Issue 44 Winter 2020/21

# ESE News

The newsletter of the European Society of Endocrinology

ISSN 2045-1563 (print) ISSN 2045-1571 (online)

# Making your voice heard in Europe

Also in this issue

Looking forward to e-ECE 2021 COVID-19: endocrinologists keep going!



# In this issue

# **Society News**

- 03 ESE White Paper to raise awareness, plus From your President
- 04 Telemedicine in endocrinology, Clinical Update on Acromegaly, and EndoBridge 2020
- 05 New ESE Advocacy Representation Scheme, plus From the ESE Office
- 06 Anton Luger, your new ECAS representative, plus journal news

## **Features**

- 07 SIMBA: effective education during COVID-19
- 08 e-ECE 2021: a festival of endocrinology
- 10 Researchers and teachers face COVID-19
- 12 Rosario Pivonello on COVID-19 and Cushing's syndrome
- 13 Luca Persani and Kristien Boelaert on COVID-19 and the thyroid

## **Editors' Selection**

14 The importance of research methodology

## At the Back...

- 15 Endocrinologists are experienced 'pandemicologists'
- 16 Endo Prize Puzzle, plus ESE diary dates

Justo P Castaño, Spain Email: justo@uco.es

Andrea Giustina, Italy Email: ese.president@ese-hormones.org

## **Editorial Board:**

Luís Cardoso, Portugal Olaf Dekkers, The Netherlands Josef Köhrle, Germany Stavroula Paschou, Greece Marija Pfeifer, Slovenia

Sub-Editor: Caroline Brewser

Design: Qube Design Associates

Website: www.ese-hormones.org

©2020 European Society of Endocrinology The views expressed by the contributors are not necessarily those of ESE



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



**ESEndocrinology** 



EuropeanSocietyofEndocrinology

The addresses used to mail this issue of ESE News were supplied by the members of ESE and are stored in Bioscientifica's database for future use. If you do not wish to receive further mailings, please advise info@euro-endo.org

ESE thanks the following for their support. Premium Corporate Members: Akcea Therapeutics, Ipsen, Pfizer, Recordati Rare Diseases, Takeda Corporate Members: Advanced Accelerator Applications, Amryt Pharmaceuticals, Diurnal, HRA Pharma, Kyowa Kirin International, Merck Serono, Novo Nordisk, Sandoz International, Siemens-Healthineers, Strongbridge Biopharma, Uni-Pharma Supporters: Chiasma, Crinetics Pharmaceuticals, Isotopen Technologien

# **Editorial**



Amongst our Society's goals is a commitment to be 'at the centre of the endocrine community in Europe, acknowledged as the reference point for endocrine science, knowledge and health'. In short, ESE aims to be the voice of endocrinology in Europe – to represent you and your needs among the policymakers and the public

This issue of ESE News highlights two major initiatives that will help make this a reality. The new ESE Advocacy Representation Scheme (EARS) enables ESE's National Affiliated Societies and their members to form a strong community of 22 500 endocrine healthcare professionals and researchers across Europe. Through EARS, you can keep up to date and share your views regarding ESE's policy and advocacy work. Find out more on page 5, including how you can sign up to EARS, and what ESE has already done to introduce an endocrine perspective into various European programmes.

Early 2021 will see the launch of ESE's White Paper on endocrinology. This will encourage the EU to bring endocrinology to the forefront of health policies, particularly in rare diseases, obesity, cancer and endocrine disruptors. It gives EU policymakers a series of expert recommendations in each area. Learn more on page 3.

The new year is upon us, and we are all looking forward, with hope, to the prospect of more positive times ahead. e-ECE 2021 in May is firmly in our sights and will be an exciting opportunity to share our passion for our field. On page 8, co-Chairs Daniela Cota and Lars Rejnmark update us on the comprehensive programme, which will bring us all the latest developments in endocrinology. You can also hear from our award lecturers on pages 8 and 9. Now is the time to prepare your abstracts, for submission by 1 February.

