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ESE News

The newsletter of the European Society of Endocrinology

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Post-truth: a return to quackery?

Why we must all stand up for science

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Turner syndrome

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

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Editor:

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

Co-Editor:

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

Editorial Board:

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

Sub-Editor: Caroline Brewer

Design: Qube Design Associates

Website: www.e-se-hormones.org

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Editorial



How did we find ourselves in this situation? How has this 'post-truth' era come about? Just a decade or two ago, we would not have believed that people could so quickly become cynical about evidence-based science, or that the power of public opinion would outweigh carefully calculated truth. Yet, here we are, and it is time we took a stand in support of our way of life as endocrine scientists.

The theme of this issue of *ESE News* therefore 'takes the bull by the horns' as we urge you all, as scientists and as members of ESE, to make your voices heard. Endocrinology and the rest of medical science needs each of us to play a part in explaining to policymakers and the public why science is the only proven truth, why it matters, and why it is the key to a healthy future for us all.

On page 8, I am joined by Professor Andrea Giustina (ESE's new President-Elect) as we examine the importance of evidence-based medicine and its foundations in the peer review process, and how these are being undermined. Meanwhile, Olaf Dekkers, a master of methodology, explains the role of rigorous design in excellent scientific studies on page 10. On page 12, Claus Gravholt introduces us to a recent example of scientific excellence, in the form of the new ESE guideline on Turner syndrome.

Fortunately, help is available to us in our quest to explain science to the wider world, and first and foremost we can call upon the services of ESE's own Media Office. On page 15, Communications Manager Lynsey Forsyth explains the many ways her team can support us in ensuring that research news is accurately reported by the media. Please see her article for ways you can benefit and get involved.

Finally, what if (dare I suggest it) we return to a world where belief counts for more than proven fact? On page 14, Wouter de Herder reminds us of more tales of dubious 'science' from the past. If that isn't enough to spur us into taking action in support of our research, I am not sure what is. So I urge you all to stand up for science today and every day, as we make our voices heard.

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

In keeping with the theme of this issue, the cover illustration is from 'The Extraction of the Stone of Madness' by Hieronymus Bosch (c1450–1516). An early form of fake science, it shows a surgeon 'curing madness' by appearing to remove a stone from the brain of the sufferer. Bosch used the funnel hat symbolically to indicate that the surgeon was a charlatan. The original painting is at the Museo Nacional del Prado, Madrid, Spain. Cover image: ©Museo Nacional del Prado.



Championing science: a pillar of freedom and prosperity

On 22 April 2017, the 'March for Science' saw more than 1 million people around the world united in support of science.

They marched in over 600 cities to defend science's role in our lives, sharing one common goal: to champion science for the common good. Although the march has ended, the movement continues, with researchers around the world speaking out against pseudoscience, poor funding and the propagation of unscientific beliefs.

This issue of *ESE News* takes up this theme, as endocrinologists worldwide also seek to defend their discipline in the face of our 'post-truth' era.

The march in April came at a convenient time, shortly after US President Donald Trump had proposed budget cuts for

scientific research and openly dismissed climate change theories. In this 'post-fact' world, it is not enough to simply continue doing science. Policymakers and the public need to be continually convinced of the very real part science plays in each of our lives. To engage the public means sharing the real impact that our work has on their well-being, the health of their families and the quality of the world we all live in.

Even without triggering any immediate changes in policy, the march was a step in the right direction. The discussion around science encouraged thousands of scientists to speak

up, initiating a conversation about how much science means to us all. It bears testament to a new generation of researchers who view public engagement and education as a responsibility rather than a luxury. Education is central to science and also provided one of the fundamental principles of the march.

As we know, science is not a trend or a fad; it is simply the pursuit of knowledge to improve our lives. The March for Science has sparked a new interest in the role of science in society and has started to break down the barriers between scientists and communities.

Visit the March for Science website at www.marchforscience.com to find out how you can still get involved to support the principles and goals of the event and protect the values of science for future generations.

On pages 8–9, you can read the opinions of ESE President AJ van der Lely and President-Elect Andrea Giustina on the need to stand up for science, while the rest of the issue reflects the importance of our never-ending quest for the truth.

Apply now for IESP

Applications are sought for ESE's International Endocrine Scholars Programme (IESP), which promotes the career development of young endocrinologists.

It aims to identify talented post-doctoral researchers who wish to train for 2–3 years in an outstanding laboratory. Recipients will benefit from a unique mentoring programme that helps them find financial support, advice and training opportunities.

Successful candidates will have their travel, registration and accommodation costs met for ECE. They will also receive free membership of ESE for 3 years and a travel bursary of €3000 to visit potential host laboratories for their post-doctoral research period.

Details, terms and conditions are at www.es-hormones.org.

The deadline for applications is 14 January 2018.

Nominations for ESE awards

Please submit your nominations for ESE award winners by **28 February 2018**.

The prestigious **Geoffrey Harris Award** recognises established researchers in neuroendocrinology.

The **European Journal of Endocrinology Award** is given to an endocrinologist who has significantly advanced the field through publication.

The **Clinical Endocrinology Trust Award** is given for clinical research at the forefront of clinical practice.

Find out more at www.es-hormones.org.



Free open access publishing in *Endocrine Connections*

ESE members were eligible for free open-access publishing in *Endocrine Connections* until 30 September, and still receive a sizeable 40% discount.* Executive Committee member Bulent Yildiz (Turkey, pictured) was among those who benefited from this offer. Here, he tells us about the research behind his free publication, on the topic of polycystic ovary syndrome and the risk of obstructive sleep apnoea (*Endocrine Connections* 2017 6 437–445).



What was the aim of this study?

Polycystic ovary syndrome (PCOS) is a common endocrine disorder, affecting up to 1 in 7 women. Patients present initially with androgen excess (hirsutism, acne, alopecia), irregular menses and infertility, but this is a lifelong syndrome associated with obesity, type 2 diabetes, dyslipidaemia and, potentially, cardiovascular disease. A growing body of literature suggests that PCOS might also be associated with obstructive sleep apnoea (OSA), which itself is known to contribute to the development of cardiovascular disease and diabetes. This meta-analysis aimed to examine

the relationship between PCOS and OSA. It is important to know whether OSA is more common in PCOS, considering both disorders are associated with cardiometabolic disease.

What did you find?

We identified eight studies conducted in adults and five in adolescents. The pooled prevalence of OSA was 22% (32% in adults and 8% in adolescents). Risk of OSA was increased 10-fold in adults with PCOS (OR: 9.74, 95% CI: 2.76–34.41), whereas adolescents did not show a significantly increased risk for OSA (OR: 4.54, 95% CI: 0.56–36.43).

What does this mean for patients?

Adult patients with PCOS need to be highly suspicious of OSA, particularly if they snore and feel tired during daytime. They should tell their doctors about these symptoms. As successful treatment of OSA improves cardiometabolic function, it is important to diagnose OSA in adult patients with PCOS who



already face a lifelong risk of diabetes and cardiovascular disease.

What are the next steps for the field?

To confirm the findings of the current meta-analysis, further studies focusing on community-based cohorts, and free from clinical referral bias, would be useful to determine whether PCOS is an independent risk factor for OSA. Longitudinal studies, ideally with many cases and controls, are needed to determine when OSA develops and which factors are involved in its pathogenesis in PCOS.

*See website for terms and conditions.



