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ESE News

THE NEWSLETTER OF **THE EUROPEAN SOCIETY OF ENDOCRINOLOGY** –
THE EUROPEAN HORMONE SOCIETY

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Endocrine inheritance

New ESE President takes the reins

Also in this issue:

A legacy of disease:
the forefront of endocrine genetics

Keeping it in the family:
brothers in endocrinology

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

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Editorial

I was delighted to see you all at the Congress in Dublin.

To attain record attendance and the largest ever number of abstracts submitted was a wonderful achievement. We also welcomed ten very active participants from the Tunisian Society of Endocrinology. Our Society is clearly going from strength to strength. Thus it was with a sense of pride that I handed the Presidency over to my very capable successor, AJ van der Lely. I wish him every success in the role, and I am sure that ESE will continue to flourish in his hands.

And so it is appropriate that this issue of ESE News has a theme of 'endocrine inheritance'. On page 7, you have a chance to meet Professor van der Lely and learn about his vision for our Society's future, as he inherits the leadership of our unique organisation. He will be pleased to hear your views about the development of this legacy.

Inherited endocrine disease is a topic that provoked much interest at ECE 2015. Recent developments have led to exciting discoveries. On pages 8 and 9, we meet two teams at the forefront of such research. Albert Beckers describes his group's recently published research on X-linked acrogigantism (X-LAG), while Martin Reincke relates his team's fortunes in unravelling the genetics behind Cushing's.

What better example of endocrine inheritance could there be than a family of endocrinologists? The Lips family (brothers Cornelis and Paul, as well as their father and members of the next generation) have all developed an interest in our discipline. What could be the reason? Turn to page 10 to find out!

The rest of the issue is packed with news of endocrine events, and the many developments at ECE 2015. I congratulate all our prize winners, many of whom are pictured on pages 11–12. I thank all the Committee members, past and present, who have worked tirelessly to further the cause of ESE, and I thank the team at the ESE Office who have supported all our endeavours.

Last but not least, I thank you, the Society's members. Without your support, energy, enthusiasm and diligence, there would be no ESE, and endocrinology would not be the strong and vibrant field that we enjoy today. It has been an honour to lead our Society. Keep up the good work – and I look forward to seeing you at future events.

Philippe Bouchard
Co-Editor of *ESE News*

From the ESE office

I am writing this column still buoyant with the success of the recent ECE in Dublin in May. It was humbling to see such fantastic attendance by more than 3500 participants from around the globe, who were able to experience the absolute best in endocrine science and practice.

My congratulations must go to Wiebke Arlt with her proactive and engaged Programme Organising Committee, particularly her co-chairs Jenny Visser and Felix Beuschlein. It was great also to meet with a large number of national society representatives at the ESE Council of Affiliated Societies (ECAS) meeting, which took place at the Congress. Discussion was of hot topics such as dual membership and a pan-European curriculum in endocrinology.

Please do let us have any feedback; we are always looking to improve what we provide for the international endocrine community, and we depend on all of you to tell us!

We said a sad farewell at ECE to President Philippe Bouchard. From the ESE Team's perspective he has been fantastic to work with, always providing fresh strategic insight and moving the Society forwards. But every cloud has a silver lining, and to welcome AJ van der Lely as our new President is a real pleasure. We look forward to working with him for the next 4 years.

Helen Gregson
ESE General Manager

ECE 2015 meets with Irish success!

ECE 2015 was a huge success, attracting a record-breaking 3529 attendees and so making this year's Congress the largest ever. Along with a huge increase in abstracts (over 1700 submitted, again a record for ECE), there was a rise in ePoster uploads, highlighting the popularity of this new format.

The Congress was opened by the Republic of Ireland's Minister for Health, Leo Varadkar, who welcomed delegates. A lively performance followed from Brian Furlong, performing music by folk legend Pete St John, and accompanied by stunning traditional Irish dance group the Liffey Side Dancers (pictured).

The AGM was extremely well attended, and we thank all the members present for helping us ensure that ESE is run the way you want it to be. Saturday saw the introduction of the nurses' pre-Congress course on acromegaly: a great addition to the nurses' programme that ran throughout the rest of the Congress.

Among the many exciting lectures, Lewis Cantley (USA) presented a riveting talk on PI 3-kinase, and C Ronald Kahn (USA) delivered the Fondation Ipsen Prize Lecture on insulin signalling and action to a crowded auditorium. This year's debate around 'How to manage hyponatraemia according to guidelines' was as close as expected, with both Wim Van Biesen (Belgium) and Joseph Verbalis (USA) presenting compelling arguments. Ultimately, the voting showed a shift of opinion from the European guidelines towards the USA approach, an interesting result from an exciting debate.

We thank all involved in making the Congress so successful, particularly Wiebke Arlt, Jenny Visser and Felix Beuschlein, Chair and co-Chairs of the Programme Organising Committee, and Chris Thompson and Mark Sherlock, Chair and co-Chair of the Local Organising Committee.