COVID-19 continues to dominate our lives, and this is reflected in this issue. On page 10, we hear from researchers and teachers about the impact of COVID-19 on their world. The past year has seen a steep learning curve in terms of our understanding of the virus' effects on the endocrine system and on patients with pre-existing endocrine disease. On page 12, Rosario Pivonello looks at its impact on patients with Cushing's syndrome, while, on page 13, Luca Persani and Kristien Boelaert examine effects on the thyroid.

Training and education need to continue, despite the pandemic, and on page 7 we hear how the team behind the SIMBA project has used free messaging and video conferencing software to support virtual learning. A series of articles on research methodology in European Journal of Endocrinology is also helping to bridge an important gap in training, in these COVID times (see page 14). The last word, for this issue, goes to Wouter de Herder. On page 15, he reminds us that we endocrinologists have long been experts in dealing with pandemics!

Justo P Castaño

- Juto Coute

# White Paper promotes endocrinology

ESE will launch its White Paper on endocrinology early in 2021. Its main aim is to explain and highlight the importance of endocrinology as a discipline to EU policymakers.

The White Paper, entitled 'Hormones in European health policies: contributing towards a healthier Europe', encourages the EU to bring endocrinology to the forefront of upcoming policies on health, such as the Beating Cancer Plan and the EU4Health Programme. The development of the White Paper has been led by the ESE Policy and Advocacy Task Force, which contributed extensively to it during the whole drafting process.

It focuses on four priority areas: rare diseases, obesity, cancer and endocrine-disrupting chemicals (EDCs). These were chosen because of their relevance to the field of endocrinology as well as current policy focus. Readers are first provided with an overview of what endocrinology is, and the functions controlled by hormones and their importance. The White Paper uses data from ESE's 2018 Mapping Endocrinology in Europe (MEnEU) survey to

'The White Paper encourages the EU to bring endocrinology to the forefront of upcoming health policies' show where endocrinologists specialise, as well as the field's multidisciplinary nature.

Each chapter (rare diseases, obesity, cancer and EDCs) describes the links between that area and endocrinology, and gives an overview of the main related EU policies. The chapters aim to identify what the EU is doing well and what could be improved, from the perspective of endocrinology. Where relevant, the chapters also contextualise the impact of COVID-19. Finally, the White Paper gives a set of concrete expert policy recommendations addressed to EU policymakers in each of the

The White Paper has been through a comprehensive developmental process lasting

several years. Drafting it combined desk-based research with quantitative input from the MEnEU survey and qualitative input from interviews with ESE experts and patients. It was submitted for consultation and review to experts of the ESE Policy and Advocacy Task Force and ESE Executive Committee. It was also reviewed and endorsed by the 54 national societies represented through the ESE Council of Affiliated Societies (ECAS).

You will be able to read the White Paper shortly at www.ese-hormones.org/advocacy.



# From your President

Dear Friends

When I became ESE President in May 2019, I had a clear vision of what I wanted to achieve under my key strategy of 'Inclusion'. I am grateful for your enormous support, which meant we could largely implement the reforms before COVID-19 arrived. The pandemic has, of course, forced us into an emergency mode of reaction which, unfortunately, must remain our focus.

I am proud of all we have achieved. When I pass ESE to my successor, the Society will be capable of playing a key role through the effective 'inclusion' of all stakeholders in our field. It can advocate at the very highest institutional level for all endocrinologists and endocrine patients, so finally obtaining recognition for their work and for the relevance of their disease, respectively.

We have 'included' more colleagues from Europe and beyond. The link with our National Affiliated Societies is stronger through EARS (the ESE Advocacy Representation Scheme, see page 5). A new Early Career Member Task Force enhances our partnership with the ESE Young Endocrinologists and Scientists (EYES). The ESE Rare Disease Committee officially strengthens our ties with Endo-ERN.

The ESE Council of Affiliated Societies (ECAS) puts our National Affiliated Societies at the centre of ESE. They now have the widest possible involvement in our core activities. Through ESE, they can speak with one strong voice at the level of European Institutions. Our policy and advocacy strategy has delivered our new White Paper (page 3). This is another important step in raising our profile, as is the European Hormone and Metabolism Foundation - Foundation of the European Society of Endocrinology (the ESE Foundation), which will soon become the home of all endocrinologists and friends of endocrinology.