Submit now at www.endocrineconnections.com

From the ESE Office

I hope you all had a fabulous summer! In the aftermath of our wonderful ECE 2017, there was 'no rest for the wicked', and we have been working hard to progress the strategic plan that we developed last year.

Really key to this is an increase in our advocacy activities, and you can read my article about our involvement with the BioMed Alliance on page 5. This is only the beginning of our increased presence within the EU, and we are evaluating the possibility of having a physical presence in Brussels by the end of 2018. We feel we are well placed to represent the needs of our members at this level, especially during these very unsettling times of budget cuts, uncertainties due to Brexit, and the general state of the world.

On a more cheery note, our new website is nearly complete. Once it has launched, you will find it at www.e-se-hormones.org! We hope it gives a more modern feel to ESE, and that it is easier to find what you are looking for: these were two of the main objectives of this substantial project.

As ever, we will only improve what we do for European endocrinology if you let us know how we can help. Do email me at helen.gregson@ese-hormones.org.

Helen Gregson
Chief Executive Officer, ESE



Luciano Martini 1927–2017

It is with sadness that we report the death of Luciano Martini, one of ESE's first Honorary Members. Professor Martini, who received his Honorary Membership in 2008, passed away on 13 July at the age of 90. He was formerly Professor of Endocrinology at the University of Milan Centre of Excellence on Neurodegenerative Diseases, Italy. He had served as President of each of the International Society of Neuroendocrinology (1980–1984), the International Society of Endocrinology (1988–1992), and the European Federation of Endocrine Societies (1994–1998).



ESE and the EU: introducing the BioMed Alliance

As part of ESE's commitment to improve the working lives of endocrinologists throughout Europe, we have significantly increased our efforts regarding advocacy.

One major step was to become an active member of the Alliance for Biomedical Research in Europe (BioMed Alliance; www.biomedeurope.org) in July 2016. This is a non-profit organisation, representing leading European research and medical societies and uniting more than 400 000 researchers and health professionals. The BioMed Alliance is committed to promoting excellence in European biomedical research and innovation, to improve the health and well-being of all European citizens.

The BioMed Alliance seeks to:

- provide a platform for members to speak with a unified voice and interact with EU policymakers on research
- provide recommendations for policy- and decision makers to facilitate biomedical research in Europe

- advocate for an EU regulatory environment to promote excellence and innovation by adopting specific policy statements
- ensure that the European Research Area has sustainable research policies and adequate funding programmes at EU level to tackle future societal challenges.

We joined the BioMed Alliance to provide strength in expertise and numbers, and to speak as a 'single voice' for biomedical and health research. The BioMed Alliance also provides access to a broad network covering EU legislation and policymakers.

What has the BioMed Alliance achieved?

One example of the BioMed Alliance's work was its involvement as a major partner during the elaboration of the final



Horizon 2020 proposal, including the creation of a Scientific Panel for Health (SPH). The SPH is a science-led stakeholder platform, aimed at focused analysis of research and innovation, identifying bottlenecks as well as opportunities, and making strategic recommendations.

The BioMed Alliance has also developed a comprehensive *Code of Conduct for Healthcare Professionals and Scientific Organisations*, to which ESE is committed (www.biomedeurope.org/code-of-conduct.html). It sets out core principles to maintain and enhance professional independence, objectivity and scientific integrity.

How is ESE involved?

At present, ESE is an active member of the working group within the BioMed Alliance which discusses CME (continuing medical education) in Europe for healthcare professionals, and the increasing involvement of the pharmaceutical industry. The intent is to publish a formal BioMed Alliance position paper in a peer review journal.

We continue to evaluate the most effective way of further increasing our advocacy activities within the EU, and will keep you updated!

Helen Gregson

Chief Executive Officer, ESE



Alliance for Biomedical Research in Europe

New European Examination in 2018

The first European Board Examination in Clinical Endocrinology, Diabetes and Metabolism will take place on 6 June 2018.* The exam is organised by ESE, in collaboration with the European Union of Medical Specialists (UEMS; www.uems.eu).

Members of ESE and of our National Affiliated Societies requested improved, internationally standardised, recognition of their level of clinical expertise. In response, we developed this exam to be high quality, clinically relevant and accessible across Europe, so that candidates can take part without incurring unnecessary travel costs.

It will be computer-based, with multiple choice questions presenting clinical scenarios to assess candidate's medical knowledge as well competency in diagnosis, investigation, management and prognosis. The tests will be taken at independently operated

assessment centres located throughout Europe.

In this way, ESE and UEMS will enable European clinical endocrinologists to assess their competence and receive certification endorsed by both organisations.

As growing internationalism provides opportunities for clinicians to work abroad, we understand the importance of universally relevant qualifications that differentiate between candidates. We hope that this exam will provide a resource which enables European endocrinologists to stand out and be recognised for their abilities.

More information, including how to apply, will be available shortly.

New ESE awards at ECE 2018

ESE will present the first Jens Sandahl Christiansen Awards at ECE 2018. A clinical award and a basic science award will each be presented to an endocrinologist for a specific piece of research or a project on metabolism.

Nominations are sought and should be made by 30 November 2017.

You can find more details at www.es-hormones.org.

*Subject to contract finalisation.



Shaping the future of endocrine science



I am delighted to take on the role of Chair of ESE's Science Committee. As you know, the Committee's main role is to ensure that basic and translational science is properly represented within the Society. We also provide an essential hub for interaction between disciplines and, by including translational research in all programmes, address the importance of bridging basic and clinical endocrinology.

New ESE Focus Areas

You will be aware that, as part of the recent strategic review, ESE identified eight Focus Areas within which to create communities, support research programme collaborations, and categorise content (see *ESE News* issue 30, page 10). These are set to provide a greater depth of understanding in each area, and so to allow us to address the specific needs of basic endocrinologists across Europe. We will also take this opportunity to integrate the areas, and to meet the associated challenges.

By nominating basic and clinical focus leads for each area and ensuring that basic endocrinologists are included in the expert panels, we will ensure that the interests of basic scientists will be prominent when planning future ESE activities.

ESE's advocacy role

As we develop the impact of endocrinology's voice in Europe, ESE will work more closely with advocacy organisations (such as the BioMed Alliance, the Initiative for Science in Europe and the European Medicines Agency). This will link their work with that of our members, and ensure your views are heard.

We will also continue to develop our own independent advocacy initiatives, such as ESE's new Working Group on Endocrine Disrupting Chemicals (see *ESE News* issue 33, page 6). In so doing, we will focus on those issues that are more specific to endocrinology. This will involve research amongst our members, and those of our National Affiliated Societies, to understand which areas will benefit most from this approach.

Meetings for endocrine research

We will, of course, continue to support established and novel meetings dedicated to endocrine research. Our courses, including the ESE Basic Course and the ESE Summer School, disseminate the latest developments in our field. We actively support other courses, particularly the annual Symposium on Hormones and Cell Regulation (Mont Ste Odile, France), which brings together early career and established endocrinologists to examine specific topics within endocrinology.

Your views and suggestions to enhance the work of the Science Committee are always welcome. Please contact me at any time via info@euro-endo.org.

Felix Beuschlein
Chair, Science Committee

Maximising excellence through ESE clinical guidelines

The Clinical Committee sees ESE's expanding collection of clinical guidelines as a major tool to improve the standard of care of patients with endocrine disease across Europe and beyond.

