypertonic saline infusion with that of the water-deprivation test. Measurement of copeptin clearly improved diagnostic accuracy. Copeptin measured after hypertonic saline infusion could therefore become the new reference standard in differential diagnosis of hypotonic polyuria.



Jens Bollerslev
European Hormone Medal

Familial osteosclerotic bone disorders have been diagnosed since radiography was introduced. Some are prone to pathological fractures, some not. The most severe forms are typically recessively inherited, while milder types show dominant inheritance.

Systematic studies of different osteosclerotic disorders in the 1980s indicated defective bone resorption as a common histomorphometric finding, whereas bone formation was considered relatively normal. The high bone mass phenotype was described in the 1990s, based on family studies of index cases

with very high bone densities. Further genetic studies revealed gain of function mutations in the *LRP5* gene in several family forms, pointing to the *Wnt* signalling pathway as pivotal for bone remodelling.

The opposite picture, osteoporosis pseudo-glioma syndrome, was found in 2001 to result from a loss of function mutation in *LRP5*. Regulation of *Wnt* signalling was discovered to be even more complicated through studies of van Buchem's disease and sclerosteosis, showing that sclerostin produced by osteocytes was another important player. Defective sclerostin leads to constitutive activation of *Wnt* with bone formation activation, followed indirectly by inhibition of bone resorption – a new concept.

Monoclonal antibodies towards sclerostin (Romososumab) are now close to clinical use in osteoporosis, with promising fracture prevention, and investigation of potential cardiovascular side effects.



Susan Webb
Clinical Endocrinology Trust Award

As endocrinologists, we consider that a patient's pituitary disease is controlled if hormone parameters are normalised and tumour growth is stabilised. However, a patient's perception of health relates to their ability to continue day-to-day activities. This is often not the case due to pain, physical or psychological limitations, or social/family issues related to their disease.

This is more relevant nowadays, as pituitary dysfunction can be controlled in most cases, by either surgery or medical therapy. In the last 2 decades, the long

term impact of prior exposure to hypercortisolism, excess growth hormone/insulin-like growth factor-I or hypopituitarism on patients' health perceptions has become apparent.

More cardiovascular, skeletal and neuropsychological morbidity persists after endocrine 'cure'. The last of these includes poorer memory, cognition, executive function or emotional coping, often leading to increased anxiety, depression and psychological distress, with an important impact on perceived quality of life.

Making patients aware, through devoted multidisciplinary teams with an understanding of these persistent problems, enables them to adapt to and accept these limitations. This engenders a positive approach to day-to-day life, together with support from family and friends. The outcome is a positive impact on patients' health perception and long term prognosis.



Contraception

New challenges and opportunities

Access to effective contraception is an essential component of reproductive health, ensuring that every child is wanted, and reducing the burden of unintended pregnancies. Contraceptive methods are not only important for individuals and couples, but play an essential part in population dynamics.^{1,2}

However, the research landscape is changing, and only a few players remain involved in this field. In addition, several ‘pill scares’ have led women to stop their method of contraception, due to a fear of hormones and the risk of thromboembolism, as well as the debate about endocrine disruptors.

These misperceptions are harmful, since one-third of all pregnancies are still unplanned. The result is abortion, which remains unsafe in countries that lack medical options.

Advances in contraception

Recent progress has included development of emergency contraception using a progesterone receptor modulator, ulipristal acetate. This is highly effective in preventing pregnancy in the 120 hours following unprotected intercourse, by inhibiting both follicular rupture and the luteinising hormone surge. However, access is not always available at the right time.

A wide array of contraceptive methods is available in most countries. These include combined hormonal contraceptives and copper intrauterine devices (IUDs). The latter can also be used by nulliparous women. Levonorgestrel-releasing intrauterine systems achieve the highest efficacy and also can decrease bleeding. Progestin-only contraception is safe for most women; however, unscheduled or increased bleeding are limiting factors for intake.

The non-oral delivery systems available to women include transdermal patches, implants and vaginal rings; these have become popular as they do not require daily attention, and compliance is improved. An interesting new method was recently approved in the USA: a vaginal contraceptive system that can be used for 1 year and delivers nesterone, a novel, well-tolerated progestin with potential added health benefits.

