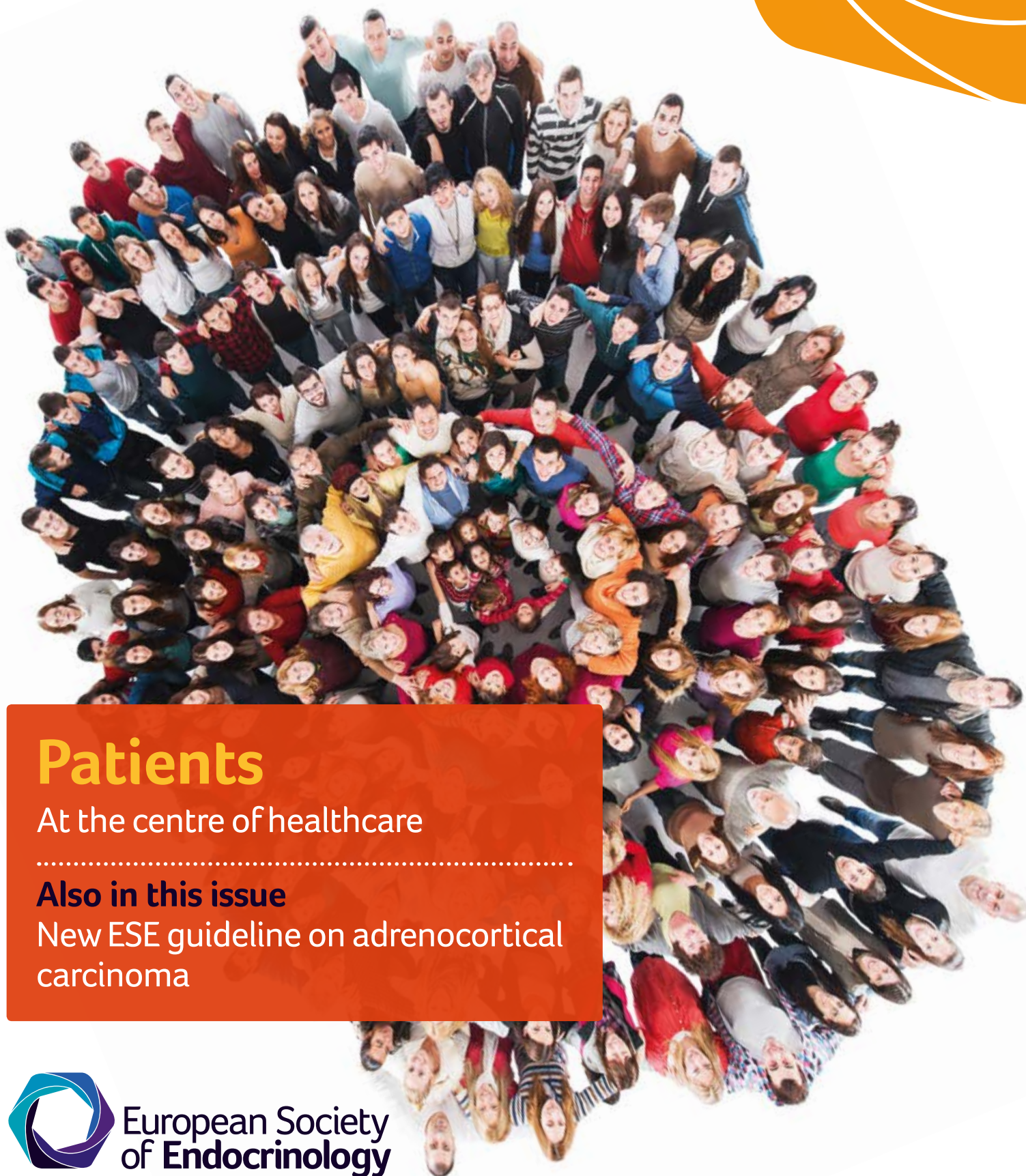


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ESE News

The newsletter of the European Society of Endocrinology

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Patients

At the centre of healthcare

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New ESE guideline on adrenocortical carcinoma



European Society
of Endocrinology



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Editor:

Wouter de Herder, The Netherlands
Email: w.w.deherder@erasmusmc.nl

Co-Editor:

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

Editorial Board:

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

Sub-Editor: Caroline Brewer

Design: Qube Design Associates

Website: www.e-se-hormones.org

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Editorial



Patients – none of our endeavours would have any purpose if it were not for patients. As members of ESE, we might spend our time elucidating complex molecular mechanisms in a lab, or identifying the most appropriate treatment protocols in the consulting room, or employing specialist nursing skills in the clinic, but in all circumstances the goal is to improve our patients' well-being.

Consequently, it is essential that we understand how the world looks from our patients' perspectives. I am sure we all think we do this as a matter of course, but this issue of *ESE News* sets out to examine the work of several people for whom 'the patient perspective' provides a particularly significant focus for their activities.

'Quality of life' is a phrase we hear increasingly often. On page 8, Alicia Santos, Elena Valassi and Susan Webb discuss the growth of this area of investigation, how to choose the best methods of making measurements, and the resulting benefits for both patient and physician.

Perhaps unsurprisingly, there can often be gaps in communication between patients and healthcare providers. Do we sometimes assume that patients have better access to information than is actually the case? How do we deal with misinformation? On page 10, Teodora Kolarova of the International Neuroendocrine Cancer Alliance (INCA) examines ways of filling the gaps and building the relationship.

On page 11, Anne-Paule Gimenez-Roqueplo explains how communication with patients in the course of genetic counselling has inspired her group's research, and boosted the transfer of findings into clinical practice.

Johan Beun provides us with an insight into his daily life on page 15. Johan is the very busy co-ordinator of AdrenalNET (a digital network for adrenal patients and their healthcare providers), as well as having lived with Addison's disease for many years. His story shows just how much difference an empowered patient can make!

The issue would not be complete without Wouter de Herder providing us with an enlightening view of the physician-patient relationship from a historical perspective. On page 14, he tells the story of Aidan Carney's search for Harvey Cushing's patient 'Minnie G'. As always, there is an interesting twist in the tale...

Finally, I am delighted to report that another ESE Clinical Guideline has just been published, this time on adrenocortical carcinoma. Martin Fassnacht and Massimo Terzolo tell us more on page 12.

Enjoy this issue – I hope it inspires you to think about our patients in a new light!

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



1st Expert Workshop on Parathyroid Disorders

Santpoort,
The Netherlands,
6–7 September 2018

The 2015 launch of ESE's clinical practice guideline on treatment of chronic hypoparathyroidism in adults (*European Journal of Endocrinology* 173 G1–G20) stimulated renewed interest in parathyroid disorders. The ESE PARAT Programme has been established to assess the new developments in our understanding and the treatment options available. Its recommendations will promote best clinical practice and education.

The programme comprises a 4-year plan for expert meetings, educational materials, research activities and publications. Led by the PARAT Steering Committee,



chaired by Jens Bollerslev (Norway), it will be supported by the ESE Focus Area on Calcium and Bone and the wider parathyroid community.

The 1st Expert Workshop on Parathyroid Disorders brought

together 30 key leaders and experts from the parathyroid field, including endocrinologists, surgeons, pathologists and researchers. The meeting focused on parathyroid cancers, primary hyperparathyroidism and

hypoparathyroidism, and aimed to identify challenges in diagnosis and management. This workshop's outcomes will inform the development of future activities.