Two guidelines were presented at ECE 2017 in Lisbon, Portugal: one on Turner syndrome, led by Claus H Gravholt (Denmark), and another on aggressive pituitary tumours led by Gérald Raverot (France).

All ESE guidelines can be freely accessed in *European Journal of Endocrinology* (EJE), and the September 2017 issue contains the new Turner syndrome publication (more details are on page 12). The guideline on aggressive pituitary tumours is proceeding through our rigorous review process, involving members of ESE and ECAS (the ESE Council of Affiliated Societies). It will also be approved by selected societies, such as the Endocrine Society, who have been invited to send representatives to

the guidelines working group.

The first three ESE guidelines were all published more than a year ago, and so we can now obtain an initial impression of their use.

ESE's first stand-alone guideline, on treatment of chronic hypoparathyroidism in adults (led by Jens Bollerslev, Norway) was published in August 2015, and was followed by a patient leaflet on this condition, translated into various languages. This guideline has been downloaded over 32 000 times from EJE's website.

Our second guideline, on long term follow-up of patients operated on for a pheochromocytoma or a paraganglioma (led by Pierre-François Plouin, France) was published in May 2016. Despite



the rarity of this condition, the article has been downloaded over 10 000 times.

Finally, the guideline on management of adrenal incidentalomas (led by Martin Fassnacht, Germany), was presented at ECE 2016 and published in August 2016. It has now been downloaded over 26 000 times.

These guidelines have been already referenced in 78 articles, demonstrating their interest and

value to the medical and scientific community. Considering the impact of this approach on clinical care in endocrine disease, the Clinical Committee is exploring new ways to further disseminate these guidelines and promote their use.

Jérôme Bertherat
Chair, Clinical Committee

The figures cited were correct as at 13 September 2017 and will have increased since.



5th Annual EYES Meeting

Porto, Portugal, 8-10 September 2017

This year's Annual Meeting of European Young Endocrine Scientists (EYES) was held in the beautiful city of Porto, Portugal. The programme covered a wide range of topics, including diabetes, obesity, pituitary pathology, endocrine tumours, adrenal and thyroid disease, and calcium and bone disorders. Delegates attended from over 20 countries across Europe, spanning east to west, and north to south.

In the opening lecture, Manuel Sobrinho Simões from the University of Porto gave an update on the latest World Health Organisation recommendations for thyroid oncology, which he developed with a team of experts. Klemen Dovc from Ljubljana University Medical

'Delegates attended from over 20 countries across Europe, spanning east to west, and north to south'

Centre, Slovenia, a successful early career researcher, gave an amazing presentation on the importance of physical activity in patients with type 1 diabetes, and how closed loop insulin delivery can be used to manage this condition.

A few other highlights from the meeting included research on sclerostin expression in atherosclerotic plaques,

intensive blood pressure control in patients with type 2 diabetes and the latest findings in brown adipose tissue regulation. Congratulations are due to Punith Kempegowda (Birmingham, UK), who delivered the best oral presentation at the meeting (see below).

The Portuguese Society of Endocrinology, Diabetes and Metabolism, and in particular

eyes 
european young
endocrine scientists
looking forward

Luís Cardoso (Coimbra, Portugal), organised a great meeting which was both stimulating and enjoyable – obrigada!

Save the date for the next Annual Meeting of EYES, which will be held in Poznan, Poland, on 31 August–2 September 2018.

Ayse Zengin, EYES

Punith Kempegowda Best Oral Presentation at EYES 2017



Punith Kempegowda is a specialist registrar in diabetes, endocrinology and internal medicine at Birmingham Heartlands Hospital, UK. He is also a researcher at the University of Birmingham and works with Wiebke Arlt.

Punith is in his third year of an academic clinical fellowship and has many research interests, including diabetic ketoacidosis and hypophysitis. He has developed a particular interest in diseases with androgen excess, for instance polycystic ovarian syndrome (PCOS) where the mechanism is unclear.

After attending the Annual Meeting of EYES for a few years,

this year Punith's presentation was selected as the best oral presentation. This means he will present his research at ECE 2018, during the EYES symposium.

Punith says, 'I find the EYES Meetings a relaxed environment, where I can have informal chats, discuss ideas and interact with great young minds. I enjoy listening to talks by PhD students and seeing how they progress through their research over the years as they attend these events. Networking at the EYES Meetings also generates opportunities for research collaborations across Europe.'



Standing up for science

Our only proven way of determining the truth

‘Truth is so obscure in these times, and falsehood so established, that, unless we love the truth, we cannot know it’

Blaise Pascal, French scientist and philosopher, 1623–1662

In 2016, the *Oxford English Dictionary*’s word of the year was ‘post-truth’. This term is defined as ‘relating to or denoting circumstances in which objective facts are less influential in shaping public opinion than appeals to emotion and personal belief’.

As scientists, the new ‘post-truth era’ sees us confronted by a change in society where our carefully accumulated peer-reviewed evidence is increasingly at risk of being undermined by a surfeit of unaccountable information, such as anecdotal stories developed through social media, unsubstantiated ‘science’ reported on unreviewed websites, and the idea that if enough people believe in something then it must be true.

Beneath all this is a very dangerous and almost orchestrated momentum, visible within society, which tries to discredit science – using it as a scapegoat for everything that goes wrong. It puts science in a position where it must fiercely defend itself against the politicians and journalists responsible, who instead squander money and generate useless rubbish. In their words, we can easily do without science.

How then can, and should, we respond? Science occupies a uniquely important position in that the evidence and facts it presents are true, even if a person doesn’t believe in them. Science has not yet provided a complete explanation of the universe around us, but it is the best and most thorough account of humankind’s endeavours to analyse and understand the natural world, for the benefit of ourselves and our fellow organisms.



So, we need to stand up for our work and that of generations that preceded us, for our benefit and for the benefit of our descendants. We must do this by engaging with the public, those in power and the media, and explaining why scientific evidence is the closest thing we have to the truth, and why this matters.

We should take every opportunity we can to achieve this. We must do this to secure the future of science, as reflected in ESE's vision of shaping the future of endocrinology to improve science, knowledge and health.

Underlining the importance of peer review

Scientific progress occurs by the iterative refinement of our understanding, building on the foundations of our previous knowledge. Such progress relies on the accuracy of scientific literature reporting on past experimental findings while adhering to correct scientific method.

Correct scientific method dictates that conclusions are developed through objective analysis of empirical or measurable evidence, obtained from the experimental challenge of a falsifiable hypothesis. It is essential to the integrity of scientific understanding that, throughout this process, the hypothesis formed is appropriate, the data obtained are accurate, the analysis is suitable and the reasoning applied is both impartial and logical. These limitations exist not to overcomplicate the scientific process, but instead to ensure the achievement of the overall goal of scientific study: the pursuit of truth.

The basis of quality control in academic publishing is the requirement that, prior to acceptance, manuscripts submitted to scientific journals should be reviewed. This review must be by an independent panel of individuals who possess appropriate expertise in the relevant field, in order to ensure that the various conditions have been adequately met.

This 'peer review' process provides a filtering mechanism, which aims to prevent the publication of scientific reports which, through the introduction of errors, subjectivity or unscientific reasoning, are not of a sufficiently high standard to positively impact scientific progress. Data evaluation by peers must not only be accepted, but sought by every researcher in the world, since involuntary errors picked up during this process may help the author to present their science at its best.

Above all, science should be the discipline which embraces the most open discussion and the greatest contrasting opinions, but these must always be based on transparency of the experimental method and data, to make every study potentially perfectly reproducible.