Thus, contrary to common thinking, hormonal contraception and IUDs are safe, provided their contraindications are respected. They have helped millions of users worldwide reach their desired family sizes.

Multi-purpose prevention

The development of multi-purpose prevention technologies (MPT) is another urgent matter to address. Indeed, HIV and unintended pregnancy remain twin burdens for women, leading to high maternal mortality, especially in low and middle income countries (LMIC).

Research into vaginal rings that combine antiretroviral and contraceptive agents, as well as microbicidal-treated diaphragms or fast-dissolving inserts (FDI), must become a priority.³

Researchers have developed an innovative dosage form for vaginal delivery using drug-eluting nanofibres.³ This user-controlled, discreet, innovative technique provides extensive coverage of mucosal tissue, and delivers appropriate molecules for dual protection. FDIs have also been developed as a new vaginal MPT.



Contraception for men

Male methods of contraception are a glaringly unmet need, despite significant progress with the use of gonadotrophin-suppressive agents associated with testosterone replacement. The combination of progestins and testosterone is efficient at inducing oligo-azoospermia in most subjects. The use of MENT (a tissue-selective androgen), or transdermal nesterone combined with testosterone, has recently shown progress.⁴ However, development requires long term studies. Consequently, no method is expected before the next decade. Until then, men are left only with the option of a vasectomy or condoms, the latter with a high risk of failure.

Advanced technologies

It is now possible to take advantage of advanced technologies, such as bioinformatics, genomics and proteomics (the 'omics'), and related tools, to develop biomarkers to identify new contraceptive targets. This opens up the prospect of innovative non-hormonal contraceptives for women and men.

Approaches to novel methods for women include inhibition of oocyte maturation, the inhibition of meiosis in the ovary or, alternatively, inhibition of cumulus-oocyte expansion leading to follicle rupture and interaction with factors involved in follicle rupture.⁵⁻⁷

In men, targeting spermiogenesis and differentiation, maturation of sperm or factors inhibiting sperm motility or transport appears promising. A few of these approaches may enter clinical testing in the next decade.⁸⁻¹²

An overview

In summary, the contraceptive needs of a significant percentage of couples have not yet been met. It is projected that, by 2050, the world population will reach 9.5 billion, an increase of 33% above the current 7.1 billion, mainly in LMIC.^{1,2}

Millennium Development Goal 5, targeting a reduction in maternal mortality and universal access to reproductive health, reaffirms the need for contraceptive options as well as access to key reproductive health services, including safe abortion, but these goals have not

yet been met. Contraceptive research and development are crucial in achieving these objectives, by finding new methods, or refining existing ones. In addition, green principles, across manufacturing and disposal, can help design products that are environmentally friendly or hormone-free.¹³

It is now critical to involve new private, public and non-governmental partners, as well as to nurture innovation in research and support younger professionals worldwide in all relevant fields, to ensure and brighten the future of contraception.

Philippe Bouchard

Sorbonne University, Paris, France

Régine Sitruk-Ware

The Population Council, New York, NY, USA

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Learning together

From the ESE Clinical Committee

The theme of this issue of *ESE News* has inspired me to focus on activities of the French endocrinology community that are relevant to the goals of ESE's Clinical Committee.

Guidelines are important tools, and ESE's guidelines are among our major investments. Two types of guideline have been developed in France that, interestingly, are complementary to ESE's guidelines since there is no thematic overlap.

Each year the French Endocrine Society releases a guideline on a specific topic, developed by their expert members, with a methodology mostly following expert opinions. As you may have seen on page 3, their 2018 guideline is dedicated to the endocrine consequences of new cancer treatments.

In contrast, other guidelines are developed by the national reference centres for rare diseases, at the request of the health authorities. These follow a specific process defined by the authorities and are published on the website of the national health agency. Congenital adrenal hyperplasia, androgen insensitivity and Cushing's syndrome are examples of topics covered by these guidelines.