To learn more, see www.ese-hormones.org/research/parat.

ESE Short-Term Fellowship Grants Deadline 30 November 2018

This ESE Grant aims to promote scientific collaboration between members of ESE. It funds research visits of between 1 week and 3 months for early career members (covering economy class travel and subsistence of the Fellow only, not research costs or costs associated with dependents).

Each Short-Term Fellowship Grant is worth up to €2500 and is awarded for exchanges between two laboratories in different countries only. The next deadline for applications is 30 November 2018.



For full details and eligibility criteria see www.ese-hormones.org/grants-and-awards/grants/short-term-fellowship-grants.

Remember to renew!



Renew your membership of ESE and stay at the centre of the European endocrine community. Here are just a few of the benefits of membership:

- Free online access to all ESE's official journals
- Reduced rate registration for ECE and other ESE events
- 40% discount on Open Access publishing in *Endocrine Connections*
- Access to ESE's wide range of grants and awards
- Networking with a membership representing over 20 000 European endocrinologists
- News updates via our email alerts and tri-annual newsletter delivered straight to your inbox
- Access to the latest science from ECE via ECE on Demand.

Members of any of ESE's National Affiliated Societies receive a discount of up to 50% on their ESE membership fees.

Renew online today: see www.ese-hormones.org/about-us/membership for full details.

ESE Adult Growth Hormone Deficiency Audit

ESE's 2-year pan-European Adult Growth Hormone Deficiency (AGHD) audit project aims to collate AGHD patient data from participating centres and to analyse, at local, national

and European levels, the best treatment practices now and in the future.

The AGHD Audit began in June 2018 across 50 countries and is led by Susan Webb of Sant Pau

Hospital, Barcelona, Spain.

Data will be captured by November 2018 to generate an interim report of findings from each participant centre. The wider sample data will

be analysed to provide two publication submissions in late 2019.

To find out more see www.ese-hormones.org/research/aghhd-audit.



Brexit's effect on European Reference Networks

In July, the UK's All Party Parliamentary Group (APPG) on Rare, Genetic and Undiagnosed Conditions held a meeting on the effect of Brexit on European Reference Networks (ERNs).



Genetic Alliance UK (www.geneticalliance.org.uk) led this briefing to the UK Parliament, in order to produce a statement outlining the detrimental effects that Brexit could have on patient care if negotiations do not provide for UK healthcare providers to continue to be part of ERNs once the UK leaves the EU.

Amongst the many eminent speakers was Márta Korbonits, Adult Chair of the Research & Science Work Package on the Endo-ERN and ESE's Scientific Programme Chair, who also represented the Biomed

Alliance (of which ESE is an active member). She highlighted that continued collaboration between the UK and the EU-27 is of paramount importance in continuing to advance rare disease research and patient care, commenting:

'The number of patients affected by a rare disease is often too small to be studied in isolation in any one country, so research collaboration is critical to provide the best care for patients. If the NHS stops taking part in ERNs, we risk patient disadvantage in the UK and also in Europe.'

Alongside rare disease medicine regulation and access, and research funding and regulation, Genetic Alliance UK has identified ERNs as one of the crucial EU initiatives that may suffer if the UK's terms for exiting the EU do not take special account of issues for people affected by rare diseases.

You can read Genetic Alliance UK's ERN statement at www.protect-erns.eu/ern-statement. You'll also find links there to case studies and, importantly, to sign the ERN petition (see below).



(L-R) Speakers Márta Korbonits, Helen Cross and Avril Daly with Genetic Alliance UK trustee Rafael Yáñez-Muñoz

Show your support for ERNs

Genetic Alliance UK are campaigning to allow knowledge about rare diseases to continue to be shared across European borders.

Help protect ERNs from the potential effects of Brexit. Sign the petition now at www.protect-erns.eu.

From the ESE Office

Much of our work over the last few months has focused on our increasing participation in policy and advocacy activities. For example, we recently responded to the development of Horizon Europe (the successor to Horizon 2020), to support the amendment to include rare disease in children as an important area.

Policy and advocacy constitute a huge area, potentially absorbing a significant amount of resource and budget. To ensure we represent you properly, and direct our efforts in the right way, we will soon be asking for your feedback through our 'Mapping Endocrinology in Europe' project. We aim to build a clearer picture of endocrinology as a discipline, its impact, and how it varies across our region.

The project's success will depend greatly on as many of you as possible completing the survey. Please look out for it and encourage your colleagues to do so too. You can find more information on page 5.

Activities leading towards our next congress – ECE 2019 in Lyon, France – are already building. The Programme Organising Committee has put together a great programme. You can find out more at www.ece2019.org, where there is plenty of information to entice you! Make sure you save 18–21 May 2019 for what is shaping up to be a fantastic meeting.

I hope you are having a wonderful autumn. Do get in touch at any time at helen.gregson@ese-hormones.org.

Helen Gregson
Chief Executive Officer, ESE



Let us hear your views!

ESE's survey will build a important picture of endocrinology in Europe



Attendees at ESE's first meeting with Members of the European Parliament in March 2018

ESE has a mission to shape the future of endocrinology, which means we must liaise with European policymakers to ensure your voices are heard.

The importance of conditions such as obesity, diabetes, osteoporosis, reproductive disorders and many rare diseases means endocrinologists have a central role in addressing a significant part of society's healthcare and financial burden. However, our discipline remains poorly understood by both

policymakers and the public, especially compared with areas such as oncology and cardiology.

Education, accreditation, access to medicine, research funding, rare diseases and guidelines are just some of the factors affecting the future of endocrinology and our patients. Our existing

engagement with Horizon Europe, the Biomed Alliance and the debate surrounding endocrine-disrupting chemicals already goes some way towards improving these areas, but we want to do more.

With your help, we can develop the necessary tools to demonstrate endocrinology's importance, including a 'White Paper': an authoritative report to inform readers concisely about the issues involved and to

present ESE's philosophy.

We will shortly be seeking your views through a survey. It will aim to gather the views of all ESE members, ESE's National Affiliated Societies and the members of those societies, in order to compile this crucial 'White Paper' and inform ongoing advocacy and policy work.

Please watch out for the survey and make sure that you and your colleagues reply, so that your voices are heard.

We all have something that makes us grand

This summer, an exciting photo project by the Spanish Association of Patients with Acromegaly used stunning images of patients with the condition to raise awareness of the disease.

The project was endorsed by the Spanish Society of Endocrinology and Nutrition Foundation and the Biomedical Research Networking Centre for Rare Diseases (CIBERER), and supported by endocrinologists Cristina Álvarez Escolá, Sonia Gaztambide, Javier Salvador,

Eugenia Resmini and Alfonso Soto, as well as Ipsen, Novartis and Pfizer.

Acromegaly affects more than 3000 people in Spain. Using patients' portraits and personal objects, the exhibition, entitled 'We all have something that makes us grand', publicised the disease with the aim of reducing the average time to diagnosis, currently estimated at 6 years.

You can find out more (in Spanish) at: www.tengoacromegalia.es/todos-tenemos-algo-que-nos-hace-grandes.