'Truth' in a world without review

In the absence of such control, the publication of erroneous data or conclusions represents a significant threat to the opinions formed and decisions made by scientists, policymakers and the wider public.

The trend of modern media towards favouring sensationalistic reporting over the less palatable traditional representation of fact, for example, has fuelled the rise in controversial and often unsubstantiated claims receiving unwarranted global attention. There are countless cases of poor representation of science in the media, many of which contribute to an overall loss of confidence in the scientific community and a distrust of scientific recommendations.

Perhaps the most famous example of this remains the reporting of the 1998 paper by Wakefield linking the MMR (measles, mumps and rubella) vaccine with the development of autism, which, despite the accumulation of a huge volume of scientific evidence to the contrary, has had a long term effect on public behaviour.

'Our carefully accumulated peer-reviewed evidence is increasingly at risk of being undermined by the idea that if enough people believe in something then it must be true'

'We need to stand up for our work and that of generations that preceded us, for our benefit and for the benefit of our descendants'

In addition, modern advances in communications provide greater opportunity for the dissemination of information without any form of filtering or regulation. While this is undoubtedly a positive development for freedom of speech and expression, there are situations where the availability of information which has not been appropriately evaluated for scientific rigour can have negative consequences.

For example, you will not be surprised to hear that social media speculation on the potential for global transmission of the Ebola virus during the 2014 epidemic in West Africa was not informed by balanced scientific debate, but by fragments taken out of context from scientific reports, and a large dose of conjecture.

In the medical profession, the emergence of mainstream 'alternative medicine' as a substitute for modern healthcare represents a risk to patient well-being. This risk is compounded by the abundance of literature and reports highlighting the benefits of such treatments, despite the lack of proper scientific evidence to support this. A belief that 'natural is best', combined with a hankering for the 'simpler way of life of the past', needs to be challenged by the very obvious reality that modern, evidence-based medicine has served to dramatically increase life expectancy over the past century.

In contrast, the same patients who refuse modern medicine are willing to ingest unlabelled pills, in total ignorance of their composition, having been prescribed them by obscure figures promising miraculous weight loss or hair regrowth, potentially posing a serious risk to their lives.

Public engagement with science

The scientific community must work with media organisations and the public to increase the understanding of the principles and importance of proper scientific reporting. It is not the job of the scientific community to introduce restrictions and controls on the freedom of opinion and expression. It is, instead, the responsibility of scientists to oppose unscientific claims and inaccurate conclusions where possible, while ensuring that the rigorous requirements of scientific research are adhered to throughout their work and that of their colleagues.

As endocrinologists, we can achieve this by explaining our science in plain language and enlisting the help of experts in public engagement (such as press officers at ESE and in our own institutions) to make sure that the media report important developments in our areas of research with accuracy, not hyperbole. We can attend courses on science communication and public engagement, and thereby seek to develop our own voices to promote the unique and irreplaceable value of peer-reviewed research in improving healthcare.

In particular, we must work closely with health authorities and political bodies, in order to help them be less influenced by the emotions of the general public – which can often be very dangerously manipulated – and to tighten the surveillance of and, eventually, the legislation in the areas covered by our expertise.

Above all, we must never stop reminding people that peer review of scientific literature represents the best available method of regulating scientific output. It should be protected by all means, to ensure that the knowledge we develop today will continue to provide a reliable foundation for future scientific progress for the benefit of all our patients who are so greatly dependent on the outcome of our scientific work.

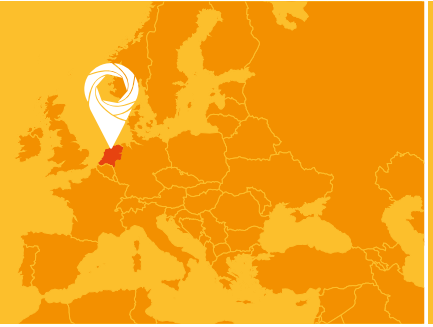
AJ van der Lely, ESE President
Andrea Giustina, ESE President-Elect



The Endo Explorer

Seeking the truth

The importance of methodology



Olaf Dekkers

Olaf Dekkers encourages us to examine the questions we pose in our pursuit of scientific understanding, and the way we determine answers.

‘There is no short cut for hard thinking about the biological and social realities and processes that jointly create the phenomena we epidemiologists seek to explain’¹

Whatever the scientific topic, the question I try to introduce is ‘What are the optimal study design and method to answer the research question under debate?’ This may sound obvious but, in my experience, very often this isn’t really posed by researchers.

I think the reason is pragmatic. In clinical research, we often start with a given dataset and consider which interesting questions can be addressed. We then search, given the information available, for the best way to analyse the data. But, for a scientific discussion, it may be helpful to challenge the dataset and ask what an ideal study should look like – and then consider how far the actual study deviates from this ideal.

Following on from this, the next question is whether the study will add meaningfully to science. If, for example, one wants to study the association between prolactinomas and breast cancer risk, then it is obviously not meaningful to study this risk in 45 prolactinoma patients.

Where endocrinology meets epidemiology

I am trained as an internist and endocrinologist, but also as a clinical epidemiologist. This has the advantage that I am able to understand the clinical relevance of research projects, while at the same time I recognise methodological pitfalls and details of the statistical analyses.

My main expertise is in creating a bridge between content and methodology. Currently, I am 50% employed by the Department of Endocrinology and 50% at the Department of Epidemiology, underlining my ‘bridge’ function. In addition, I have a master’s degree in philosophy. I have always considered philosophy an inspiring part of my life, and it is a pleasure to teach students philosophy of science.

A method-oriented expertise

My own research activities are not very focused on one topic (a disease or even a pathway), which is a direct consequence of a method-oriented expertise. Also, I do not have a well-defined research team, but work together with different national and international research groups.

I have a specific interest in meta-analyses and have been involved in the publication of several of these. This interest was triggered during an Endocrine Society meeting a decade ago. In a lecture, the absence of an association between acromegaly and mortality after transsphenoidal surgery was claimed, because the studies published on the topic were all, except one, non-significant. The result of a potential meta-analysis was immediately clear to me. As all the studies showed a slightly increased mortality risk, no doubt a meta-analysis would increase the precision of a combined estimate, and show an increased mortality risk. Indeed it did (see Figure).²

Valuable Danish data

In 2014, I spent a research year at the Department of Clinical Epidemiology in Aarhus, Denmark, where I worked in close collaboration with Jens Otto Jørgensen. Why Denmark? Denmark is well known for the fact that all medical data are captured in different databases that can be linked for research purposes. From a methodological point of view, the whole country can be seen as a cohort. This has the advantage that studies on rare diseases or rare outcomes can be performed without compromising the precision of study effects too much. A second advantage is that inhabitants cannot be lost to follow-up, as medical data are registered routinely.

In such a setting, it is possible to study the prolactinoma–breast cancer association, by linking prolactinoma data to (breast) cancer registers. This research question requires a large number of patients but also long term follow-up. We performed a study in 2457 patients diagnosed with hyperprolactinemia. The mean follow-up was 8 years. We could not find an increased breast cancer risk (standardised mortality ratio 0.99).³

Pitfalls of database-driven research

In the near future, we will see a further increase in database-driven research. Larger trans-national collaborations will be established, but routine care data will also be easier to access, as is already the case in Scandinavian countries. In addition, the recently established European Reference Networks aim to combine clinical data from different countries.