The European dimension is key to progress in rare endocrine diseases. At the national level, the French Ministry of Health

launched a plan in 2005, renewed in 2016, to identify reference centres. In endocrinology, 21 were identified across 7 different fields, each covering a group of rare endocrine diseases (e.g. pituitary disorders, disorders of sex development, adrenal disorders, insulin sensitivity disorders, etc.). The centres are organised in a national network for rare endocrine diseases, with competent centres to cover the various regions, patient associations, research labs, diagnostic labs and so on.

This organisation mirrors, at the national level, the European Reference Network for Rare Endocrine Conditions (Endo-ERN) at the European level. A strong interaction between the national and European initiatives is clearly essential to maximise progress.

With so many things to learn and share from national experience in France and elsewhere, ESE undoubtedly has a major role to play in exchange of knowledge and tools. Our annual Congress provides a great opportunity to do so.

Jérôme Bertherat

Chair, ESE Clinical Committee



The Endo Explorer

Understanding pituitary tumours



Team members: (L–R) Alexandre Vasiljevic, Hélène Lasolle, Philippe Bertolino, Moitza Principe, Yajie Zhao, Marie Chanal, Gérald Raverot, Ana Hennino and Zhichong Wu

Gérald Raverot and Philippe Bertolino's team in Lyon has been brought together to study the genetics of pituitary tumours and the impact of their microenvironment.

Pituitary neuroendocrine tumours represent the second-most common intracranial neoplasms in adults. Despite extensive research that has already led to significant advances in the field, pituitary tumours still present major clinical and scientific challenges. Their cellular and functional diversity, combined with their complex evolution, make the clinical analysis and management of pituitary neoplasms difficult when it comes to identification of aggressive pituitary tumours and customisation of targeted, personalised therapies

Developing solid research into these neoplasms is therefore not trivial, and requires a wide range of expertise to be gathered together in order to cover all the technical and scientific challenges, as well as access to relevant biological material within the proper institutional environment.

Joining forces

In 2014, in order to better understand the aggressive behaviour of pituitary tumours and to develop novel therapeutics, we decided to join forces and build a team. We took advantage of our respective expertise in studying the genetics and behaviour of aggressive pituitary tumours¹ and in developing model systems to study MEN1 (multiple endocrine neoplasia type 1) tumours' genetics/plasticity and endocrine disorders. The research team we assembled was based on the legacy of the work initiated by Jacqueline Trouillas at the Hospices Civils de Lyon (HCL).

Our aims were simple but ambitious: pave the road for a better understanding of pituitary tumour genetics and comprehend the function of their microenvironment.

In building such a project, we also aimed to take advantage of our geographic location between the National Reference Centre on Pituitary Tumours (HYPO) at the HCL and the Cancer Research Centre of Lyon

(CRCL; Inserm U1052, www.crcl.fr). We wanted to bring together a trio comprising an expert endocrinologist (Gérald Raverot), neurosurgeon (Emmanuel Jouanneau) and neuropathologist (Alexandre Vasiljevic) with a team of fundamental researchers (led by Philippe Bertolino).

In this way, we could:

- (a) tackle the limitations that researchers face in accessing a large number of human biopsies with matching clinical data that fulfil their scientific needs, and also
- (b) bring the use of patient-derived material to the next level of research, through the top-notch technical resources available at our research institute, CRCL.

Addressing our research aims

While our Tumour Environment and Pituitary Oncology Group has a short history, our co-headed team has developed a unique experimental pipeline. This makes it possible to access more than 100 fresh biological samples/tumour biopsies per year, with complete clinical traceability from clinical characterisation to histological analysis post-surgery.

Getting access to such biological material rewarded us far beyond our expectations and opened up the possibility of developing approaches that we could not have imagined previously. These included patient-derived-xenograft mouse models and tumour-microenvironment-derived patient cell lines. More importantly, having access to such biopsies, matching clinical data and histological material was of great help when we achieved the transcriptomic profiling of more than 80 tumours (the HYPOPRONOS cohort) and the genomic analysis of 200 tumours by CGH (comparative genomic hybridisation) array (the PITUIGENE cohort).