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Working with patients in mind

ESE's Clinical Committee always bears in mind that its ultimate, ambitious goal is to improve the situation for patients with endocrine diseases. To achieve this, we aim on one hand to integrate patients' perspectives into the activities we develop for health professionals, and on the other hand to interact directly with patients and produce material for them and their relatives.

The assessment of patients' quality of life has been the focus of much clinical research in endocrinology. For the patients, this is clearly a significant parameter which they can perceive directly, in contrast to the medical parameters monitored by their physician.



Studies of quality of life relating to various endocrine diseases have been very helpful in identifying patients' needs. Such studies have contributed to our understanding that medical parameters, although of paramount importance, are not always enough to really evaluate the consequences of a disease and the outcome of treatment.

In Cushing's syndrome, the European Register on Cushing's Syndrome (ERCUSYN, which is owned by ESE and supported by the Clinical Committee) addressed this important issue (see also pages 8–9). The results were central to realising how much quality of life is altered in this disease, despite successful treatment.

We also view ESE guidelines as major tools in improving the care of patients with endocrine diseases, and we now aim to integrate quality of life as a major end point in our guidelines. Future guidelines will be developed systematically with the participation of the patients' representatives, to ensure patients' views are taken into account.

Guidelines are developed primarily for healthcare professionals, but patient leaflets will now be produced as accompanying material. These constitute important educational materials for patients and relatives, enabling the active and fruitful involvement of the patients in the management of their diseases.

Jérôme Bertherat
Chair, Clinical Committee

Supporting Early Career Clinical Endocrinologists

Our second Early Career Clinical Endocrinologists Session is taking place as this issue of *ESE News* is published, alongside EndoBridge 2018 in Antalya, Turkey.

The first session, during last year's EndoBridge, was developed through the ESE Council of Affiliated Societies (ECAS) as a workshop reviewing the aims, expectations, challenges and threats faced by early career clinical endocrinologists. It discussed how European endocrinology should advance, from their perspective.

Early career representatives of 16 National Affiliated Societies and of EYES (the European Young Endocrine Scientists) took part in the session, which examined:

- the current situation in education and career development
- the support offered by the National Affiliated Societies and ESE
- expectations for the future of clinical endocrinology.

Amongst the conclusions, delegates said they would welcome more educational and



career support from the Societies, with increased opportunities to take part in meetings. In addition to the support currently offered by ESE, they sought practical help, including opportunities for self assessment and greater access to clinical cases, webinars and postgraduate course content.

They felt that improved visibility of institutions where they could gain experience, better access to mentors, opportunities to develop practical skills, and training in writing grant applications and papers would all be beneficial, with more specialist education located in tertiary centres rather than small hospitals.

Participants looked forward to the field growing, with improved diagnosis and clinical care, increased European collaboration, and a more harmonised education structure. Concerns surrounded the limited number of opportunities for education, and a lack of career security. Delegates also wanted more forums to discuss opportunities and projects.

This year's session is focusing on communication between endocrinologists and healthcare professionals, specifically:

- referral from primary care to an endocrine unit
- shared care between primary

- care and endocrinology
- dismissal from an endocrine unit back to primary care
- referral from an endocrinologist working in the community to a hospital endocrine unit
- collaboration between endocrinology and related specialities.

Representatives of each of the National Affiliated Societies will join leading experts, looking at how the Societies and ESE can best support early career clinical endocrinologists and patients.

Watch out for updates in future issues of *ESE News*.



Wonderful international friends

6th EYES Meeting, Poznań, Poland, 31 August–2 September 2018

As August became September, the weather in Poland was surprisingly warm and, in turn, we warmly welcomed the participants of the 6th Meeting of European Young Endocrine Scientists (EYES). The meeting was supported by ESE and the Polish Society of Endocrinology and attracted participants from 12 European countries, with interests across both basic and clinical research.

Before the regular sessions began, participants could take part in practical workshops: one for clinicians (thyroid ultrasound) and two for researchers (transcriptomic and genomic studies in endocrinology).

The role of genetics in contemporary endocrinology was also the subject of the first invited lecturer, Katarzyna Ziemnicka (Poland). Torquil Watt (Denmark) presented a plenary lecture on the development and use of quality of life assessment tools in thyroid diseases.

Participants were able to present their own results in sessions covering a broad range of topics (thyroid, pituitary and gynaecological endocrinology, to name a few). These saw a broad audience and, as is traditional at EYES meetings, each ended with a vivid discussion. Every delegate could find a subject of particular interest. There was also space for

exciting case reports, molecular biology experiments and next-generation sequencing studies.

Beata Małachowska (Poland) was the recipient of the award for Best Oral Presentation (see below), for her survey of lysophosphatidic acid among patients with HNF1B-MODY syndrome.

During the meeting, there was also time to discover the city of Poznań, with its unique 'Eastern energy, Western style' atmosphere.

EYES meetings are unique in many aspects. As one of the participants commented, 'You come once and you will not miss the next.' They provide a

eyes 
european young
endocrine scientists
looking forward

truly open forum where young endocrinology enthusiasts with diverse backgrounds have the opportunity for endless, inspiring and fruitful discussions. They start in the conference room and finish late in the night. They allow us to get closer to each other and are an excellent environment for making new friends and forging future collaborations.

Thank you Poznań and the local team of organisers!

Adam Czyżyk
Local Organising Committee

Meeting Beata

Beata Małachowska won the Best Oral Presentation award at EYES 2018. She is a fourth year PhD student at the Department of Biostatistics and Translational Medicine (Medical University of Łódź) and Postgraduate School of Molecular Medicine (Medical University of Warsaw), Poland, under the supervision of Wojciech Fendler.

We were curious to know a little bit more about her and her work, so Ljiljana Marina of EYES asked Beata a few questions.

Tell us about your background

I graduated in 2014 from the Medical University of Łódź. To advance my skills in research methodology, I have undertaken several postgraduate courses. My research started in 2011 at the Polish Registry for Pediatric and Adolescent Diabetes project, co-ordinated by Wojciech Młynarski – a leader in the field of paediatric diabetology in Poland. I continued working in this field, with a particular focus on HNF1B-MODY and its pathogenesis. I also expanded my skills into the field of transcriptomic biomarkers.

What is your area of interest?

The title of my PhD thesis is 'Metabolomic profiling of acute diabetes complications among children with type 1 diabetes', which investigates the use of metabolomics studies



in paediatric diabetes. My current research includes the use of advanced biostatistics, data-mining algorithms and bioinformatics tools for data processing combined with molecular biology and high-throughput data.

Was this your first EYES meeting?

Yes, and I was really amazed by the high level of research projects and the great

organisation of the conference. I was very surprised that my work was selected as the Best Oral Presentation, as there were many other interesting research projects and great presentations during the conference.

Will you be coming to EYES 2019?

I hope I will be able to attend the meeting next year, not only to present my new research project but also to see all the people I've met in Poznań.

How do you see yourself in the future?

I hope to still work on diabetes projects, but it would also be exciting to switch to a different topic and focus more on computational biology.



Quality of life

Its importance in treating our patients

In recent decades, quality of life has received growing interest from the medical community. A PubMed search shows that 27 907 articles on quality of life were published in 2017, and numbers seem to rise progressively every year (see Figure).