Such large and combined datasets pose great opportunities. But, at the same time, methodological challenges will increase, and the mere fact that a large number of patients can be included does not make a study valid. I think this point should really be stressed, as large numbers will make all studies statistically significant, but unfortunately *P* values do not present a measure of validity.

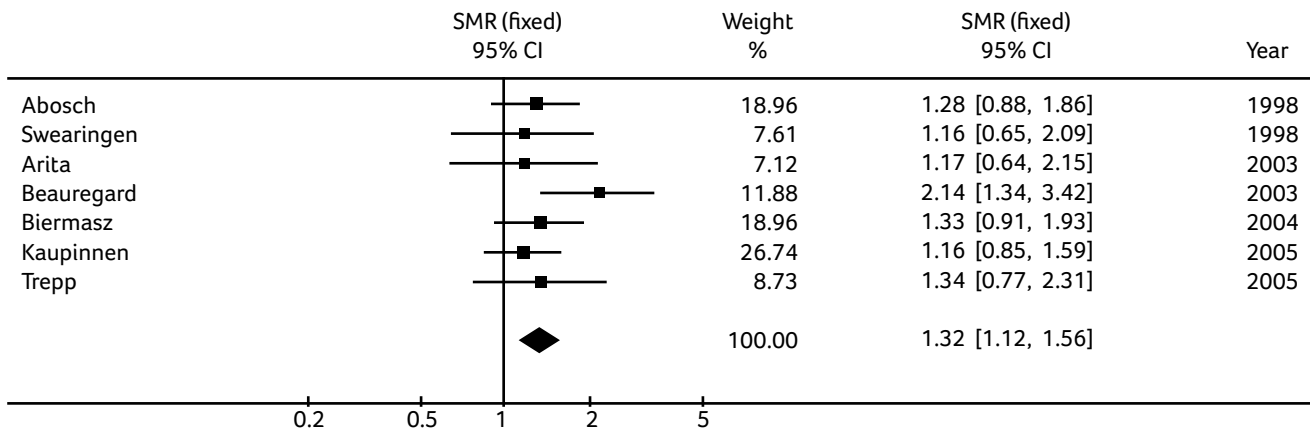


Figure Meta-analysis on standardised mortality ratios (SMRs) in studies in which more than 80% of the acromegalic patients had been treated by transsphenoidal surgery. (From Dekkers *et al.* 2008 Mortality in acromegaly: a metaanalysis. *Journal of Clinical Endocrinology & Metabolism* **93**(1) 61–67, by permission of The Endocrine Society.)

Crucial data, for example body mass index, are often not well-recorded in databases, and disease definitions differ among countries. Moreover, these databases are not always easy to handle statistically. This underlines the need for close collaboration between methodologists and content experts when setting up or analysing large datasets.

Adopting new research methods

More generally, research methods are becoming more technical and challenging. Instrumental variable analysis, network meta-analysis, inverse probability weighting and multiple imputation are just a few techniques that are becoming more popular.

I try to implement more modern methods, such as these, if they could increase the validity of a study. An example is a network meta-analysis on oral contraceptive use and venous thrombosis risk that we performed a few years ago.⁴ Such a technique allows a comparison between various treatments in one meta-analytic design, even if head-to-head comparisons are lacking. I also do more fundamental methodological research, thereby trying to assess under which circumstances newer methods outperform standard methods.

The importance of understanding methodology

There are two sides of the research coin: doing research and reading research. Whereas researchers often receive training in methodology, this is not automatically true for readers of research. However, reading and interpreting a scientific paper requires methodological skills.

I am curious as to how many clinicians know what is meant by ‘an extension of multivariable Bayesian hierarchical random effects models for multiple treatment comparisons’. Such an article is simply meant to answer the question ‘What is the best treatment?’ And without knowledge of the study design and analysis, it can be difficult to judge the validity of study results. For this reason, I also teach residents and medical specialists how to read scientific papers.

The development of ESE guidelines

This interpretation of science is also crucial for the development of guidelines. Four years ago, Pia Burman (then Chair of the Clinical

Committee) started the initiative to develop guidelines for ESE, and I have been involved as a methodological expert since then. ESE’s first stand-alone guideline was published in 2015, others have since followed, and new ones are underway.^{5–8} (You can read about the latest guideline, on Turner syndrome, on page 12.)

It really is an intriguing process to come up with reasonable recommendations in a field where not many randomised trials are performed and published. The starting point is that you cannot abstain from recommendations because the evidence is of low quality, or even absent. On the other hand, if randomised trials are lacking, this does not make observational studies automatically valid. Making recommendations thus is a balancing act, where evidence (often low quality) plays a role, but so do clinical experience, costs or patient preferences.

This balancing act is not unique to guidelines, but probably central to science, as a discussion about a scientific truth is generally not decided in a single paper. This requires the incorporation of study results in a broader discussion of several other papers, not only clinical but also from basic science.

Science is not about obtaining the truth based on a single study; it concerns slowly moving towards truth in a non-linear way.

Olaf Dekkers

Departments of Clinical Epidemiology and Endocrinology, Leiden University Medical Centre, The Netherlands

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Caring for girls and women with Turner syndrome: ESE's new guideline



ESE's new clinical practice guideline for Turner syndrome is the result of an international effort to reduce the burden of morbidity throughout the lifespan.

Turner syndrome (TS) is a condition which requires the involvement of many different medical specialists from intra-uterine life until old age. The care of females with TS also necessitates close collaboration of those specialists at different times.

When we started the process of developing this new guideline, we therefore established a set of criteria. The most recent guideline was from 2006 (published in 2007) and the recommendations had become outdated and were largely based on expert opinion. We wanted to involve as many different scientific societies as necessary, covering all aspects of TS care. As well as involving known international TS experts, we wanted to include young and upcoming specialists. Our aim was that the guideline should be evidence-based as far as possible, and so we used GRADE (Grading of Recommendations, Assessment, Development and Evaluations) to analyse the knowledge base. We were keen that the process should be transparent and that all 60+ experts would be genuinely involved in the work. It was important to us to have involvement from many different countries, and preferably from all continents.

A collaborative effort

The resulting guideline¹ is thus the result of the work of many specialists covering all aspects of the care of females with TS across the entire lifespan. They have also benefited from the input of many societies (including ESE, the Pediatric Endocrine Society, the Endocrine Society, the European Society for Pediatric Endocrinology, the European Society of Human Reproduction and Embryology, the American Heart Association, the Society for Endocrinology and the European Society of Cardiology). Specialists from yet more professional societies participated in work groups that developed the guideline consensus statement. We also included patient advocate groups in all the working groups, aiming to include the voice of the TS patients throughout the entire process.

Participating delegates thus came from many different backgrounds and this resulted in the guideline process being an open, democratic and transparent endeavour, starting with simultaneous initial meetings in Europe and the USA, followed by a joint consensus meeting in Cincinnati, OH, USA, in 2016. After this meeting, a writing group put the final document together, with all contributors approving the final guideline manuscript.

A comprehensive product

The finished guideline, published recently in *European Journal of Endocrinology*, extends over 70 pages. We were asked if it really had to be this long. And the answer to that question is of course – YES! The guideline is quite extensive, but we believe that it is very operational and useful in the clinical setting.