‘Our aim is to contribute to the creation of an EU network dedicated to improving knowledge of pituitary tumour biology’



Emmanuel Jouanneau

In addition to the identification and characterisation of novel markers of pituitary tumours that these analyses led to in prolactinomas,² they suggested that the different subgroups of pituitary tumours are not equal when it comes to genomic rearrangements.³ Having access to fresh tumour biopsies also led us to initiate mapping of their specific microenvironment, through systematic immuno- and stromal population phenotyping (the PitME/HypoMet projects).

A European network for the future

Multi-omics approaches have proved their value in terms of clinical discoveries. Our team is now willing to take that direction, and we plan to further extend this research regarding the genetics of primary versus relapsed tumours from the same patients.

This should definitively help us to (a) better understand the genetics of pituitary tumours and (b) identify the driver genes associated with their origin and aggressive behaviour. However, it is important to emphasise that this huge challenge cannot be taken on by our group alone.

Recent efforts, supported by ESE, have underlined the need for a collaborative European network combining clinical and basic research. This is why we are now willing to push forward the opportunities of EU collaborations and share our expertise and large sampling capabilities with scientific and clinical partners. Our aim is to contribute to the creation of an EU network dedicated to improving knowledge of pituitary tumour biology.

Gérald Raverot

Centre de Référence Maladies Rares Hypophysaires (HYPO), Hospices Civils de Lyon–Universitaire Claude Bernard Lyon 1, Lyon, France

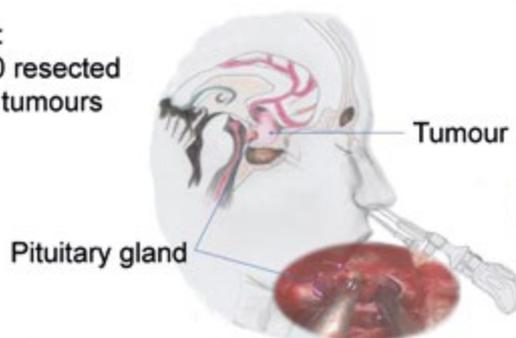
Philippe Bertolino

Cancer Research Centre Lyon (CRCL), Inserm U1052, CNRS UMR5286, Universitaire Claude Bernard Lyon 1, Lyon, France

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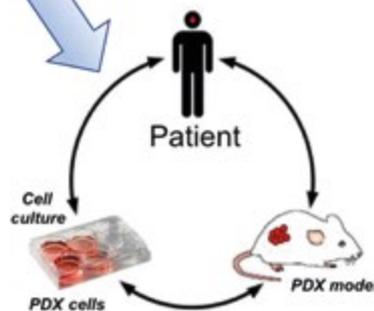
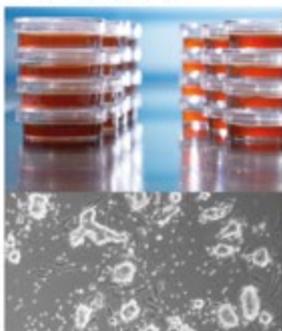
Patients:
100–150 resected
pituitary tumours



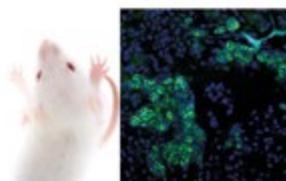
nr	gender	age	hist	size	hormonal	WHO grade	cellular	mitosis	ki67	ki
1	M	58	Mac	10	Norm	1	100%	0	0%	0%
2	M	47	Mac	10	Norm	1	100%	0	0%	0%
3	M	50	Mac	10	Norm	1	100%	0	0%	0%
4	M	50	Mac	10	Norm	1	100%	0	0%	0%
5	M	50	Mac	10	Norm	1	100%	0	0%	0%
6	M	50	Mac	10	Norm	1	100%	0	0%	0%
7	M	50	Mac	10	Norm	1	100%	0	0%	0%
8	M	50	Mac	10	Norm	1	100%	0	0%	0%
9	M	50	Mac	10	Norm	1	100%	0	0%	0%
10	M	50	Mac	10	Norm	1	100%	0	0%	0%
11	M	50	Mac	10	Norm	1	100%	0	0%	0%
12	M	50	Mac	10	Norm	1	100%	0	0%	0%
13	M	50	Mac	10	Norm	1	100%	0	0%	0%
14	M	50	Mac	10	Norm	1	100%	0	0%	0%
15	M	50	Mac	10	Norm	1	100%	0	0%	0%
16	M	50	Mac	10	Norm	1	100%	0	0%	0%
17	M	50	Mac	10	Norm	1	100%	0	0%	0%
18	M	50	Mac	10	Norm	1	100%	0	0%	0%
19	M	50	Mac	10	Norm	1	100%	0	0%	0%
20	M	50	Mac	10	Norm	1	100%	0	0%	0%