This increasing interest also applies to clinical practice. Even if clinical and laboratory tests give us essential information on the course of a disease, we would be missing part of the picture if we did not take into account the patient perspective and outcome, by measuring quality of life.

What is quality of life?

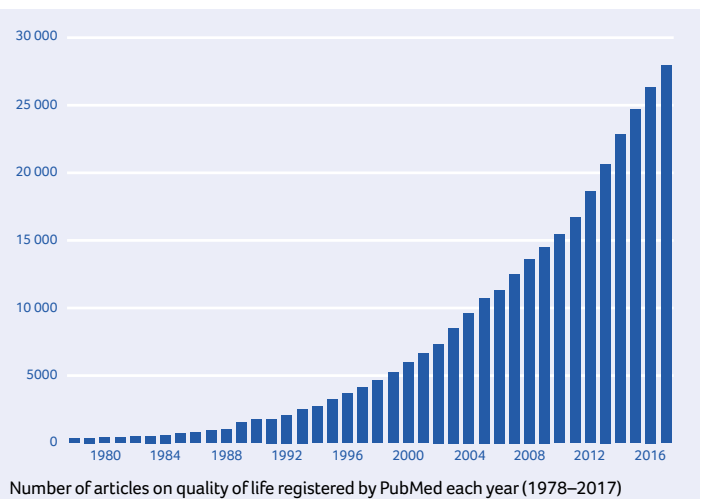
According to the World Health Organization (WHO), quality of life is defined as 'an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'.¹ Therefore, quality of life is a personal perception, which will differ between people with the same clinical conditions. Taking into account quality of life information can help clinicians better understand the worries and needs of each individual patient and even adjust clinical management.

How is quality of life measured?

Many methods are available to measure quality of life. What is important is to use tools that are validated and have shown good psychometric properties.

Questionnaires can be easy to use and administer in clinical practice. They can be divided into generic questionnaires (which may be used in any disease or in healthy individuals) and specific questionnaires (developed to evaluate the specific quality of life aspects of a certain disorder).

Furthermore, there are those which, even if they may not be directly considered quality of life questionnaires, can measure specific domains which can have an important impact on quality of life (such as depression, fatigue, sexual function and pain).





How can this better help our patients?

Using quality of life questionnaires in daily practice can improve our understanding of patients and enable us to focus on those aspects that are most important for each particular individual in daily life. Quality of life assessment can also help healthcare providers to register (and therefore manage) some aspects that otherwise might be missed during clinical follow-up (mood alterations, pain or sleep problems, for instance).

It can also improve the patient-clinician relationship. This is more important than one would think, as a better relationship may have a positive effect on health outcome.²

Including a short quality of life evaluation in daily practice and registering it in clinical files can also help us to better evaluate the patient's clinical course and compare changes from one visit to another. This can provide positive encouragement for patients, informing them about their improvement, or enable us to focus on and explore aspects which may worsen from one follow up to the next.

Choosing the best technique

The selection of the method to use may vary depending on the particular patient and the time available to devote to them. If disease-specific tools are available, it is best to use them (alone or combined with a generic approach), as they collect information about specific aspects of the disease which generic methods may not consider. On the other hand, if a particular problem is suspected (such as depression), a domain-specific questionnaire may be used as a screening tool to establish if the patient needs further evaluation or treatment.

Even if there is a tendency to focus on and only register total scores when using questionnaires, in clinical practice the answers to specific items can be particularly helpful in understanding a patient's status and to make decisions on management. For instance, if a patient states, when completing the generic questionnaire EuroQoL5D, that they have extreme pain and discomfort, or that they are extremely anxious or depressed, this may require further evaluation (and treatment if necessary).

How does research help to predict quality of life outcome?

The growing literature on quality of life can help us to better understand a patient's perspective, to identify patients at higher risk of suffering from low quality of life and, therefore, to provide early treatment or complementary interventions if necessary.

Of course, it is important to remember that each single individual is different and the general conclusions from studies may differ from what we find in a particular case, so we need to be cautious.

An example of recent research

One recent study that focused on quality of life featured a large cohort of patients with Cushing's syndrome.³ It included data on 595 patients from the European Register on Cushing's Syndrome (ERCUSYN), a prospective database collecting information on management, diagnosis, health-related quality of life and long term follow up.

Quality of life data were analysed in patients with Cushing's syndrome of pituitary (PIT-CS, 71%) and adrenal (ADR-CS, 29%) origin at three time points: (a) at diagnosis (baseline), (b) at the first post-operative visit and (c) at last follow up. Patients completed two quality of life questionnaires: the generic EuroQoL and/or the disease-specific CushingQoL (developed to assess quality of life in patients with Cushing's syndrome).

'Quality of life assessment can also help healthcare providers to register (and therefore manage) some aspects that otherwise might be missed during clinical follow-up'

'Quality of life is a personal perception, which will differ between people with the same clinical conditions'

Whereas there was no difference in quality of life scores between PIT-CS and ADR-CS patients at baseline, the former scored worse on three specific items in the CushingQoL questionnaire (pain, wound healing and physical appearance) within 1 year of surgery. This finding suggests that psychophysical status in PIT-CS patients may take longer to recover than in ADR-CS patients. At last follow up, after a median of 38 months, PIT-CS patients had lower total CushingQoL score, and scored worse on four CushingQoL items when compared with ADR-CS patients, including leisure time, every day activities, memory and worries about future health. However, when only patients in remission were analysed, no differences in any of the quality of life parameters were observed between the PIT-CS and ADR-CS subjects. Indeed, remission was the single most important predictor of beneficial outcome for the CushingQoL questionnaire in the entire series, indicating that hypercortisolism per se is the main reason for quality of life impairment in Cushing's syndrome, regardless of aetiology.

Of note, presence of depression at diagnosis was also associated with a worse total CushingQoL score at last clinical visit, indicating affective disorders' role as main determinants of long-lasting impaired well-being, even when remission is achieved. Older age was also associated with poorer quality of life.

Alicia Santos, Elena Valassi and Susan M Webb

Endocrinology/Medicine Departments, Hospital Sant Pau, and Universitat Autònoma de Barcelona, Spain



REFERENCES

1. World Health Organization 1993 *Quality of Life Research* 2 153–159.
2. Kelley et al. 2014 *PLoS One* 9 e94207.
3. Valassi et al. 2018 *Clinical Endocrinology* 88 787–798.



Patient advocacy

Working with healthcare providers to close the gaps

Patient advocacy groups have an essential role to play, working in partnership with the medical community to identify issues and improve diagnosis, care and research. The quality of communication between the patient and the medical team has an enormous impact on the quality of care. Understanding each other's perspective is the key.

This is even more important in a complicated disease setting such as the world of neuroendocrine tumours (NETs), where collaboration is of instrumental significance.

Collaboration is the principle underlying the work of the International Neuroendocrine Cancer Alliance (INCA): the global voice in support of NET patients. INCA is an umbrella organisation representing 20 patient advocacy and research groups from around the world.

Addressing differences in perception

Employing its network and effective partnership with the medical community, INCA recently championed a survey to identify unmet needs and align patient and medical points of view. The survey included 443 patients and their families (338 respondents), patient advocates (35 respondents) and healthcare professionals (70 respondents) from 26 different countries. Many differences in perception between patients and healthcare professionals surfaced.