One does not have to read the entire document to take care of a specific issue in relation to a clinical problem. Rather, the guideline can be used as a reference on an 'as needed' basis. The guideline's length, of course, is also due to our goal of covering all aspects of TS. There is guidance for growth-promoting treatment during childhood and adolescence, puberty induction with sex hormones, oocyte donation during adulthood, cardiovascular care and a focus on neurocognitive problems, as well as many other issues.

Analysing the evidence

We also took a systematic evidence approach to the scientific literature and used GRADE to examine four pertinent questions:

- (1) What is the effect of growth-promoting treatment in TS?
- (2) What is the probability of achieving viable pregnancy after oocyte donation in TS?
- (3) What is the effect of blood pressure treatment on clinical outcomes in TS?
- (4) What is the best approach to oestrogen replacement in TS?

While we were able to address the first two questions using the GRADE approach with reasonable certainty, we did not find enough scientific evidence to precisely answer questions concerning best practice in oestrogen replacement in TS. Furthermore, it was clear that almost no research has addressed questions concerning treatment of hypertension (which occurs early and is common in TS). Consequently, one of the conclusions of the guideline process is that there is a great need for additional investigation in some areas to further improve the care of females with TS.

New areas in the guideline

The guideline recommendations cover many areas and, of course, we cannot completely revolutionise optimal care in TS. However, within the section on diagnosis and genetics, we define what should be called TS and what should not. We also focus on delayed diagnosis and the frequent occurrence of non-diagnosis, suggesting new avenues. We discuss inclusion of TS in newborn screening programmes to avoid long diagnostic odysseys and non-diagnosis.

Growth and puberty are key issues of concern, and we present new recommendations for optimal growth-promoting treatment and induction of puberty, in particular that the age for pubertal induction is now recommended to be between 11 and 12 years.

Regarding fertility, which is judged by adults with TS as the most important determinant of quality of life, there are several new recommendations. Many women with TS are now able to achieve pregnancy after oocyte donation, and the birth of a healthy child, if such a pregnancy is well-planned and preceded by a thorough cardiovascular work-up.

Detailed cardiovascular recommendations are based on a wealth of new data from several centres around the world. Our review elucidated the frequent occurrence of congenital cardiac malformations, including some previously described (bicuspid valves and coarctation of the aorta), but has broadened this to include entities such as elongated aortic arch, aortic dilation and dilation of the branching arteries. We emphasise that magnetic resonance imaging or other techniques should be used much more liberally.

We also discuss rigorous treatment of the frequently occurring hypertension, especially during pregnancy. The transition process from paediatric to adult care is examined, along with a proposal to strengthen this process. The guideline includes recommendations for appropriate care during adulthood, while covering all known comorbidities that affect individuals with TS. Neurocognitive impairment frequently affects people with TS, and we present new operational recommendations for neuropsychological care.

'Within the section on diagnosis and genetics, we define what should be called TS and what should not'

Future directions for better care

We urge the creation of multidisciplinary clinics around the world and stress that care of individuals with TS should take place in such units. This will ensure optimal care from childhood through adolescence into adulthood. We believe that medical centres around the world should implement policies to this end.

Claus H Gravholt

Aarhus University Hospital, Aarhus, Denmark

Philippe Backeljauw

Cincinnati Children's Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH, USA

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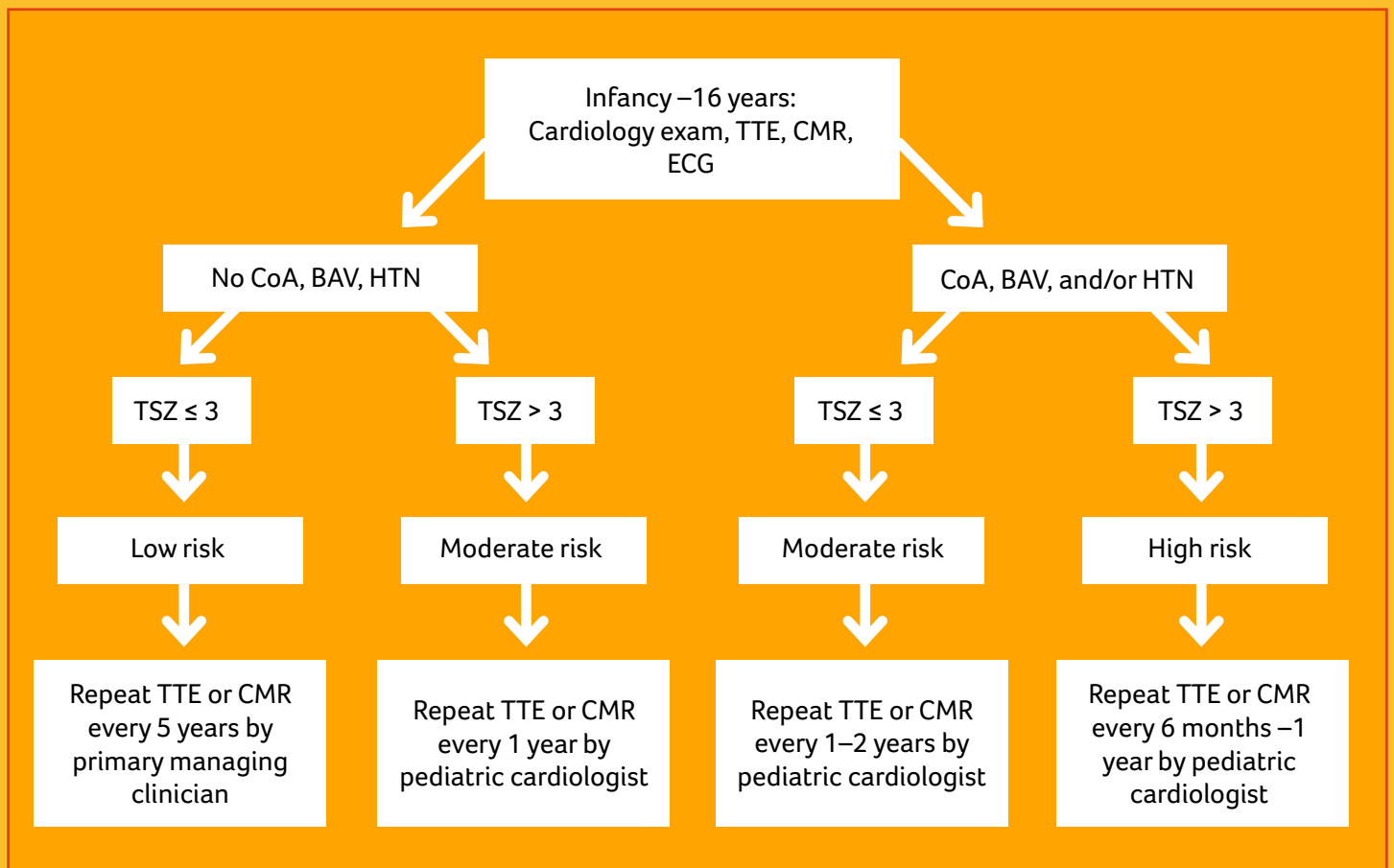
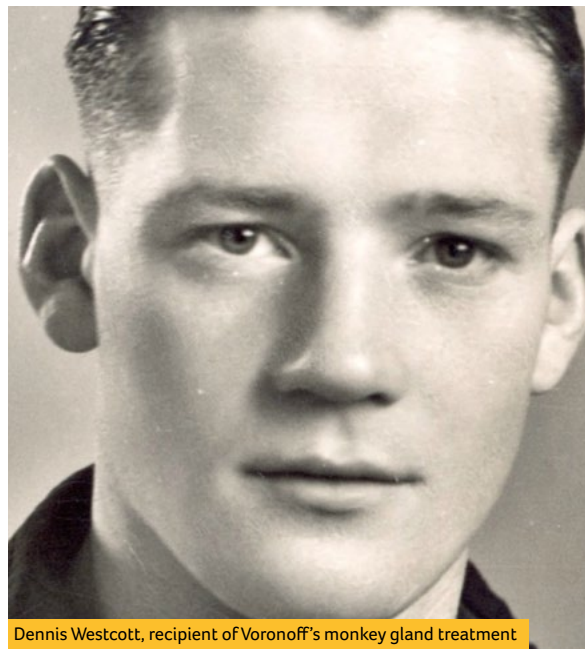
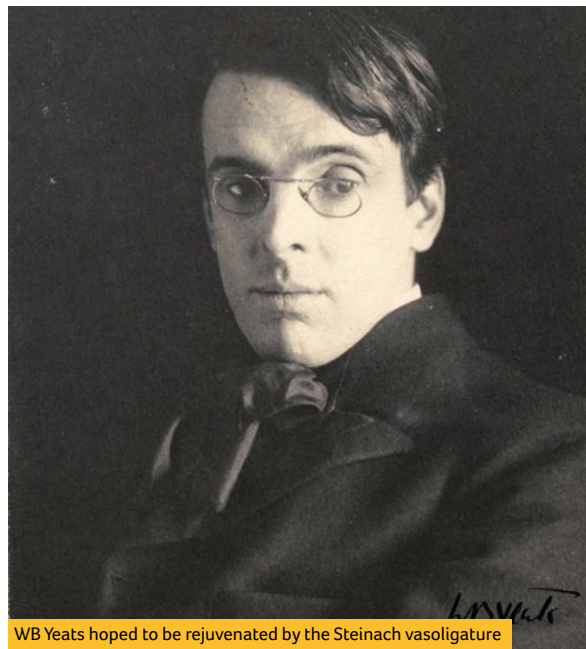