Carl Djerassi 1923–2015


Image courtesy of the Chemical Heritage Foundation

Innovative chemist Carl Djerassi will be forever associated with norethisterone, a synthetic form of progesterone. Following its synthesis by his team in the 1950s, its oral effectiveness led to Gregory Pincus' creation of 'The Pill' that heralded the sexual revolution of the 1960s.

But Professor Djerassi's achievements were far more extensive. Throughout his career, Djerassi worked in industry. At CIBA he developed Pyribenzamine, one of the earliest anti-histamine preparations. Then at Syntex in Mexico he developed synthetic steroids, originally seeking therapies for arthritis. It was while working on corticosterone substitutes derived from diosgenin (from wild inedible yams) that he created norethisterone. In the late 1960s he formed Zoecon, a company which developed environmentally sensitive pest control using adapted insect growth hormones to block insect metamorphosis.

Alongside this career, Djerassi was also Professor of Chemistry at Wayne State University in Detroit, MI, USA, and later at Stanford University, CA, USA. At Stanford, he developed techniques such as mass spectrometry, which have been so important in the life sciences. He received many awards, notably both the US National Medal of Science (for his role in developing the contraceptive pill) and the US National Medal of Technology and Innovation (for his contributions to environmentally sensitive insect control).

Djerassi was an all-rounder, also excelling as a novelist, playwright and art collector. His death marks the passing of a truly remarkable man.

ESE President visits Portuguese Congress

The Portuguese Congress of Endocrinology 2015 took place in Funchal, Madeira, on 22–25 January.

ESE President Philippe Bouchard addressed the meeting, speaking about ESE, its 44 affiliated national societies and 10 specialty societies, and discussed ESE initiatives, such as ECAS (the ESE Council of Affiliated Societies) and EYES (the European Young Endocrine Scientists), as well as membership benefits. ECE 2017 is to be held in Lisbon (20–23 May 2017).

A symposium on type 1 diabetes in Africa followed. Participants from Angola, Cape Verde and Mozambique described the problems of access to insulin therapy. The participation of the ESE President on the discussion panel alongside Shaukat Sadikot, President-elect of the International Diabetes Federation, and Francisco George, the Portuguese Director-General of Health, should call attention to this issue.

NEW journal-based learning

ESE has worked closely with Bioscientifica, the publisher of *European Journal of Endocrinology*, to develop a new online journal-based learning programme, so supporting the education of clinicians-in-training and early career scientists, and to keep senior healthcare professionals up to date.

Selected articles now include questions written in collaboration with experts. Learners will get real-time scores, including explanations of the answers, and can download certificates of completion, which can be uploaded to their UK NHS ePortfolios to demonstrate learning.

The programme is free to use. You simply need to register at **http://bioscientifica.knowledgedirectweb.com.**

2nd Combo Endocrinology Course

1–4 October 2014, Viotia, Greece

Young doctors representing a variety of medical specialties from around the world gathered at the Evangelistria monastery. They were welcomed by Evanthia Diamanti-Kandarakis (President) and other internationally renowned endocrinologists.

Lectures discussed the topic systematically from diagnosis to management, considering future perspectives. The workshops were most challenging, where attendees analysed interesting cases under the supervision of experienced tutors, before becoming speakers in a virtual congress setting.

Opportunities to socialise with peers and experts arose during meal and coffee breaks, as well as at the traditional dinners with dance and music, and there was a very friendly atmosphere.

Thanks are due to Professor Diamanti-Kandarakis for organising this successful course, along with all the speakers and tutors. We look forward to the 3rd Combo Endocrinology Course on 1–3 October 2015 in Athens, focusing on sports endocrinology!

For more details see **www.comboendo.gr.**

EUROPIT 2014

24–26 November 2014, Annecy, France

The 4th European Multidisciplinary Postgraduate Course on Pituitary Tumours (EUROPIT) saw pathologist Jacqueline Trouillas, endocrinologist Márta Korbonits and neurosurgeon Michael Buchfelder once again gather physicians from all fields involved the care of patients with pituitary tumours: endocrinologists, neurosurgeons, oncologists and pathologists.

From a group of highly qualified candidates, 24 students were selected from 10 European countries. They were taken on an odyssey in pituitary science by over 20 of the most knowledgeable lecturers in the field. Diverse topics included mutation hotspots in Cushing's pituitary adenomas by Marily Theodoropoulou, and tips for writing a successful manuscript by Hans Romijn, as well as a hot debate on the controversy in radiotherapy between Fredric Castinetti and Albert Beckers.

The students presented a wide range of cases, leading to interesting discussions and, in some cases, new research collaborations. Best of all were the constant conversations between faculty and students during lunches and dinners!

After 3 intensive but rewarding days, the conclusion was obvious – co-operation between specialties is essential in improving the field of pituitary tumours! Don't forget to apply for EUROPIT 2015.