These were subsequently addressed at the joint patient–physician symposium during the European Neuroendocrine Tumor Society Conference. This constituted a significant step forward, as historically patients had not been actively involved in such meetings.

An unmet need for information

In this digital era, many patients are ready and well-equipped to better understand their disease, and the amount of misinformation that is available is of great concern. It is therefore crucial that all NET patients are provided with accessible and accurate information at different stages of their disease pathway. The INCA survey identified a significant unmet need for information that is easy to understand, with most patients finding general information on NETs on patient association websites.¹

Informed patients can be active partners in the management of their disease, and this triggers improved outcomes. However, in the INCA survey, 84% of patients reported that their needs for information about treatment options were not fully met at the time of diagnosis and there was an obvious discrepancy between the perspectives of patients/

patient advocates and healthcare professionals about the quality of information provision.

Patient involvement in research

Notably, there was, however, a shared view among all three groups of survey respondents that patients were not involved enough in NET research at the design stage. All groups thought that neuroendocrine cancer research was under-resourced in comparison with other forms of cancer research.

Greater involvement of patients in research is bound to yield many benefits for both patients and researchers, including:

- a better understanding of patient priorities and their expectations from NET research
- consideration of how it feels to be involved in research as an individual patient, looking at the practical impact on everyday life
- improved communication and understanding of research programmes, clinical trials and their results through the use of lay language
- more effective advocacy regarding the need for funding for NET research to potential funders: governments, non-profit organisations and individuals
- better awareness of important clinical trials within the patient community, so increasing enrolment and improving patient knowledge of treatments in development.

Collaboration between patient and clinical leaders to get patients more involved in the process of agreeing research priorities, and advocating for more research funding, builds a compelling argument which is set to make change happen.

Adopting a patient-centred approach

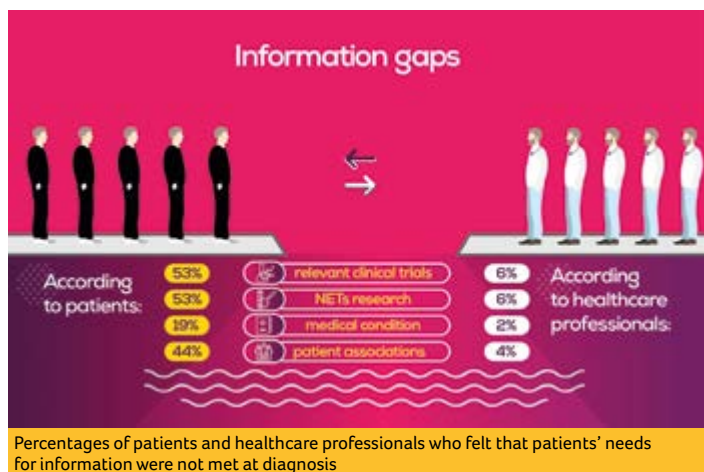
Like the European Reference Network (ERN) on Rare Endocrine Conditions (Endo-ERN), ERN-EURACAN (the ERN for Rare Adult Solid Cancers) has the concept of European Patient Advocacy Groups (ePAGs) embedded in its structure. Hence, ePAG representatives work to make sure the patient perspective is reflected in the ERN's decisions. Ten experienced patient advocates currently serve as ePAG representatives within ERN-EURACAN. The exchange of perspectives and experience between these ePAG members and the various healthcare providers dedicated to rare solid cancers is very constructive and enlightening.

In summary, global co-operation between NET patient organisations and medical communities may achieve greater influence on all fronts where there are major gaps in fulfilling the informational needs of patients, ensuring access to the highest standards of care and facilitating patient involvement in research.

Teodora Kolarova

Executive Director, INCA

www.incalliance.org and www.netcancerday.org



REFERENCE

1. INCA 2017 *Unmet Needs in the Global NETs Patient Community* www.incalliance.org/wp-content/uploads/2016/08/2017-11-08-UnmetNeeds_in_the_global_NETs_community.pdf.



The Endo Explorer

Counselling patients in genetic disease



Anne-Paule Gimenez-Roqueplo with her colleagues

Anne-Paule Gimenez-Roqueplo's group in Paris, France, has worked on the genetics of pheochromocytoma and paraganglioma (PPGL) for 15 years. Communication with patients and genetic counselling form a crucial part of their work, as she relates.

The number of known PPGL susceptibility genes has dramatically increased from 3 in the 1990s to more than 15 today. Around 40% of patients with PPGL carry a germline mutation in one of these genes. The ESE guidelines¹ recommend offering a genetic test to every patient affected by the disease.

Over the last 15 years, we have led fundamental and clinical research programmes in this area and published papers in high impact journals. We have, however, always kept in mind the importance of quickly translating our research findings into routine practice at the Department of Genetics in the Georges Pompidou European Hospital (HEGP) in Paris.

Meeting the needs of patients

In 2002, we founded an oncogenetic clinic for patients with rare cancers, including neuroendocrine tumours, led by a multidisciplinary team. This is open to at-risk patients and their families.

During an initial consultation, patients meet a geneticist or genetic counsellor to learn the consequences for them and their relatives should a causative mutation in a susceptibility gene be identified. Then, they meet a psychiatrist or psychologist to discuss the potential psychological impact of a positive or negative result, to be best prepared for the results.

After both consultations, if patients decide to proceed with the genetic test, they sign an informed consent form, and the blood sampling is performed and sent to the Molecular Genetics Laboratory at HEGP.

Defining the results

In the lab, we have developed an innovative method for PPGL genetic testing, based on a custom panel which allows sequencing (by next generation sequencing) of all the main PPGL genes in both germline and tumour DNA. The biological interpretation of identified genetic variations can be tricky. So, we have also established complementary methods to prove whether or not the identified variation is the causative mutation, responsible for the disease.

Once the definitive result of the genetic test is determined, it is explained to the patient during in a further consultation. Mutation carriers are directed to a referral centre with appropriate expertise to ensure a favourable outcome.

Who uses our service?

Our multidisciplinary team has performed more than 4000 consultations since opening. Patients fall into three categories:

1. Recently diagnosed patients

The first group comprises patients recently diagnosed with PPGL, whose physicians would like to know their genetic status. Indeed, a positive genetic status is of major importance in patient management, because the identification of a mutation may carry a higher risk of development of new tumours or metastases. The geneticist looks for personal and clinical information relating to a specific predisposition syndrome during the patients' interviews.

2. Relatives of those with PPGL

Our clinic is also attended by asymptomatic individuals who have a first degree relative with a PPGL where PPGL genetic testing has identified a causative mutation. Because mutations in PPGL susceptibility genes are transmitted along an autosomal dominant inheritance pattern, the risk of carrying a paternal or maternal mutation is 50% for offspring. The geneticist explains the consequences of a positive result, which comprises the outcome of initial screening including biological and imagery tests, and of long term surveillance.

3. Possible child carriers

So far, we have received more than 90 children who are at risk of carrying a mutation in one PPGL susceptibility gene. In a preparatory consultation, we talk to both parents to define together how and when the test would be carried out. We also explain to the parents the means, adapted to the age group, for informing their child.