Enhanced collaboration with

sister societies includes an agreement to prepare joint clinical guidelines with the Endocrine Society, and setting up the International Liaison Committee.

In these difficult times, we have ensured the Society's financial sustainability to support our objectives and new activities. I am proud that we achieved a 'break even' financial position in 2019, and that we now have a Finance Committee. Despite the challenges of 2020, it is likely that the financial outcome will be far better than initial possible projections! This positive outlook would not have been possible without our supportive industry partners.

Finally, our prompt reaction to the pandemic provided essential support to the entire endocrine community, including crucial information, and activities such as our online Congress and educational events.

I look forward to working with you for the rest of my term. I know I will leave ESE in good,



trustworthy hands, that are stronger than ever.

Stay safe, my friends, and see you at e-ECE 2021!

Andrea Giustina
President of ESE
Twitter: @EsePresident

You can find a full version of this article at www.ese-hormones. org/giustina\_reflections

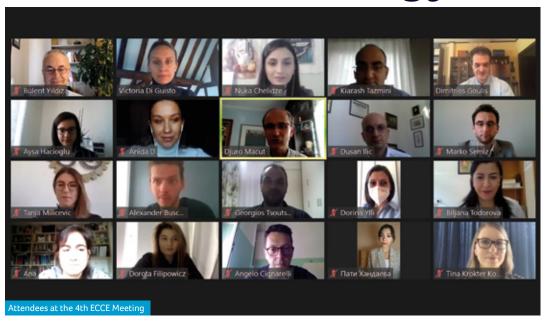
# Telemedicine in endocrinology

The 4th Early Career Clinical Endocrinologists (ECCE) meeting on 22 October focused on 'Telemedicine in endocrinology: clinical, administrative and educational procedures'.

The online event attracted 23 early career participants, representing 20 countries. Discussion spanned the aims, expectations and challenges regarding application of telemedicine to endocrinology, from the perspective of early career clinical endocrinologists. As well as clinical, administrative and educational procedures, the event considered how European endocrinology should advance. One aim was to identify the similarities and differences between European countries, to better inform future support. The main outcomes were as follows.

## Benefits of telemedicine:

- It can be used for urgent care.
- It can provide specialist care for chronic diseases (much needed in rural areas).
- In addition to history-taking, information from remote patient monitoring (e.g. glucometers) can be transmitted to the health provider.
- It is effective in diabetes, reducing HbA1C by an additional 0.5% compared with usual care.
- It can substitute for many in-person contacts during the COVID-19 pandemic.



## Limitations of telemedicine:

- Difficulties with technology may interfere with the delivery of care.
- It can impede important clinical elements (e.g. physical presence, emotional connection).
- It is difficult to conduct a physical examination, despite peripheral devices (e.g. digital stethoscopes).
- The 'digital divide':
  - Some patients may prefer in-person appointments.
- Telemedicine is not appropriate for all patients with endocrine disease.
- Undeveloped and/or nonharmonised telemedicine infrastructure and knowledge on the ground in European is a serious limitation.

The national societies and ESE could collaborate to address these challenges. Regulatory issues must be considered, such as:

- Data security: patients should be advised about privacy issues, and health providers should enable all encryption modes.
- Health insurance coverage: this varies by country and health insurance provider.
- Licensure: as country boundaries do not limit video transmission, cross-border telemedicine may be subject to licensure issues.
- Prescribing: most insurance providers prohibit delivery of medication via the internet.
   The meeting was moderated by Djuro Macut (Serbia), Bulent Yildiz

(Turkey) and **Dimitrios G Goulis** (Greece), and is organised annually by the ESE Council of Affiliated Societies (ECAS). The 5th ECCE meeting in October 2021 will be on 'Use of decision support systems in endocrinology'.

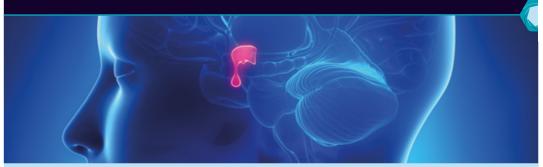




The 8th Annual Meeting of EndoBridge was held online on 22–24 October 2020. The 3-day scientific programme included state of the art lectures and interactive expert discussion panels on challenging and interesting clinical cases. Simultaneous translation into Russian, Arabic and Turkish was provided. A record level of participation saw over 1600 delegates from 92 countries.