Daniel S Olsson
Sahlgrenska University Hospital, Sweden

Save the date
3rd EYES Annual Meeting
24–26 September 2015
Modena, Italy
Register now at:
www.eyes-meeting.eu

Your new EYES Board

At ECE 2015, Gefsi Mintziori replaced Dominik Schulte (Germany) as co-Chair of the EYES Board, and we welcomed new members Tatjana Isailovic and Elahu Sustarsic. We thank Dominik for all his work for EYES during his term of office. Your Board members are now Max Bielohuby (co-Chair, Germany), Gefsi Mintziori (co-Chair, Greece), Anneke van den Beukel (The Netherlands), Filip Gabalec (Czech Republic), Tatjana Isailovic (Serbia), Carmelo Quarta (Germany) and Elahu Sustarsic (Germany).

New Board members Elahu Sustarsic and Tatjana Isailovic

3rd Annual Meeting of EYES

24–26 September 2015, Modena, Italy

The EYES Annual Meeting is the occasion to promote networking between young endocrinologists in Europe. This year's meeting will feature areas from diabetes and obesity, through thyroid, reproductive, adrenal and bone disorders, to neuroendocrinology and endocrine tumours. The programme spans 3 days of oral abstract sessions, interest group discussions, special lectures and a workshop. The meeting is held in collaboration with EnGIoI, the Italian young endocrinologists.

Register now at www.eyes-meeting.eu! We look forward to seeing you in Modena.

Joining forces in sexual medicine

The 17th Congress of the European Society for Sexual Medicine (Copenhagen, Denmark, 5–7 February) was an opportunity for young endocrinologists to participate with young urologists, gynaecologists and psychiatrists in a round table discussion. Gefsi Mintziori represented EYES in this session with colleagues from the European Society of Residents in Urology (ESRU), the European Network of Trainees in Obstetrics and Gynaecology (ENTOG) and the European Federation of Psychiatric Trainees (EFPT).

Education in sexual medicine education was the primary objective, and this event was an excellent platform for young clinicians and scientists to discuss challenges, share ideas and learn from one another.

EYES on Madeira

Dominik Schulte represented EYES at a session on young endocrinologists' perspectives in Europe during the Portuguese Congress of Endocrinology 2015 in Funchal, Madeira, on 22–25 January.

Dominik's talk on 'ESE, EYES and co-operation' was followed by Catarina Moniz (Lisbon, Portugal) on 'Foreign internships during residency: advantages and challenges', and Mariana Martinho (Penafiel, Portugal) on 'Difficult clinical management in peripheral hospitals'.

Luís Cardoso (Chair of FinE, see right) was recommended as ambassador for Portugal on the EYES Committee, and the Portuguese Society of Endocrinology, Diabetes and Metabolism (SPEDM) agreed to support an application for the 2017 EYES meeting to be held in their country.

Fórum do Interno e do Jovem Endocrinologistà (FInE)

Translating as the 'Residents and Young Endocrinologists' Forum', FInE was founded in Portugal in 2013 under the patronage of the then President and Vice-President of the Portuguese Society of Endocrinology, Diabetes and Metabolism (SPEDM), Helena Cardoso and Margarida Bastos respectively.

FInE's main goals are to promote mutual exchange of knowledge between residents and young specialists, and to develop a fruitful environment where the difficulties of residents' training and young endocrinologists' careers can be addressed.

We are active in three main areas:
- endocrinology training
- young specialists' careers
- continuing medical education.

We strive for a uniform residency programme across Portugal by discussing training inequalities and suggesting improvements. Secondly, we endeavour to promote public awareness of the consequences of a 'sell-out' of endocrinology for patients and endocrinologists. FInE also organises a symposium at the annual meeting of SPEDM, and hopes to hold thematic courses and meetings.

Experiencing different scientific environments and networking are of upmost importance to early career endocrinologists, and we look forward to forming links with similar groups across Europe. In short, FInE is a platform where residents, young specialists and researchers share experiences, concerns and suggestions in a pleasant environment. The common ground is our will to share and co-operate in order to take endocrinology to the next level.

Luís Cardoso
Chair, FInE Committee

Four years on...

Basic Science within ESE

L–R: László Hunyady, Márta Korbonits, Wiebke Arlt, Maris Laan, Ilpo Huhtaniemi, Justo Castaño and Josef Koehrle at ECE 2015

The first ESE Science Committee was established 4 years ago, with myself as Chair and Wiebke Arlt, Justo Castaño, László Hunyady, Josef Koehrle, Maris Laan, Ruben Nogueiras and Philippe Bouchard (ESE President) as members. The Committee's remit was to strengthen basic science amongst ESE activities, and we should reflect now on our achievements.

Basic/translational science courses

ESE Summer School (Bregenz, Austria) is an annual workshop for young scientists, covering a new topic each year. It has been run by ESE since 2012.

Symposium on Hormones and Cell Regulation (Mont Ste Odile, France) has been co-organised by ESE for the last 4 years. It has taken place for 40 years and is of the highest scientific quality.

ESE Circulating Basic Science Course sees annual workshops on different topics in different European locations: neuroendocrinology in Amsterdam (2014), reproductive endocrinology in Edinburgh (2015), and metabolic aspects in Porto, Portugal (2016).