After a reflection period, when both parents agree to proceed and have informed their child, we receive the children during a second consultation. We take the time needed to respond to their questions before the blood sampling. The result of the test is given to the child in presence of both parents. If it is positive, the child will be quickly directed to a specialised endocrinological paediatric centre.

Empowering patients and physicians

Our practice of PPGL genetic counselling has surely put patients and physicians in a stronger position for the management of such rare genetically determined neuroendocrine tumours. In addition, because we meet affected patients and families weekly for years, this approach has inspired our research and greatly boosted the transfer of our significant findings into clinical practice and real life.

Anne-Paule Gimenez-Roqueplo

Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Department of Genetics, Paris Descartes University, France

REFERENCE

1. Plouin *et al.* 2016 *European Journal of Endocrinology* 174 G1–G10.



Adrenocortical carcinoma: the latest ESE guideline



ESE's latest clinical practice guideline addresses adrenocortical carcinoma (ACC).¹ While these tumours are rare, they are highly aggressive and no truly evidence-based guidelines were available. Guidance was therefore urgently needed, as chairs of the guideline panel Martin Fassnacht and Massimo Terzolo explain.

Adrenocortical carcinoma is a rare cancer with an annual incidence of about 1 per million, meaning just 750 cases per year across all the countries of Europe.

About 50–60% of these patients present with autonomous adrenal hormone excess (mostly Cushing's syndrome, androgen excess or a mixture) and 30–40% suffer pain or abdominal discomfort due to the abdominal mass (the average size of the tumour is about 11 cm). An increasing number of cases (10–15%) are diagnosed as adrenal incidentalomas.

In general, clinical outcome is poor with a median overall survival of about 3–4 years. However, prognosis is heterogeneous (even within a given tumour stage) and prognostication is challenging.

Surgery is well established as first line therapy in localised ACC. However, many other questions in the management of this tumour remain unanswered. Therefore, and because Europe traditionally leads in clinical research on adrenal tumours, in 2016, ESE's Clinical Committee decided to address this issue as the next clinical practice guideline.

Just as for the recent adrenal incidentaloma guideline,² the European Network for the Study of Adrenal Tumors (ENSAT) was invited to join forces with ESE, and we were asked to gather an interdisciplinary expert group.

Multidisciplinary working is key

As adrenal tumour researchers in Europe and around the world are well connected, it was quite easy to find ten experts across five disciplines (endocrinology, surgery, oncology, pathology and epidemiology) who were willing to establish the first evidence-based guideline for ACC (see photo).

We also involved the European Society of Endocrine Surgeons, the Endocrine Society, the European Society of Pathology, the American–Australian–Asian Adrenal Alliance (A5), the European Reference Network on Rare Endocrine Conditions (Endo-ERN) and the European Reference Network on Rare Adult Solid Cancers (ERN-EURACAN), all of whom finally endorsed the guideline.

The importance of interdisciplinary teamwork is also demonstrated by the first and perhaps most important single recommendation. Here it says: 'We recommend that all patients with suspected or proven ACC are discussed in a multidisciplinary expert team meeting (including healthcare providers experienced in the care of adrenal

tumours, including at least the following disciplines: endocrinology, oncology, pathology, radiology and surgery) ... In addition, this team should have access to adrenal-specific expertise in interventional radiology, radiation therapy, nuclear medicine and genetics, as well as to palliative care teams.'

The key open questions

At the beginning of the guideline development process, we discussed the different clinical scenarios in which guidance is needed. During the first face-to-face meeting of the guideline panel in November 2016 in Birmingham, UK, we established a list of 30 important clinical questions in the management of patients with ACC that the guidelines needed to address.

The next step involved us agreeing on the four most relevant overarching clinical questions, for which a detailed literature search and review were subsequently performed. These questions were:

- Pathology: what is needed to diagnose an ACC?
- Which are the best prognostic markers in ACC?
- Is adjuvant therapy able to prevent recurrent disease or reduce mortality after radical resection?
- What is the best treatment option for macroscopically incompletely resected, recurrent or metastatic disease?

With the help of Olaf Dekkers (The Netherlands), endocrinologist and experienced ESE guideline methodological expert, we systematically reviewed the literature according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system. The first search revealed 5988 papers, of which 111 studies (including only 2 randomised studies) finally met the predefined inclusion criteria and could be included in the analyses.

'Adrenocortical carcinoma can be a devastating condition in some patients. As we have concluded in compiling the guidance, a multidisciplinary team with broad expertise is crucial for the best clinical outcome. However, for true progress, we require more clinical and translational research'



What are the key recommendations?

By means of many telephone and email conversations and after two additional meetings (in Frankfurt, Germany (September 2017) and Leiden, The Netherlands (March 2018)) we were able to come up with a total of 61 recommendations. Consensus was reached upon discussion; minority positions were taken into account in the rationale that accompanied every recommendation.

Apart from the need for a multidisciplinary expert team meeting, which we have already mentioned, the following recommendations are central:

- (1) Every patient with (suspected) ACC should undergo careful clinical assessment, a detailed endocrine work-up to identify autonomous hormone excess, and adrenal-focused imaging.
- (2) An adrenal mass suspected to be an ACC should be resected only by surgeons experienced in adrenal and oncological surgery, and requires a review afterwards by an expert adrenal pathologist.
- (3) The subgroup of patients most likely to benefit from adjuvant therapy with mitotane has been defined (e.g. ACCs with at least one of the following: ENSAT stage III, or R1 resection, or Ki67 > 10%).
- (4) In advanced ACC not amenable to complete surgical resection, local therapeutic measures (e.g. radiation therapy, radiofrequency ablation, chemoembolisation) are of particular value, because adrenal surgery is usually not helpful in the case of widespread metastatic disease. In these patients, we recommend either mitotane monotherapy or mitotane, etoposide, doxorubicin, and cisplatin, depending on the proposed prognostic parameters.

We also offer recommendations about tumour staging, prognostic factors, genetic testing, management of mitotane treatment, salvage therapies and other supportive measures. Finally, we suggest directions for future research.

The review process

After drafting a first version, the guidelines were open for review. We asked three clinicians with particular expertise in ACC (Mouhammed Habra (USA), Electron Kebebew (USA) and Britt Skogseid (Sweden)) for their expert opinions and all members of ESE and ENSAT, as well as patient representatives, for their comments. In addition, we presented the guidelines at ECE 2018 in Barcelona.

At end of July 2018, the guidelines were accepted for publication in *European Journal of Endocrinology* and made available online as a preprint. All the comments of the different reviewers as well as our responses are available as supplementary data in the online version of the guidelines.

We thank the Clinical Committee of ESE for giving us the chance to chair this challenging, but very interesting, endeavour. We are grateful to everybody who commented on the guidelines and particularly to our great team of guideline panellists.

It is undeniable that ACC can be a devastating condition in some patients. As we have concluded in compiling the guidance, a multidisciplinary team with broad expertise is crucial for the best clinical outcome. However, for true progress, we require more clinical and translational research on this rare aggressive disease.

Martin Fassnacht

University of Würzburg, Germany

Massimo Terzolo

University of Turin, Italy

REFERENCES

1. Fassnacht et al. 2018 *European Journal of Endocrinology* **179** G1–G46.
2. Fassnacht et al. 2016 *European Journal of Endocrinology* **175** G1–G34.