Diagnostic
and clinical
data

Primary culture



Formalin-
fixed
paraffin-
embedded
tissue



PDX model

(FSH/Dapi)

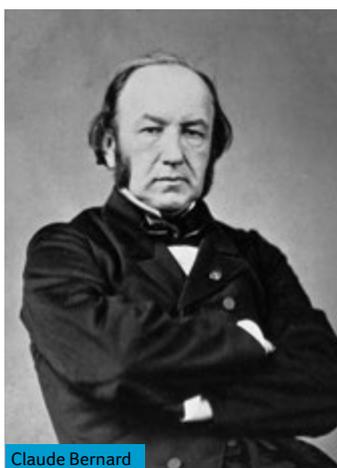
Accessing more than 100 fresh samples per year has enabled us to gather matched clinical data and histological material, as well as to develop tumour-microenvironment-derived patient cell lines and patient-derived-xenograft (PDX) mouse models



Collège de France, Paris

Two famous French godfathers

Pioneers in physiology and endocrinology



Claude Bernard

Two giant French physicians were world-renowned leaders in the field of physiology and basic endocrinology. Now the European Congress of Endocrinology is moving to France for 2019, we should honour them, by briefly discussing why they are important, even now, for modern endocrinology.

Claude Bernard

Claude Bernard was born on 12 July 1813 in Saint Julien, Rhône, France. Aside from his achievements in medicine, he was also a playwright and dramatist.

He studied at the Faculty of Medicine of the University of Paris, and began working as an intern under François Magendie (1783–1855) at the Hôtel-Dieu. In 1841, he became Magendie's research assistant at the Collège de France. He was an enemy of charlatanry and oratory, and can be considered as one of the founders of experimental medicine and physiology.

Among his many discoveries and achievements, his concept of the milieu intérieur, or internal environment, which the organism maintains constant in order to enable normal tissue function, is pivotal. However, this new concept had no impact in his lifetime.

Bernard also discovered that the secretions of the pancreas broke down fat molecules into fatty acids and glycerine.

Claude Bernard died on 10 February 1878 in Paris.

One of his many famous sayings was 'I consider the hospital the antechamber of medicine; it is the first place where the physician makes his observations. But the laboratory is the temple of the science of medicine.'

Charles-Édouard Brown-Séquard

Charles-Édouard Brown-Séquard was born on 8 April 1817 in Port Louis, on the island of Mauritius. His father was a naval officer from Philadelphia (PA, USA), while his mother was French. Brown-Séquard was raised by his mother alone after his father was lost in a shipwreck.

In 1846, he received his doctorate in medicine from the University of Paris. In 1878, he succeeded Claude Bernard as Professor of Experimental Medicine at the Collège de France, and also became a French citizen.

Although he made several important contributions to different fields of medicine, his contribution to endocrinology focused on his studies and theories on the internal secretion

of substances we nowadays call 'hormones' (1889).

He became more (in)famous because of his rejuvenation organotherapies, which used subcutaneous injections of liquid extracts from the testicles of guinea pigs and dogs. One of his study subjects was the investigator himself.

Brown-Séquard died on 1 April 1894 in Paris.

Wouter de Herder

Editor, *ESE News*

FURTHER READING

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A day in the life of...

...an endocrinologist in France



(L-R) Georgios Papadakis, Peter Kamenicky, Sylvie Salenave, Jacques Young, Helena Mosbah, Philippe Chanson, Luigi Maione

06.30

At the sound of the alarm clock, I get up, have breakfast and leave home for a 30-minute car journey to Bicêtre Hospital. We are very lucky, because the Endocrinology and Reproductive Diseases Service that I head, the medical school and our lab, INSERM U1185, are on the same campus with all the hospital and research facilities.