Grants for basic scientists

ESE Basic Science Meeting Grants enable early-career scientists to attend ESE events.

ESE Short-Term Fellowships allow early-career scientists to visit another laboratory group for 1 week–3 months, to perform experiments not possible in the home laboratory.

ESE Endo International Endocrine Scholars Programme provides funding and mentoring for talented early-career endocrinologists to attend ECE and to visit a laboratory for postdoctoral training.

European endocrine basic scientists' network

This discussion forum includes a basic science ambassador from each ESE affiliated society. It spreads information about ESE's basic science activities and generates ideas for new ESE initiatives.

So, many of the initial goals have been achieved, but challenges remain for the Committee, which will now be chaired by Márta Korbonits. I thank outgoing members László, Ruben and Wiebke for their invaluable contributions, and wish the new Committee the best of success.

Ilpo Huhtaniemi
Chair, ESE Science Committee

Clinical challenges:

Glancing backwards, looking forwards

As a newly elected Executive Committee member in 2011, I took the Chair of the new ESE Clinical Committee with some hesitation. However, looking back, I am most grateful for this rewarding opportunity. I was fortunate to recruit a group of outstanding endocrinologists, and am proud of what we have accomplished.

L–R: Pierre-François Plouin, Sofia Llahana, Martin Fassnacht, Olaf Dekkers, Pia Burman, Jens Bollerslev and Anton Luger in Dublin (Andrea Giustina (inset) and new member Claus Gravholt were unable to attend)

We have initiated European guidelines in areas where no consensus was available. Two will be finalised this year, on management of hypoparathyroidism, and management of adrenal incidentaloma. They will be published in *European Journal of Endocrinology* (EJE).

Special Interest Groups (SIGs) have been set up to address specific topics. The first, on polycystic ovary syndrome, presented their recommendations at ECE 2014. The second has dealt with phaeochromocytoma and paraganglioma, and the novel data, presented at ECE 2015, will provide a firm basis for recommendations on management. A third SIG on aggressive pituitary tumours has recently started work. The SIGs receive support for 3 years, and publish their work in EJE.

Development of symposia for endocrine nurses at ECE has been accompanied by formation of a dedicated nurse group, led by Sofia Llahana, to further extend nurse activities. I should also mention our co-operation with national Addison's disease support groups to provide a standardised European emergency card (see www.ese-hormones.org/professional).

I am convinced that the Clinical Committee will further contribute to improved, evidence-based management of patients with endocrine disorders across Europe. I wish the new Chair, Jérôme Bertherat, a warm welcome to a most dynamic group, and can promise 4 years of fun and stimulating work with the Committee!

Pia Burman
Chair, ESE Clinical Committee

Greetings from your new President

We welcome new ESE President, Professor AJ van der Lely, who took over the reins of the Society at ECE 2015 in Dublin. Here, he gives an insight into his view of the future of endocrinology and of ESE.

First, I thank all the ESE members who entrusted me with the role of President. It's really a great honour for me, and I am delighted to start working with an excellent Executive Committee, where I'll meet friends with great experience in serving ESE, as well as new members.

Here are just a few words to introduce myself. I'm 58 years old, and based at the Erasmus University Medical Center in Rotterdam, The Netherlands, where I am Vice-Chair of the Department of Medicine, and Chair of the Section of Endocrinology. I consider myself a clinical and translational endocrinologist, working in neuroendocrinology and endocrine gastroenterology.

I was Treasurer on the Executive Committee of ESE until 2013. With this experience in mind, I do think that the ESE is all set to meet enormous challenges as they arise.

A change of scene

For example, many new regulations will dictate how we collaborate with our sponsors. This will mean great changes to the scenery at congresses, as 'old style' exhibition areas will more or less disappear. Congress attendance is also under pressure, as many countries have changed the rules that allowed pharmaceutical companies to invite guests to congresses abroad. Moreover, the introduction on a large scale of web coverage of meetings might decrease attendance even further. But problems can be challenges as well, and under pressure we just have to perform better.

With an excellent Executive Committee, and with the professional and skilled support of the ESE Office, we must evolve into a modern, strong, international society. Finding new ways to collaborate with industry, in which we 'team-up' to develop teaching programmes for the multiple target populations of ESE, including endocrine patients, is just one example.

Mutual benefits

Another is the recent initiative to work better with ESE's affiliated societies, in the form of ECAS (the ESE Council of Affiliated Societies). This collaborative venture must evolve into a win–win situation, in which ESE, via ECAS, is better equipped to reach out to its members, and in which ECAS can use ESE as a perfect international platform.

ESE is a society with individual memberships, and I strongly believe it must remain so. We shouldn't go back to the EFES (European Federation of Endocrine Societies) structure. However, we are the biggest international endocrine society, as I see the Endocrine Society more as a national society with clear international ambitions. Being the biggest means we have a responsibility to act clearly as an international society.