The ESE–ENSAT guideline panel: (L–R) Alfredo Berruti (Italy), Olaf Dekkers (The Netherlands), Radu Mihai (UK), Massimo Terzolo (Italy), Harm Haak (The Netherlands), Ronald de Krijger (The Netherlands), Tobias Else (USA), Eric Baudin (France), Guillaume Assie (France) and Martin Fassnacht (Germany)



Whatever happened to Minnie G?

Aidan Carney hunted for Cushing's first patient. Now, in a surprising turn of events, it appears that Cushing documented an early case of Carney complex...

Carney complex (CNC) is characterised by myxomas of the heart and skin, hyperpigmentation of the skin (lentiginosis) and endocrine overactivity. It may present with clinical features of Cushing's syndrome due to (adrenocorticotrophin-independent) primary pigmented nodular adrenocortical disease.

CNC has been linked to mutations in the regulatory subunit of the protein kinase A type I-alpha (*PRKAR1A*) gene. It was reported for the first time in 1985 by the Irish-born pathologist Aidan Carney, who was working in the Mayo Clinic in Rochester, MN, USA.¹

Carney meets Cushing

In 1995, Aidan Carney also tracked down and re-analysed the first case of Cushing's syndrome, as reported by and named after the famous neurosurgeon Harvey Williams Cushing (1869–1939).²

In his 1912 monograph, *The Pituitary Body and its Disorders, Clinical States produced by Disorders of the Hypophysis Cerebri*,³ Harvey Cushing describes a case of a 23-year-old woman MG, later to become

known as Minnie G, but whose correct first name was in fact Maita.

She was born in Ukraine in 1887 and had emigrated with her family to the USA in 1906. For at least 7 years she had presented with a spectrum of unusual features, which are nowadays easily recognisable as the signs and symptoms of Cushing's syndrome, before she was referred to Cushing at the John Hopkins Hospital in Baltimore, MD, USA, in 1910.

Radiography of the skull showed 'a somewhat thinned-out sella of normal configuration but of small size' (= 0.9x1cm). Cushing attributed her disorder to presumptive 'basophil hyperpituitarism'. He performed a subtemporal decompression of low grade hydrocephalus and attempted to explore the interpeduncular area.

After her discharge from the hospital, Cushing never saw her again, but he was regularly updated on her clinical condition, either by the patient herself or by physicians who were taking care of her. On the basis of this information, Cushing stated for the last time in 1932 that Minnie G was 'in reasonably good



Harvey Cushing's patient Minnie (Maita) G at presentation. Reproduced from Cushing 1912 *The Pituitary Body and its Disorders, Clinical States produced by Disorders of the Hypophysis Cerebri*. Philadelphia, PA, USA: JB Lippincott Company.

health, though some stigmata of her malady still persist'.⁴

Aidan Carney found out that Minnie G died in 1958 in Brooklyn, NY, USA, at the age of 70. Quite surprisingly, atherosclerotic heart disease was recorded as the cause of death, and no mention of Cushing's syndrome was given. An autopsy was never performed.

He also concluded from the information in the medical records, as well as from information provided by Minnie G's family members, that the Cushing's syndrome in Minnie G, although ameliorated, had persisted until her death. Harvey Cushing had never removed a (basophil) pituitary tumour from Minnie G. The cause of Cushing's syndrome in Minnie G will forever remain a mystery.

Cushing meets Carney

Interestingly, in 2017, the team of Maya Lodish at the NIH, Bethesda, MD, USA, together with researchers from Yale University, New Haven, CT, USA, examined the post-mortem material of a 34-year-old acromegalic male patient (GBS) described in 1914 by Harvey Cushing with a clinical

presentation and post-mortem findings suggestive of CNC.⁵ They discovered and reported (more than a century after surgery had been performed by Cushing) a mutation in the *PRKAR1A* gene.

So it would appear that Carney and Cushing have each encountered the other – although I am sure they never met in real life!

Wouter de Herder

Editor, *ESE News*
Erasmus MC, Rotterdam,
The Netherlands

REFERENCES

1. Carney *et al.* 1985 *Medicine (Baltimore)* **64** 270–283.
2. Carney 1995 *American Journal of Surgical Pathology* **19** 100–108.
3. Cushing 1912 *The Pituitary Body and its Disorders, Clinical States produced by Disorders of the Hypophysis Cerebri*. Philadelphia, PA, USA: JB Lippincott Company.
4. Cushing 1932 *Bulletin of the Johns Hopkins Hospital* **50** 137–195.
5. Tsay *et al.* 2017 *Journal of the Endocrine Society* **1** 1312–1321.

Also see:

Cushing 1913 *Peter Bent Brigham Hospital Surgical Service Notes* 21. Yale School of Medicine, New Haven, CT, USA: Cushing Brain Tumor Registry.



A day in the life of...

...a healthcare network co-ordinator



07.30

Beep! Beep! The alarm goes off. In less than a second, a dozen tasks go through my mind. But first I must take my hydrocortisone tablets to get this old body working. I have suffered from Addison's disease for 44 years, and the start of the day is still difficult. Then I pick up my iPad and check the healthcare news.

Problems fly across the screen: medicines which aren't covered by insurance anymore, eHealth packages failing to get introduced, and an email from a patient who can't find the doctor they need! I have work to do.

08.30

BijnierNET (www.bijniernet.nl) is a national, digital community for people with adrenal gland disorders and their healthcare providers. We regularly receive emails from patients seeking assistance – often people who have been receiving hospital treatment for some time, but who aren't doing very well.

Unfortunately, not all internal medicine specialists/ endocrinologists have noted the new Quality of Care Standard for Adrenal Disorders (www.endo-ern.eu/wp-content/uploads/2018/06/20180604-samenvatting-kwaliteitstandaard-UK.pdf). Patients turn to BijnierNET as a last resort. We try to advise them, so their conversation with

their endocrinologist can be meaningful. In some cases, we suggest they switch to one of the designated centres of expertise.

09.30

The first meeting of the day begins, through Skype. It is with a representative of a fund which might support BijnierNET. It's important we have the financial means to carry out at least basic activities. These include publishing a blog (at least 44 times per year), maintaining the website (which has received over 30 000 unique visitors so far in 2018), and enabling the board to discuss healthcare innovations.

The blog helps keep attention focused on the fact that there's always room for improvement in the care provided to those with an adrenal gland condition. By working together, internal medicine specialists/ endocrinologists, specialist nurses and patients can make that a reality.

After the meeting, I have to write a report to formulate a successful request for a grant.

11.00

Mail! This email is one that I hadn't expected. The SOS cards in Denmark have run out, and we must get more printed, quickly. I need a quote from the printer, and to make sure that the partners accept the financial consequences. Every country in Europe has issues like this, on the path to making innovations in adrenal care a reality.

Many more emails to the printer follow, then mails to Denmark, Sweden and the Dutch Adrenal Society NVACP (www.bijniervereniging-nvacp.nl; the patients' organisation), so that the information in their web shop can be updated.

It's time for a cup of coffee and some hydrocortisone tablets for my afternoon dose.

13.00

I meet with the developers of the AdrenalApp, which has been downloaded over 3500 times, and is a great tool for people with an adrenal gland condition. Last week we discussed its new 'diary' feature with a psychologist. This lets people register how they feel from day to day (human memory isn't the most reliable record).