EndoBridge 2021 will take place in Antalya, Turkey, on 21–24 October 2021.
You can find out more at www.endobridge.org.

# Clinical Update on Acromegaly



This popular ESE course took the form of three webinars on 27–29 October 2020 covering:

- Diagnostic dilemmas in acromegaly
- The burden of acromegaly

• The current and future landscape in management

Talks from leading experts were supported by patient videos and case presentations. Each webinar concluded with a discussion. All sessions are available to delegates on ESE On Demand (www. eseondemand.org). The course content will be available as a report.

# Listen up! It's time to join EARS

The new ESE Advocacy Representation Scheme (EARS) launched in October, following careful consultation with ESE Council of Affiliated Societies (ECAS) representatives. EARS enables our National Affiliated Societies and their members to engage with ESE's policy and advocacy work, so ensuring endocrinologists' voices are heard across Europe.

# Why are policy and advocacy so important?

ESE's mission statement, 'Shaping the Future of Endocrinology', requires us to interact with stakeholders, so that the importance of endocrine health is recognised when healthcare policies and research programme support are developed.

# Why should you join the EARS community?

The main reason for you to get involved is that we are stronger together. ESE is the VOICE for ENDOCRINOLOGY in Brussels. The EARS scheme means we will represent a community of over 22 500 endocrine healthcare professionals and researchers across Europe, as well as the patients they care for. This community cannot remain unheard!

# What does joining EARS mean?

You will:

- receive regular e-newsletter updates on ESE's policy and advocacy work
- be consulted on our policy and advocacy activities
- have your voice heard as part of Europe's endocrinology community
- be able to access resources, such as the ESE White Paper (see page 3)
- be invited to relevant events,
   e.g. during ECE and on topics
   such as research funding.

Joining is FREE for members of ESE's National Affiliated Societies (represented by ECAS), as your society will pay the small fee of €2.50 on your behalf.

# What does ESE's policy and advocacy work include?

It focuses on three areas of strategic importance to the European and global healthcare agenda:

- achieving greater healthcare effectiveness and resilience through health promotion and disease prevention, particularly post-COVID-19 recovery and its impact regarding endocrine and metabolic diseases
- supporting the 'Mission on Cancer', contributing to the 'Beating Cancer Plan' and stimulating research on endocrine origins and consequences
- engaging in EU debates on climate change and the environment, particularly endocrine disruptors.

# What has ESE achieved so far?

Over the last 12 months, we have focused on inserting the hormone health perspective into the **Horizon Europe** research programme, the **Beating** 

Cancer Plan, support to rare diseases within the European Reference Networks and, more recently, driven by the impact of the COVID-19 pandemic, the EU4Health Programme. The Commission's Green Deal and, as part of that, the Chemical Strategy for Sustainability need to include a strong emphasis on endocrine disruptors, a major contributor to susceptibility to many non-communicable diseases. To read more, visit www. ese-hormones.org/advocacy.

We look forward to welcoming you into the EARS Community – so we can amplify our collective voice in Brussels.

Martin Reincke ESE President-Elect Anton Luger ECAS Representative

# Join EARS today:

sign up at https://bit.ly/JoinEARS

# 'We look forward to welcoming you into the EARS Community – so we can amplify our collective voice in Brussels'



# From the ESE Office

At last, it feels like there may be the opportunity for optimism! At the time of writing, the longhoped-for news of a vaccine against COVID-19 has recently looked like becoming a reality. Furthermore – without wanting to get too political – change at the White House is imminent. In an otherwise reasonably dry 'good news' year, these developments feel like a cause for celebration.

2020 was unprecedented for everyone – and for ESE this was no different. We had to pivot our activities and change at rapid speed, converting plans

and launching new ones – all on a massively steep learning curve. I am hugely proud of what was achieved in supporting our community and continuing to provide our services. I would like to thank our wonderful leadership and my amazing team for making it possible. And to you, our members, many on the frontline and working so unbelievably hard under stressful circumstances – THANKYOU.