Meeting members' needs

We must run high quality congresses, in the English language, of course. However, in addition, we should develop ways to provide our members with a more tailored approach when we organise events in their region. This might be by providing simultaneous translation and by handing out translated course materials. This would be another project in which ECAS would be instrumental.

Due to the ongoing scientific differentiation within endocrinology, spanning so many fields, ESE faces the challenge of acting as 'superglue' to hold these entities together as one impressive powerhouse. Our congresses and courses must address all these areas in a way that will keep bringing basic scientists and clinicians into our meetings.

I hope I have made it clear to you that the new Executive Committee is ready to address the multiple challenges that ESE will face. We will keep you updated via *ESE News* and other means and, for sure, we will see each other at the annual Congresses. Don't forget, we need you, dear friends!

AJ van der Lely
President, ESE

Background

AJ van der Lely serves, or has served, on the Editorial Boards of *Clinical Endocrinology, Journal of Endocrinological Investigation, Clinical Interventions in Aging, Journal of Clinical Endocrinology & Metabolism, Endocrinology,* and *Nature Reviews in Endocrinology.* He is Past-President of the Dutch Endocrine Society and Secretary of the European Union of Medical Specialists (UEMS), Section of Endocrinology.

Until mid-2013, he served as Treasurer of ESE, and until mid-2014 he was a member of the Executive Board of the International Society of Endocrinology.

He is also scientific adviser and co-founder of Alizé Pharma SAS in Lyon, France. This small biotech company is developing a des-acyl ghrelin analogue in phase 1–2 for two indications (diabetes and Prader-Willi syndrome). His main research areas are pituitary diseases and the role of gut hormones in health and disease.

The Endo Explorer

Gigantism: a mystery explained

The discovery of a new genomic cause of gigantism lay down a winding path, as travelled by Albert Beckers.

My interest in gigantism began about 30 years ago, and it is a problem to which I keep returning. Although pituitary gigantism is rare, I have come across several such patients in my career. The burden of their disease never fails to make an impression on me. I don't think that pituitary gigantism has been taken seriously enough in the past. As a rare disease, it has been difficult to study in depth, but the will and the means are now available.

A journey of discovery

I am particularly interested in pituitary tumours, their causes, their variable presentation and their epidemiology. Stemming from the discoveries of genetic causes of syndromic pituitary adenomas (e.g. *MEN1*), I defined a new population termed familial isolated pituitary adenomas (FIPA) as a clinical disease in the 1990s.

It would be nice to think that research takes a straight road from A to B, guided by GPS, but in reality you just have to follow where the results lead. Since that initial work on FIPA, we have had an interesting time with collaborators around the world, expanding upon and studying the cohort. Aaltonen's group discovered the role of the *AIP* gene in pituitary adenomas, which led us to study this gene in the FIPA setting and elsewhere.[1] These adenomas' characteristics led us to refocus on gigantism, once we found significantly more *AIP* mutated acromegaly patients were giants.

Characterising gigantism

By that time, our collaborative group had amassed data on dozens of patients with pituitary gigantism, and I felt it was time for the first specific in-depth study on its characteristics. Working with over 40 clinical centres and many national statistics authorities, we assembled more than 200 patients with pituitary gigantism. I look forward to sharing the final results soon.

While undertaking that study, we made a fascinating genetic discovery regarding a particularly dramatic form of pituitary gigantism. One of our closest research partners, Constantine Stratakis (NICHD, NIH, Bethesda, MD, USA) came to me with an unusual genetic finding in two kindreds with gigantism, one familial and one sporadic. This was a duplication at chromosome Xq26.3 spanning a region unreported in the setting of growth disorders at the time.

Compelling phenotype

Using our dataset, we looked for other instances of the same duplication, and were amazed to find multiple cases that allowed us to focus on a small region of four coding genes. Clinically, though, the phenotype was the most compelling element, as all the patients were young children (typically under 3 years), previously normal at disease onset, who then developed profound growth hormone and usually prolactin hypersecretion due to macroadenomas and/or hyperplasia. Most cases are sporadic and female, but two FIPA kindreds with mother to son transmission were identified, so I was happy we could explain part of FIPA's aetiology!

Since the original publication in *New England Journal of Medicine*,[2] together with Dr Stratakis and others, we continue to study patients (we have identified more than 20 cases) and further refine the phenotype that we termed X-linked acro-gigantism (X-LAG) syndrome. Recently, together with our colleague Wouter de Herder, we looked into the historical literature on gigantism and found many of the tallest humans had a pattern of disease matching X-LAG syndrome, including the tallest person recorded, Robert Pershing Wadlow (1918–1940).[3]

Over the last 15 years I have enjoyed delivering a lecture entitled 'The secret of giants and gigantism: a mystery explained'. I am glad we have elucidated part of the mystery, and I look forward to applying this knowledge to improve awareness and management of this unique disease.