The latest version enables people to complete a questionnaire at intervals that suit their schedule and that of their healthcare provider(s). The data can be saved in PDF format, better informing discussions between patients and endocrinologists, and so enabling more accurate assessment of requirements for medication and psychological support, etc.

The diary function will soon be rolled out in Germany and Denmark, in conjunction with our partner organisations (Addison Foreningen i Danmark and the Deutsche Gesellschaft für Endokrinologie).

15.00

Back in the car, I recall the a young patient with congenital adrenal hyperplasia (CAH) who once said, 'Johan, you're no help to me!' I wonder if she's more satisfied with our work now?

She told me there wasn't enough information for young people with adrenal gland insufficiency, which led us to create a series of animated video clips. Now our YouTube channel has been expanded with mini-documentaries, featuring parents of children with CAH, work which was only made possible by securing a grant.

The young lady will be well into puberty by now. But how is she doing, and what do she and her fellow teenagers need from us to make a smooth transition to adult care? A concerned mother recently told us that her daughter won't take her emergency bag when she goes out. It's too big – it won't fit in her bra. I really hadn't thought of that during the design phase!

There is evidently much to do to help young people lead a normal life. I'm stuck in traffic, and take the opportunity to call my team members and exchange ideas about the transition from child to adult care.

17.00

Another Skype meeting, this time with international colleagues in Denmark, Germany and Norway. The achievements of small groups like this in the last 2–3 years are amazing. Meeting the needs of adrenal patients requires us to work beyond our own borders and not in silos. Global action in healthcare is what's needed, please.

17.30

Finally, I prepare for a plenary training day for nurses next week. Together with our medical universities, we created an eLearning programme so that nurses could become more familiar with adrenal diseases. Nearly 100 have trained in the last 12 months – a great success. But there's always so much more to do!

Johan G Beun
Co-ordinator,
BijnierNET/AdrenalNET

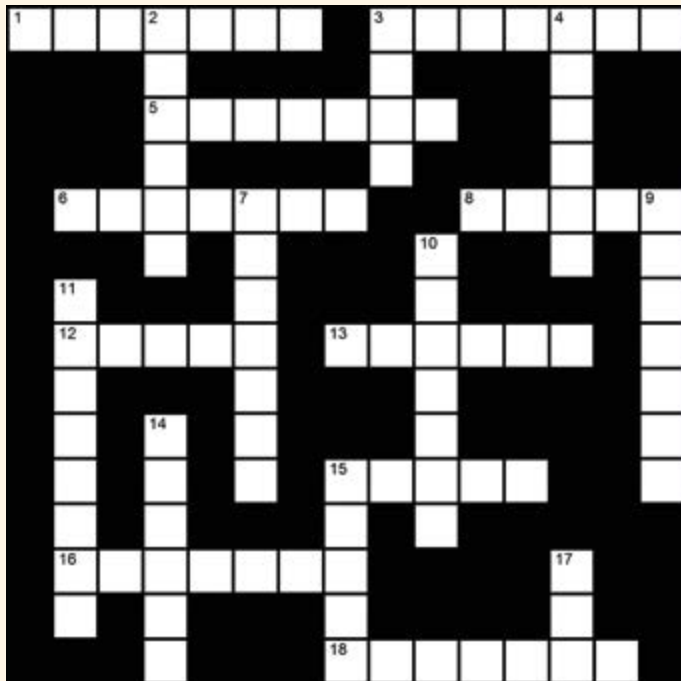
Please visit www.bijniernet.nl or www.adrenals.eu (the international hub) or email info@adrenals.eu. Many thanks to Jacqueline and Peggy for their support.



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.



Congratulations

Our winner from issue 36 was Christoph Haudum (Austria).

Answers to the puzzle in issue 36

Across 3. Fallopio, 5. Robert, 7. Ghrelin, 9. Nikola, 1. Tesla, 12. PMS, 14. Boyle, 15. Gabriello, 18. Stiles, 19. MRSA, 20. Stevia

Down 1. Crooked, 2. Hirsutism, 4. Laser, 6. Ankyloglossia, 8. PCOS, 10. Ankylosis, 11. Threonine, 13. Scab, 16. AMH, 17. Ezra

This issue's solutions are all famous patients in endocrinology.

Across

- 1 This famous writer and patient co-founded Diabetes UK (1,1,5)
- 3 See 4 down
- 5 See 11 down
- 6 See 12 across
- 8 See 14 down
- 12 **and 6 across** Talk show host with thyroid disease who received the Presidential Medal of Freedom (5,7)
- 13 **and 18 across** A German Chancellor with thyroid disease who recorded a Mozart piano concerto (6,7)
- 15 **and 2 down** Swedish actress who suffers from osteoporosis (5,6)
- 16 See 4 down
- 18 See 13 across

Down

- 2 See 15 across
- 3 See 7 down
- 4 **and 3 & 16 across** A learning disability campaigner with Addison's disease, sister to a US President (6,7,7)
- 7 **and 3 down** This patient with gigantism starred in two Bond films (7,4)
- 9 See 17 down
- 10 See 15 down
- 11 **and 5 across** 19th century French artist believed to have had pycnodysostosis (8-7)
- 14 **and 8 across** Film director exempted from military service due to type 2 diabetes (6,5)
- 15 **and 10 down** Russian President with hypothyroidism (5,7)
- 17 **and 9 down** After surgery for thyroid cancer, this rock star sings an octave lower (3,7)

Did you know?



The world's tallest patients

Robert Pershing Wadlow (USA, 1918-1940) is still considered to be the tallest man who ever lived, at 272cm (8ft 11.1in). Sultan Kösen (born Turkey, 1982) is the tallest living man, at 251cm (8ft 2.8 in). Both were/are acromegalic giants.

Over the past two decades, our increasing understanding of the molecular and genetic aetiologies of pituitary gigantism and acromegaly have yielded several genetic causes, including multiple endocrine neoplasia types 1 and 4, McCune-Albright syndrome, Carney complex, familial isolated pituitary adenoma (*AIP* gene mutations), pituitary adenoma association due to defects in familial succinate dehydrogenase and *MAX* genes, and the recently identified X-linked acrogigantism.



Save the date

For more information about any ESE event see www.e-se-hormones.org.

23rd ESE Postgraduate Training Course on Endocrinology, Diabetes and Metabolism

8-11 November 2018

Minsk, Belarus

Europit 2018

14-17 November 2018

Anney, France

6th Serbian Congress of Endocrinology

18-21 November 2018

Belgrade, Serbia

6th Slovenian Congress of Endocrinology

22-24 November 2018

Bled, Slovenia

Pituitary Society Workshop – Updates in Pituitary Tumor Diagnosis & Management

28-30 November 2018

Stellenbosch, South Africa

ICE 2018

1-4 December 2018

Cape Town, South Africa

11th ESE Clinical Update

11-12 January 2019

Abu Dhabi, UAE

12th International Conference on Advanced Technologies & Treatments for Diabetes (ATTD 2019)

20-23 February 2019

Berlin, Germany

21st European Congress of Endocrinology

18-21 May 2019

Lyon, France

Deadlines

30 November 2018

ESE Short-Term Fellowship

Application deadline