07.30

I have a strong coffee in my office while browsing my emails. A nurse calls in to ask for clarification on a pituitary stimulation test that must be performed on a patient.

07.45

My secretary and I schedule some urgent appointments, and then programme admissions. I list all the biochemical measurements and visits needed for endocrine assessment of new patients or patients whom we regularly monitor.

08.30

The first of three patients who are booked for a supplementary consultation arrives. He presents with a macroprolactinoma. I explain the illness and start dopamine agonist therapy right away. The next patient has

acromegaly; he lives abroad, is passing through France and needs a prescription. At the end of his visit, I ask a nurse to test him for IGF-I. The third patient has Graves' disease: her treatment, which began a month ago, needs adapting.

10.00

At our Clinical Research Unit, I meet a patient who is included in a clinical trial. I explain the next steps of the protocol, and check that everything is going well. A resident takes the opportunity to ask me for advice about a patient admitted for evaluation of pituitary mass effects before surgery.

10.45

It is time for the weekly seminar given by an invited scientist. The medical staff gather with the basic scientists from the research lab, the biochemists and geneticists working in the Molecular Genetics and Hormonology Department, and the endocrine paediatricians.

12.00

At today's inpatient review meeting, medical students and residents summarise the charts of some patients who have posed problems. We decide to schedule some of the cases for the monthly Neuroendocrine

Multidisciplinary Meeting or the next Endocrine Tumours Multidisciplinary Meeting.

13.30

I have a quick lunch of a sandwich and fruit, and a briefly check through my emails.

14.00

Now it's time to cross the hospital to go to the medical school, where I give a course to medical students on the semiology of endocrine diseases. As a Professor, I must deliver regular courses, and am also responsible (with the rest of my team) for the initial training of 12 medical students, who attend the ward each morning for a trimester, as well as 6 residents on a 6-month rotation.

16.00

I go to our lab, INSERM U1185, to review the results of one of our PhD students, together with Peter Kamenicky (our service's Associate Professor) and Say Viengchareun (a basic scientist in the lab). We agree on the journal to which we will submit the paper.

17.00

I chair the monthly meeting of our University Hospital's Global Medical Committee. We evaluate which medical position will be selected for recruitment of doctors. It's a difficult job, where we must respect balance between the different specialties, comply with limited resources and make good strategic decisions.

19.00

Back at my office, I try to sort the 60 or so emails that have arrived since this morning, talk to the assistants, and have a quick look in the ward to see some of my patients who have recently been admitted, while the junior doctors are still present.

19.30

Before leaving, I knock on the door of Professor Jacques Young, my closest collaborator for almost 20 years. We chat about the service, the hospital, the university (he is very involved in its scientific committee), and about our respective clinical and basic studies ... then also about France and world news.

20.15

I leave the hospital.

20.45

Before dinner, my wife and I have a well deserved glass of wine. Then, I take another look at my emails and work a little on a review that I need to write, while listening to 'France-Musique' on the radio. Finally, I read my French newspaper, *Le Monde*, and fall asleep!

Philippe Chanson

Hôpitaux Universitaires Paris-Sud, Hôpital de Bicêtre and Université Paris-Sud, Le Kremlin-Bicêtre, France