Albert Beckers
Chief, Department of Endocrinology, CHU de Liège, Belgium

References

1. Beckers *et al.* 2013 *Endocrine Reviews* **34** 239–277.

2. Trivellin *et al.* 2014 *New England Journal of Medicine* **371** 2363–2374.

3. Beckers *et al.* 2015 *Endocrine-Related Cancer* **22** 353–367.

In this special issue on inheritance, The Endo Explorer visits two groups who have successfully explored the inheritance of endocrine disease.

Cushing's: a genetic conundrum

Martin Reincke reflects on his team's approach to a perplexing puzzle.

Fortuna fortes adjuvat: fortune favours the brave. When our team moved to the Ludwig-Maximilians-University in Munich in 2004, a close colleague quoted this old Latin proverb. He was encouraging us to look for the unexpected and to disrespect natural 'borders' in science. And so we did, but it was a couple of years before our brush with good fortune.

Ask big questions on important topics

Our lab had been dedicated to adrenal research for a long time, but in 2006 we decided to stop reacting to new hot topics discovered by others. Rather, we asked ourselves, 'What are the big open questions in adrenal disease or, more directly, which diseases are most neglected?'

Where could our research have the strongest impact? Our answer was primary aldosteronism. The screening tests were unreliable, subtype differentiation by adrenal vein sampling was a nightmare, and its pathophysiology was largely unknown. How could we overcome this? We thought we should first acknowledge that our care for patients with primary aldosteronism was unquestionably of low quality. So, with colleagues across Germany, we started a national patient registry and biobanking facility, and documented this clinical misery in publications.

Since 2009, all prospective patients diagnosed in eight centres in Germany and one in Poland have been documented (over 700 so far). Using the datasets and bioprobes we collected, we started hypothesis-driven research on the pathophysiology of primary aldosteronism. With the advent of exome sequencing, we had the tools to unravel the genetics of aldosterone-producing adenomas, and so we did.[1]

The Cushing's disease story

Subsequently, we began similar projects in other areas. We always started with an important research question, or a scientific *terra incognita*, or both. One question related to Cushing's disease, a dreadful syndrome characterised by increased body weight and fat accumulation at the trunk, elevated blood pressure, depression, infections, myopathy, decreased reproductive function and more.

We initiated a Cushing's registry in 2012, and were puzzled that the genetic events leading to corticotroph adenoma formation in Cushing's disease were still unknown. Clearly, because mutations did not occur in the known genes and pathways responsible for adrenocorticotrophin (ACTH) secretion, here was a *terra incognita* worth exploring.

The first step was collection of appropriate corticotroph tumour material and corresponding normal DNA by our team's neurosurgeon, Michael Buchfelder in Erlangen. Using exome sequencing on ten samples, Tim Strom from the Helmholtz Centre in Munich discovered recurrent somatic hotspot mutations in the ubiquitin-specific protease 8 (*USP8*) gene, which had never before been implicated in endocrine disease.

Over the next 18 months, main players from three labs (Silviu Sbiera, Martin Fassnacht and Felix Beuschlein from our lab, Marily Theodoropoulou from the Max Planck Institute for Psychiatry in Munich, and Masayuki Komada from the Tokyo Institute of Technology) dedicated most of their effort to unravelling the underlying pathophysiology of *USP8* mutations.[2]

In short, wild type USP8 recycles a key protein, epidermal growth factor receptor (EGFR), from the cellular sink, the lysosome. The newly identified mutations activate USP8 irreversibly, leading to uncontrolled recycling of EGFR and unrestrained production of ACTH. Elucidation of the genetic mechanism responsible for a significant fraction of cases of Cushing's disease provides a new diagnostic tool, and may lead to new approaches to treatment using USP8 inhibition.

A network of collaborators

To quote another proverb, success has many fathers! These were our excellent collaborators: colleagues at the German Cushing Registry (funded by the Else Kröner-Fresenius Stiftung), international and national research partners, and our European research consortium through the ERA-NET programme devoted to Cushing's syndrome, of which Felix Beuschlein and Martin Fassnacht are members. Many more people in our labs, often very young and extremely gifted, invaluably contributed to the project. And finally, needless to say, fortune favoured us: our competitors' paper was published 3 months later than our own.

Martin Reincke
Director, Medizinische Klinik und Poliklinik IV, Ludwig-Maximilians-University, Munich, Germany

References
1. Beuschlein *et al.* 2013 *Nature Genetics* **45** 440–444.
2. Reincke *et al.* 2015 *Nature Genetics* **47** 31–38.

L-R: (back) Mirjam, Paul, (front) Cornelis and Adriaan Lips

A family active in clinical endocrinology:

predisposition, common interest, or both?

Several members of our family share a common interest in the history of enlightenment and endocrinology: developments by observation, rationalism, tolerance, boundless curiosity and dedication. Despite this, there does not appear to be a specific gene responsible for predisposition to endocrinology!