Figure Suggested monitoring protocol for girls with TS from infancy to 16 years of age. TTE, transthoracic echocardiography; CMR, cardiac magnetic resonance imaging; ECG, electrocardiogram; CoA, coarctation of aorta; BAV, bicuspid aortic valve; HTN, hypertension; TSZ, Turner syndrome specific Z-score of the aorta (as explained in the guideline text). (From Gravholt et al. 2017 *European Journal of Endocrinology* **177** G1–G70.)



Dennis Westcott, recipient of Voronoff's monkey gland treatment



WB Yeats hoped to be rejuvenated by the Steinach vasoligature

How to stay young and vigorous? Part 2

Science or nons(cience)

In the last issue of *ESE News*, I reflected upon the unsuccessful rejuvenation experiments of the French physician and physiologist Charles-Édouard Brown-Séquard (1817–1894), using injections of testis extracts. As the current issue contemplates ‘fake science’ in the post-truth era, it seems appropriate to remember that Brown-Séquard was not the only expert researcher in this field. Let’s have a closer look at two other heroes in the field of rejuvenation research...

Voronoff's monkey gland experiments

First let me introduce a French surgeon of Russian extraction, Serge Abrahamovitch Voronoff (1866–1951), who became famous for his ‘monkey gland’ experiments.^{1,2}

From the 1920s onwards, Voronoff transplanted thyroids from chimpanzees and human thyroid lobes into hypothyroid humans. Subsequently, he started transplanting the testicles of executed criminals into millionaires. However, when demand outstripped supply, he instead used monkey testicles to rejuvenate these rich males.

Among his clients/patients was his brother Georges, as well as players from the UK football teams Wolverhampton Wanderers (‘Wolves’) and Portsmouth, who were ‘rejuvenated’ in accordance with Voronoff’s approach. Seemingly by this means, Wolves’ striker Dennis Westcott became top

scorer, with 38 goals in the 1946–1947 First Division Football League season! Are we looking at the first cases of doping here?

Voronoff also transplanted a human ovary into a female monkey, and then tried to inseminate the monkey with human sperm. Once welcomed as a hero in the gland transplantation field, Voronoff’s experiments did not prove to successfully retain youth and, at the end of his very prosperous career, he was unmasked as a charlatan.

The Steinach vasoligature

Secondly, the Austrian physiologist Eugen Steinach (1861–1944) conducted similar transplantation experiments in humans. He became convinced that the testes/testosterone was responsible for sexual behaviour. This led him to develop the famous ‘Steinach vasoligature’, unilateral vasectomy, which (according to Steinach) would shift the balance from sperm

production towards increased hormone production in the affected testicle, again to rejuvenate the male.

Among the famous patients who underwent this procedure (this time carried out by the Australian-British sexologist Norman Haire) was, in 1934, the famous poet William Butler Yeats (1865–1939).³ Might it not have been coincidence that, in the same year, Yeats (then aged 69) began a relationship with the 27-year-old actress and poet Margot Ruddock, and his production of poetry got an enormous boost?

But history repeated itself, and the once famous Steinach, nominated for the Nobel Prize several times, was forced to spend the last part of his life in exile in Switzerland.

Time for a new wave?

Recently, the team of the Russian scientist Vladimir Mironov has been the first to successfully

transplant a 3D printed thyroid gland into a mouse.⁴ Are we also close to transplantable 3D printed testes for humans? If successful, will this open the avenues for a new wave of rejuvenators? Certainly, at this time, supply will probably no longer be rate-limiting.

Is endocrine rejuvenation, therefore, re-achievable in the 21st century? Will it follow the historical path of endocrinology – and the rejuvenation of ESE, its 10-year-old Society!

Wouter de Herder
Editor, *ESE News*

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A day in the life of...

...the ESE Media Office



The ESE Media Team aims to ensure that endocrinology, and ESE, are responsibly and accurately represented by the press and other media, and that members are supported to work effectively with journalists. Here, Communications Manager Lynsey Forsyth describes how she spends her time – and the opportunities available for you to get more involved.

09.00

Every morning I analyse the media, looking for endocrinology-related stories. Science, including hormone stories, is very often misrepresented.

Journalists can contact the ESE Media Office for expert opinions on hormone-related stories they are covering. We can then get accurate and responsible comments from ESE members to accompany the stories, or even provide advice that 'kills' badly angled reports. I am passionate about this key function, and the importance of involving ESE members.

Today, there are several interesting stories, and I am pleased our members' quotes have been included in some cases. Although shortened in places, they have helped balance the reporting and reduced sensationalism.

I compile a selection of the most interesting relevant stories for the ESE Daily Alert to inform members about endocrinology in the news and its treatment by the media.

10.30

Running the on-site press office at ECE is always a major highlight for ESE Media Office staff. During the event, we selected research to highlight to media outlets via press releases, and this year we generated great press coverage.

I remember chatting to one of the authors in Lisbon, who had completed a few press interviews about his presentation. He had enjoyed the experience and was pleased the journalists asked insightful questions, which had encouraged him to think about his work in a much broader context.

We were at ECE not just to set up these interviews, but also to prepare interviewees for handling the media (e.g. by guiding practice interviews or helping draft statements for a non-specialist audience).