As always, remember you can contact me with your thoughts and feedback at helen.gregson@ese-hormones.org.

Let us hope that 2021 brings a 'new dawn'. We will be here to support you. Take care and stay safe.

# **Helen Gregson**Chief Executive Officer, ESE





# Anton Luger, your new ECAS representative



ESE welcomes Anton
Luger (Austria) as the new
representative of ECAS (the
ESE Council of Affiliated
Societies). ECAS aims to
raise the profile of European
endocrinology through
greater collaboration
between ESE and the national
endocrine societies of Europe.

Anton teaches and has collaborations in research projects at the Medical University of Vienna, Austria. He sees patients in two hospitals and at his office in Vienna.

In Anton's own words, he describes his passion for endocrinology as follows: 'As a young doctor, I fell in love with the pituitary gland and have remained faithful. Diabetes was another field that fascinated me, with the numerous innovations in the past decades that improved the care and thereby the quality of life of affected patients so tremendously.'

Here, Anton tells us about his thoughts on endocrinology in Europe today, and his aims for his 4-year term in the role of ECAS representative.

# What are the main challenges for endocrinologists in Europe?

There are tendencies to shorten training in endocrinology in several countries, and to divide endocrinology into separate disciplines. We need to oppose these initiatives fiercely and make sure that adequate resources are allocated to endocrinology. Its central place in medicine needs to be acknowledged.

# What opportunities should we grasp?

At the national and European levels, forces should be joined to represent endocrinology as a central discipline that deals with the major threats to health and economy. Obesity and diabetes are diseases responsible to a great extent for the major causes of morbidity and mortality, i.e. cardiovascular diseases and cancer.

Efforts made by ESE towards this goal, through lobbying in Brussels, need to be strongly backed up by all European endocrinologists in the interest of their individual futures and that of their specialty.

# What attracted you to a leading role in ECAS?

I was always interested in exchanging ideas and hearing of experiences in other countries. A constructive dialogue guarantees development of optimal strategies to strengthen the position of our specialty. The current times are challenging in any respect but, at the same time, ESE is building up strong political representation at the European level in Brussels, and this needs the strong support of all national societies.

# How would you like ECAS to develop during your tenure?

We should enhance the collaboration of endocrinologists and their institutions across all European countries with the goal of harmonising training, and standardising and optimising treatment of patients with endocrine diseases. This can only be successful through close collaboration of all individual endocrinologists, the national societies and ESE.

# What advice do you have for European endocrinologists?

It is not so important in which field within endocrinology you land. Everything is fascinating in this discipline, so long as you are determined to get to the bottom of it and don't stop to ask questions. Dogmata are relevant, questioning them is even more important.

All National Affiliated Societies who are members of ESE are automatically members of ECAS. Affiliated Society Membership is open to national endocrine societies in Europe and in countries bordering the Mediterranean Sea, as well as pan-European and international sub-specialist endocrine societies. To find out more, see www.ese-hormones.org/ecas.

# ECAS ESE Council of Affiliated Societies

# New Editor-in-Chief for *Endocrine Connections*



ESE is proud to announce that Professor Adrian Clark is the new Editor-in-Chief of *Endocrine Connections*, the official open access endocrine journal of ESE and the Society for Endocrinology.

Adrian is Honorary Professor of Endocrinology at Barts and the London School of Medicine and Dentistry (UK). To aid the transition, he will work jointly with current Editor-in-Chief, Josef Köhrle, throughout January 2021.

# Journal website enhanced



The brand new homepage of European Journal of Endocrinology has been launched, following extensive research and development, in close liaison with the Editorial Board. These changes ensure you can easily find the

information or articles you need.

As a member of ESE, you can access all journal content free of charge. This is even easier than before! To explore the journal, just go to https://eje.bioscientifica.com.



# SIMBA: effective education in the COVID-19 pandemic

The COVID-19 pandemic has had a significant impact on medical education and clinical training worldwide. SIMBA (Simulation via Instant Messaging – Birmingham Advance) is an international initiative to support virtual learning, led by doctors and enthusiastic medical students.