Endocrine roots

Our father Adriaan Lips (b 1907) was a physician (internist) interested in metabolic processes. His thesis on the effects of eating on metabolism was entitled 'Contribution to the knowledge of specific dynamic action of nutrients'. It involved animal studies on the effects of nutrients on metabolism and the nervous system by spirometry. He admired the French physiologist Claude Bernard (1813–1878), and often cited him, 'The biological integrity of the human body is more than the sum of specific components'. This concept would later lead to discovery of hormones that mediate the cross-talk in the body and regulate homeostasis.

Immediately after the Second World War, he travelled to the USA with a colleague to report medical developments, and wrote a monograph 'Progress in medicine during 1940–1945'. He predicted the importance of endocrinology and biochemistry, and said he would have studied biochemistry if he had to choose again, but that he would have missed his patients. He did not direct us into internal medicine, but his example and principles may have guided us.

A growing interest

The two of us, Cornelis and Paul, followed very different pathways to endocrinology.

Cornelis (b 1940) performed studies on hereditary endocrine tumour syndromes. From 1972, he detected several families with multiple endocrine neoplasia (MEN), writing a thesis 'The MEN syndrome type 2A in a large family in The Netherlands' (1978). Later, his work involved metabolic and molecular biological studies into the genetics of such syndromes. These showed that hereditary tumour syndromes have comparable mechanisms of activation of proto-oncogenes or inactivation of suppressor genes by germline mutations. The life expectancy and quality of life in these hereditary tumour syndromes have increased considerably.

Paul (b 1952) became interested in the consequences of hip fractures after seeing patients in a nursing home during an internship. He wrote a thesis 'Metabolic causes and prevention of femoral neck fractures' (1982) involving vitamin D metabolism, bone histomorphometry of iliac crest biopsies and possible pathophysiological clues. Subsequently, he was involved in epidemiological studies on vitamin D, the effects of hormones and mechanical forces on bone, and clinical trials in osteoporosis and with vitamin D.

We were both involved in training young doctors in endocrinology at the end of specialisation in internal medicine. We have incidentally collaborated on parathyroid function tests and published together. We have common cultural interests and both enjoy the good things of life.

Fresh shoots

Family trends are continuing with Mirjam (b 1982) whose thesis (2014) was on 'Roux-en-Y gastric bypass and calorie restriction: differences and similarities of endocrine and metabolic effects in obesity and type 2 diabetes mellitus'. A nephew, Alexander (b 1988), is currently studying medicine after graduating in biomedical sciences.

Our personal histories have been paralleled by developments in medical science. Collaboration between clinicians and basic scientists has been fruitful. Specific, responsible disease gene mutations are identified, progress in healthcare is obtained through investigation, and targeted treatment is available. Prevention will further improve life expectancy and quality of life. On the other hand, a philosophical attitude, with discussion of social values, is worthwhile in decreasing patients' isolation and dependency. Psychologists will support individual patients. The next generation may solve some of the medical, philosophical and social questions that remain open.

In summary, in our family, observation, rationalism and dedication, as well as boundless curiosity in clinical endocrinology, were general characteristics. A familial predisposition is not proven. We realise that collaboration with our colleagues, active in clinical and basic science, was worthwhile and provided an extra dimension. In addition, we are grateful to our patients who were always partners in all activities.

Nature, nurture, or both? The family environment, setting examples, and developments in translational and clinical endocrinology may have been the common pathway in our lives.

Cornelis J Lips
formerly at University Medical Center Utrecht, The Netherlands

Paul Lips
VU University Medical Center, Amsterdam, The Netherlands

Lecture videos coming soon at
www.ece2015.org!

New Executive Committee Members

We welcome two new members to the ESE Executive Committee.

Jérôme Bertherat is Professor of Endocrinology at Paris Descartes University and Chief of the Endocrinology Department, Cochin Hospital. He is Head of the National Centre for Rare Adrenal Diseases and his research team at the Cochin Institute is studying genomics and signalling in endocrine tumours, with a particular interest in Cushing's syndrome and familial adrenal tumours.

Márta Korbonits is co-Centre Head of the Department of Endocrinology at Barts and the London School of Medicine. Her interests include hormonal regulation of the metabolic enzyme AMP-activated protein kinase and pituitary tumours, including familial cases. She has a large collection of familial isolated pituitary adenoma families and works on the clinical characterisation and molecular aspects of this disease.

Prize lecturers at ECE 2015

Carlos Dieguez

Geoffrey Harris Prize Lecturer

'Understanding energy sensors, understanding neuroendocrine function'

Carlos Dieguez is based at the University of Santiago de Compostela in Spain where he is Professor of Physiology and Director of the Centre of Investigation into Molecular Medicine and Chronic Diseases. Over the last 15 years, his group has focused on the physiopathology of obesity at the hypothalamic level, including the regulation and neuroendocrine actions of ghrelin and leptin and the discovery of new potential drug targets.

Robert Semple

***European Journal of Endocrinology* Prize Lecturer**

'Insulin action in common metabolic disease: too little, too much, or both?'