Now the Congress is over, I must finish my report on the impact of the press coverage. Once complete, I email the coverage highlights to all the authors who were involved with the ECE press releases. My media report includes article metrics, as well as geographical spread, to give us a measure of the impact of the entire media coverage for ECE 2017.

13.00

Right now, we are preparing a press release on an exciting upcoming article in *European Journal of Endocrinology* (EJE). All work published in EJE is of a high standard but, to attract media attention, the article must also have a wider appeal: perhaps something affecting the population at large, something

that challenges current thinking, or (more generally) something people would talk about in a bar.

When EJE accepts a paper of interest, and the authors agree to a press release, we send them a questionnaire to provide us with the broader context of the work, so we can quickly draft the release for circulation to media contacts. It is sent to journalists with an embargo date, before which they are not allowed to publish anything. This drives interest and encourages them to cover the story for the paper publication date, with no fear of being 'scooped'. Today's focus is on a press release for a clinical guideline for a common endocrine condition, which is likely to have a broad appeal to the medical media and the general public.

14.30

The ESE media line rings while I am drafting the press release. A journalist from a major European publication is seeking an expert on endocrine disruptors to comment on the recent EU classification changes of these chemicals. The journalist's deadline is extremely tight – she needs comments by the end of the day, which is very common.

I scan ESE's database of 'media ambassadors': members who have volunteered for just this purpose. More volunteers are always welcomed to increase our subject and language coverage. I email the journalists' specific queries to everyone with appropriate expertise and ask for responses before the deadline. It is now my top priority to get balanced and insightful comments to go with this story.

15:00

I receive another email, listing the papers that are about to be accepted for EJE. I must scan these quickly to find any that are suitable for a press release. If I delay, the paper could appear online before we arrange a release and create an embargo. The stories won't appeal to journalists if they are already freely available online. Though interesting, I don't see any reports that will capture the mass media's attention this week.

16:00

Excellent! One of the media ambassadors sends me comments on the endocrine disruptor questions, suitable for a non-expert audience. I forward these to the journalist and ask for a link to the finished article. Tomorrow, if appropriate, we may promote this piece on our social media channels.

Simultaneously, I receive another media enquiry, this time via email, with a more relaxed deadline. The journalist works for a specialist medical publication and is writing an article on a paper that has just been accepted by EJE. They need a copy, so I send them a PDF and offer to co-ordinate contact with the authors if they need more information for their story.

17:30

Time to head out of the office for the evening – and to look forward to another busy day tomorrow!

Lynsey Forsyth

Communications Manager, ESE

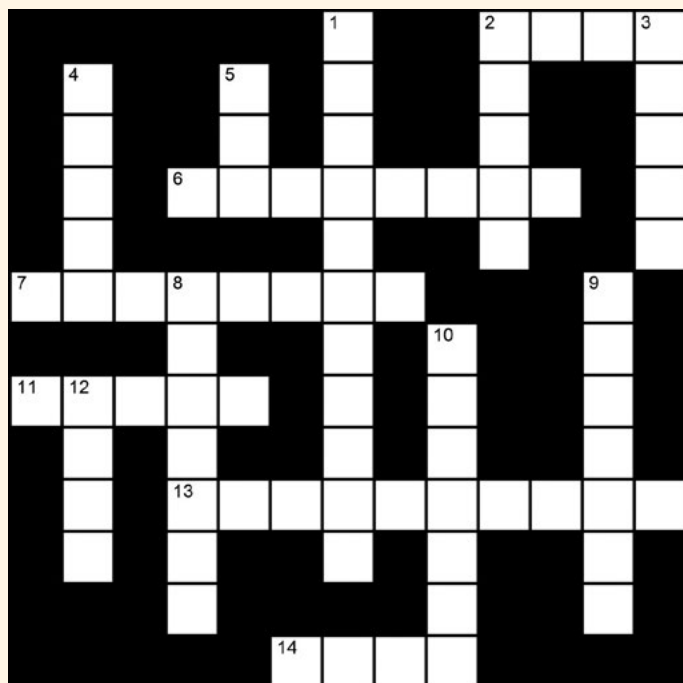
See www.es-hormones.org if you would like to find out more about the ESE Media Office. If you are interested in getting involved, contact media@bioscientifica.com.



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 winners from issue 33 were Mubina Hodzic (Bosnia and Herzegovina), Alison Forhead (UK) and Aftab Khattak (Ireland).

Answers to the puzzle in issue 33

Across 2. Asprosin, 5. Nelson's, 6. Glucose, 8. Carlsson, 12. PYY, 13. Reserpine, 15. Arvid, 16. Ecdysteroids.

Down 1. Xenopus, 3. Pineal, 4. Mesentery, 6. Geoffrey, 7. CCK, 9. Laevis, 10. Harris, 11. Vitamin D, 14. Iodine.

Endo Prize Puzzle

Across

- 2 *The New York Sun* falsely claimed elaborate life forms had been found on this celestial body in 1835 (4)
- 6 US priest who, in 1896, defrauded investors with his supposed way of extracting gold from seawater (8)
- 7 _____ Man: skull described in 1912 as a fossil link between apes and man; later proved a fake (8)
- 11 Cytokine stimulating white blood cell formation (abbr.) (5)
- 13 Type of self-limited subacute thyroiditis, first described in 1904 (2,8)
- 14 Cytogenetic technique using fluorescent probes to locate specific sequences (abbr.) (4)

Down

- 1 South Korean who falsely claimed in 2004 to have created a stem cell line from the world's first cloned human embryo (5,3-3)
- 2 Prefix meaning black (5)
- 3 Nuclear chemist who falsely claimed to have found element 118, ununoctium, in 1999 (5)
- 4 Organelle which organises and packages proteins and lipids into vesicles (5)
- 5 Essential amino acid, precursor of catecholamines (abbr.) (3)
- 8 Filipino tribe whose 'discovery' in 1971, living a Stone Age existence, may have been faked (7)
- 9 _____ Giant: a 10-foot 'petrified man', exhumed in New York state in 1869; found to be fake (7)
- 10 Dutch surgeon who, in 1783, wrote a false account of a Javan tree that killed everything for miles (7)
- 12 One of the cell-signalling pathways triggered by activated RAS (abbr.) (4)

Did you know?



Texas giants

You may have heard of the famous Texas Giants Baseball Academy, but the original Texas Giants were four brothers who formed part of a Barnum and Bailey sideshow in the USA in the 1800s.

Famed for their stature, Augustus 'Guss' Orion Shields stood at 6ft 9in (206cm), John Franklin 'Frank' Shields at 6ft 10.5in (210cm), Jack Robinson Shields at 6ft 11in (211cm) and Shadrick 'Shade' Archibald Shields at 6ft 8in (203cm).



Save the date

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

Europit

20–23 November 2017
Annecy, France

10th ESE Clinical Update

12–13 January 2018
Abu Dhabi, UAE

22nd ESE Postgraduate Course on Endocrinology, Diabetes & Metabolism

22–25 February 2018
Budapest, Hungary

ECE2018

20th European Congress of Endocrinology

19–22 May 2018
Barcelona, Spain

Deadlines

30 November 2017

Jens Sandahl Christiansen Awards

Nomination deadline

30 November 2017

ESE Short-Term Fellowship

Application deadline

14 January 2018

ESE International Endocrine Scholars Programme

Application deadline

29 January 2018

ECE 2018

Abstract deadline

28 February 2018

ESE Awards (see page 3)

Nomination deadline

6 April 2018

ECE 2018

Early bird registration deadline