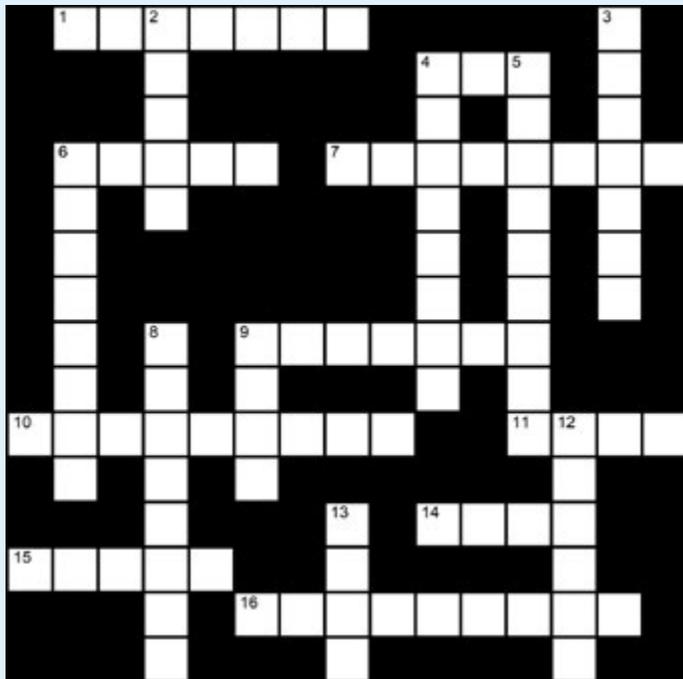




The Endo Crossword



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.



Solution

Answers to the puzzle in issue 37

Across

1. HG Wells, 3. Kennedy, 5. Lautrec, 6. Winfrey, 8. Lucas, 12. Oprah, 13. Helmut, 15. Britt, 16. Shriver, 18. Schmidt

Down

2. Ekland, 3. Kiel, 4. Eunice, 7. Richard, 9. Stewart, 10. Yeltsin, 11. Toulouse, 14. George, 15. Boris, 17. Rod

Across

- 1 Brothers from Lyon, creators of the first motion picture (7)
4 One of two codons corresponding to **4 down** (3)
6 French joint recipient of the 1965 Nobel Prize (5)
7 Woman symbolising the French Republic, often wearing a Phrygian cap (8)
9 Famous Lyonnais puppet (7)
10 Recipient of an MD from Lyon, an Ordre National de la Légion d'Honneur and the 1977 Nobel Prize (9)
11 Industry for which Lyon was famed in the 1400–1600s (4)
14 Largest fundamental research organisation in Europe (abbr.) (4)
15 French joint recipient of the 1965 Nobel Prize (5)
16 Location of Lyon's ancient theatre and basilica (9)

Down

- 2 French joint recipient of the 1965 Nobel Prize (5)
3 French physician, inventor of the stethoscope (7)
4 Amino acid from which melanin is derived (8)
5 Passageways in Lyon, enabling workers to carry **11 across** to the river (9)
6 Roman name for Lyon (8)
8 Triple A syndrome, characterised by achalasia, alacrima, and adrenal abnormalities (8)
9 French endocrinologist after whom the parathyroid glands are sometimes named (4)
12 French public research organisation dedicated to human health (abbr.) (6)
13 Name for widely distributed cells producing peptide hormones (abbr.) (4)



Did you know?



What would Jonah have made of this?

In humans, we know that we can use scalp hair to assess stress exposure by measuring hair cortisol levels combined with hair growth rate and age.¹

But listen to this! To determine stress exposure in huge baleen (so-called 'toothless') whales, it is possible to use their earplugs. These form over an animal's lifespan and consist of lipid- and keratin-based semi-annual bands. By combining age estimates with cortisol measurements in

historical specimens and material from recent strandings, researchers have been able to examine stress levels in whales throughout the 20th century.²

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Save the date

For more information see www.eese-hormones.org/meetings.

24th ESE Postgraduate Training Course on Endocrinology, Diabetes and Metabolism

7–10 March 2019

Bled, Slovenia

ECE2019

21st European Congress of Endocrinology

18–21 May 2019

Lyon, France

European Board Exam

12 June 2019

Various locations

Deadlines

4 February 2019

ECE 2019

Abstract deadline

20 February–20 March 2019

European Board Exam

Applications open

28 February 2019

Geoffrey Harris Award

Nomination deadline

28 February 2019

European Journal of Endocrinology Award

Nomination deadline

28 February 2019

Clinical Endocrinology Trust Award

Nomination deadline

28 February 2019

Jens Sandahl Christiansen Awards

Nomination deadline

1 March 2019

Small Meeting Grants

Application deadline

4 April 2019

ECE 2019

Early bird registration deadline