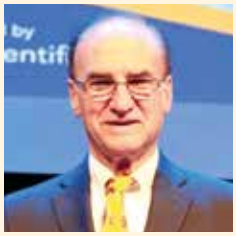
Wellcome Trust Senior Research Fellow and Honorary Consultant Endocrinologist at the University of Cambridge, UK, Robert Semple aims to identify novel genetic defects underlying insulin resistance and related conditions, to improve diagnosis and treatment of patients, and to draw inferences, through physiological studies, about the pathobiology of common forms of metabolic disease.

Sir Stephen O'Rahilly

European Hormone Medal Lecturer

'Obesity and insulin resistance: lessons from human genetics'

Professor O'Rahilly is Director of the University of Cambridge Metabolic Research Laboratories and of the MRC Metabolic Diseases Unit, Cambridge, UK. His research with Sadaf Farooqi, Tony Coll and Giles Yeo focuses on disorders of energy balance. They examine the causes of highly penetrant forms of human obesity, and how more common genetic variants predispose to common forms of obesity. A further collaboration with David Savage and Robert Semple examines mechanisms of human insulin resistance and the metabolic syndrome.



C Ronald Kahn

Fondation Ipsen Prize Lecturer

'Insulin signalling and action'

C Ronald Kahn is Chief Academic Officer at Joslin Diabetes Center, and Mary K Iacocca Professor of Medicine at Harvard Medical School, Boston, MA, USA. His research includes alterations in insulin signalling in diabetes, obesity and insulin-resistant states; how different adipose depots affect metabolism; and the impact of genes, ageing and the environment on these processes.

Andrew Hattersley

Clinical Endocrinology Trust Award Lecturer

'From base change to better care in diabetes'

Andrew Hattersley is Professor of Molecular Medicine and Consultant Physician at the University of Exeter, UK. As well as defining the genetic aetiology of monogenic diabetes, Professor Hattersley's research on the genes involved in neonatal diabetes, and on maturity onset diabetes of the young, has led to revision of guidelines for their management. He co-led UK research on genetic polymorphisms predisposing to type 2 diabetes, and is investigating personalised treatment for that disorder.

Congratulations to all our award winners at ECE 2015

Young Investigator Award winners

Maha Al-Asmakh (Qatar), Anna Angelouisi (USA), Shobhit Bhansali (India), Ludivine Drougat (France), Sjoerd Joustra (The Netherlands), Takuya Kikuchi (Japan), Julika Lietzow (Germany), Olaia Martinez-Iglesias (Spain), Luis Gustavo Perez-Rivas (Germany), Andrew Powlson (UK), Maria Estrella Sanchez Rebordelo (Spain), Daniele Santi (Italy)

Poster Prize winners

Cornelie Andela (The Netherlands), Yacir Benomar (France), Antonia Brooke (UK), Daniela Fernandois (Chile), Jonathan Hazlehurst (UK), Johannes Hofland (UK/The Netherlands), Philip Johnston (USA), Tim Korevaar (The Netherlands), Avigdor Learner (UK), Aristides López Márquez (Spain), Jonathan Mueller (UK), Silviu Sbiera (Germany), Hyekyoung Sung (Canada), Alexia Vinel (France), Isabel Weigand (Germany), Leon Wert-Lamas (Spain)

ESE Endo International Endocrine Scholars

L–R: Stavroula A Paschou (Greece), Silvia Leon Tellez (Spain), Lisa Owens (Ireland), Alejandro Ibáñez Costa (Spain), with Wiebke Arlt (Chair, second right). 2014 winner Mora Murri (Spain) also gave a presentation at ECE 2015.

Honorary Members & Special Recognition Award winners

L-R: New Honorary Members Furio Pacini, Eberhard Nieschlag and Andrzej Milewicz with AJ van der Lely (ESE President, second left). Martin Schlumberger was unable to attend. In addition, Professor Nieschlag and Fotios Pavlatos (not present) received Special Recognition Awards.

Save the Dates!

ESE Summer School
2–6 August 2015
Bregenz, Austria

2nd Translational ESE Bone Course
17–18 September 2015
Brescia, Italy

3rd EYES Annual Meeting
24–26 September 2015
Modena, Italy

40th Symposium on Hormones and Cell Regulation (ESE)
8–11 October 2015
Mont Ste Odile, France

EndoBridge 2015
15–18 October 2015
Antalya, Turkey

17th ESE Postgraduate Course on Endocrinology, Diabetes and Metabolism
19–22 November 2015
Tirana, Albania

7th ESE Clinical Update
15–16 January 2016
Abu Dhabi, UAE

3rd ESE Basic Endocrinology Course
17–19 February 2016
Porto, Portugal

18th European Congress of Endocrinology (ECE 2016)
28 May–1 June 2016
Munich, Germany

Deadlines:

30 August 2015
40th Symposium on Hormones and Cell Regulation (ESE)
– registration deadline

31 August 2015
Endobridge 2015 – abstract deadline

30 September 2015
ESE Small Meetings Grants
– application deadline

30 November 2015
ESE Short-Term Fellowships
– application deadline

1 December 2015
3rd ESE Basic Endocrinology Course
– abstract deadline

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