SIMBA uses accessible and free messaging and communication platforms (WhatsApp and Zoom) to deliver remote, case-based simulations in diabetes and endocrinology. It enables the delivery of effective, virtual education that is compatible with ongoing social distancing policies. It has been championed by Punith Kempegowda and Eka Melson from the University of Birmingham's Institute of Metabolism and Systems Research.

## **How it works**

During SIMBA sessions, participants interact with their allocated moderator (usually a trained medical student) via WhatsApp. Each simulation session adapts four challenging real-life clinical situations incorporating various learning points. After a simulation, participants join an interactive video conference via Zoom, where each case is discussed in detail by a consultant endocrinologist. Feedback is sent to all participants in the following week, using an adapted version of the global rating scale.

Since its introduction in July 2019 with the Pituitary 1.0 session only for clinicians in the UK, SIMBA has become recognised internationally and consequently increased its capacity to accommodate up to 100 participants worldwide, completely free of charge.

The eighth and most recent SIMBA session focused on complex type 1 diabetes mellitus cases. A total of 59 participants from 17 countries interacted with 22 moderators. The session was lively, with 7880 messages exchanged between participants and moderators. Analysing the surveys from the session, participants demonstrated improved confidence post-simulation in managing simultaneous pancreas–kidney transplantation (P=0.0001), new onset type 1 diabetes in the elderly (P=0.0001) and hypoglycaemic unawareness (P=0.0003).

## A range of benefits

Participants' feedback from all SIMBA sessions has shown that trainees gained confidence in managing complex endocrinology and diabetes cases through solving the challenging clinical scenarios during simulation and having a discussion with the expert managing those cases. Additionally, feedback from our most recent diabetes session suggests that the SIMBA method of practice-based learning was impactful to their personal and professional learning and the topics were applicable to their clinical practice.





# SIMBAR

Simulation via Instant Messaging - Birmingham Advance

Medical students acting as moderators also develop a variety of skills from the experience. The exposure to clinical case management early in medical education familiarises students with vital aspects of clinical practice. The experience acts as a revision tool, but also teaches fundamental qualities, such as leadership, time-management and teamwork skills. Within SIMBA, there are numerous opportunities for student volunteers to work and collaborate with specialists to successfully organise SIMBA Endocrinology sessions.

## **New developments**

The most recent initiative from the SIMBA Team is CoMICs (Concise Medical Information Cines). These are short videos consisting of illustrations and infographics created by medical students and junior doctors, to provide bite-sized information on various diseases and conditions. The information



on each topic is based on national and international guidelines pitched at an easily intelligible level and reviewed by world-renowned experts. Medical students creating CoMICs gain valuable experience in medical education, revision of key concepts, and the opportunity to work directly with leaders in the field. New content is released weekly as part of our '#CoMICWednesday' drive. Follow us on Instagram (simba. comics) and Twitter (@SimbaComics) for access to all episodes.

The SIMBA Endocrinology stream has so far successfully organised six sessions focusing on a range of specialist topics, such as diabetes, pituitary, adrenal and thyroid pathologies. There will be three SIMBA Endocrinology sessions annually which are free to attend. However, places are limited and offered on a first come, first served basis. The next session will be on metabolic bone diseases in February 2021.

For more information about our work, please follow us on Twitter (asimbasimulation), or explore our website at https://bit.ly/simbasimulation.

Vina Soran, Rachel Nirmal, Meri Davitadze and Punith Kempegowda on behalf of the SIMBA Team





# **Key dates**

# **eECE 2021**

23rd European Congress of Endocrinology

Submit your abstracts by

1 February 2021

The early bird registration deadline is

6 May 2021

www.ece2021.org

# A festival of endocrinology

22-26 May 2021

It is time to look forward to the next European Congress of Endocrinology. Once again, we will provide you with the best clinical and scientific updates and breakthroughs in our field. You will have the opportunity to interact with thousands of colleagues and to attend lectures from top scientists and clinicians in the area of your interest.

e-ECE 2021's rich, varied and exciting programme can be tailored to your needs. It will fully cover the eight ESE Focus Areas:

- Adrenal and Cardiovascular Endocrinology
- Calcium and Bone
- Diabetes, Obesity, Metabolism and Nutrition
- Endocrine-Related Cancer
- Environmental Endocrinology
- Pituitary and Neuroendocrinology
- Reproductive and Developmental Endocrinology
- Thyroid

With 12 award and plenary lectures, we will bring you excellence in basic and clinical research. Amongst the many subjects these lectures will cover, you will enjoy the latest discoveries in the fight against obesity and diabetes, the impact of body clocks in endocrinology, and the most recent advances in thyroid cancer and Cushing's disease. The Programme Organising Committee has introduced some changes that we hope you will appreciate, including plenary lectures entitled 'One year in pituitary' and 'One year in bone', which will provide an overview of the most relevant findings in these fields over the past 365 days.

A total of **30 symposia** will form the backbone of e-ECE 2021, with more than 90 international speakers providing inspiring lectures covering all fields of endocrinology. One symposium on rare endocrine diseases will be a joint session between Endo-ERN and ESE. Of course, as is now traditional, we will also have an EYES (ESE Young Endocrinologists and Scientists) session organised by our early career members.

The programme will include **15 meet the expert sessions**, giving you the chance to discuss very diverse topics with clinical experts. These span the management of craniopharyngioma, new treatments for thyroid ophthalmopathy, and sarcopenic obesity, to name just a few. In addition, **4 basic science meet the expert sessions** will cover the mechanisms underlying remodelling of adipose tissue, molecular genetic testing in thyroid cancer, genome-wide association studies in diagnosis of osteoporosis, and the impact of endocrine-disrupting chemicals on neural stem cells.

The **5** new scientific approaches sessions include a new technical breakthrough in the 3D study of the adrenals, the latest methodologies allowing replacement and regeneration of  $\beta$ -cells, and use of zebrafish as a model to predict endocrine disruptor action. A **round table session** will allow an exchange of views with politicians and representatives from Brussels on advocacy strategies addressing endocrine disruptors.

Finally, **5 debates** in the field of diabetes, bone, thyroid, adrenals and environmental endocrinology will animate e-ECE 2021. They are expected to catch your attention!

Certainly, you will help make e-ECE 2021 a true success by submitting your abstracts and presenting your work through posters, short talks and late breaking communications. Submit your abstracts by 1 February 2021 via www.ece2021.org.

We have put together what we believe will be THE endocrine event of 2021. We hope that you will be part of it!

## Daniela Cota

e-ECE 2021 Basic Science Co-Chair

## **Lars Rejnmark**

e-ECE 2021 Clinical Co-Chair

# **Our award lecturers**



Niels E Skakkebæk European Hormone Medal

Human birth rates are decreasing in industrial countries, and are below levels where populations can be sustained. Although socioeconomic analyses suggest the trends are due to behavioural changes, adverse health factors may also be at play. In Europe, we have epidemics of infertility resulting in an increasing need for assisted reproduction. In Denmark, 9–10% of children are now born after medical assistance. Female infertility due to delays in pregnancy planning causing 'oocyte ageing', combined with

a partner's poor semen quality, may often be aetiological factors. We have focused on links between increasing trends in testicular germ cell cancer and decreasing semen quality. Our work has provided evidence of a testicular dysgenesis syndrome (TDS). The symptomatology of TDS includes cryptorchidism, decreased spermatogenesis, low sperm counts and risk of testicular germ cell cancer. In patients with TDS, we detected a cell pattern giving rise to seminomas and non-seminomas. These precursor cells (germ cell neoplasia *in situ*) are gonocytelike and express embryonic genes, including *OCT-4*. We believe a spectacular increasing trend in testicular cancer among young men is a 'canary in the coal mine' for adverse effects of an industrialised lifestyle on human testicular development and function.

# Our award lecturers continued



Vera Popovic-Brkic Geoffrey Harris Award

It has been a fantastic journey to see growth hormone (GH) secretagogues reach their current clinical status. I spent fruitful years studying the actions of synthetic GH-releasing peptide-6 on human GH secretion. Amongst our many findings was a safe and reliable test for adult GH deficiency. Identification of a novel peptide gastric hormone, ghrelin, led to use of a highly selective oral ghrelin mimetic (macimorelin) in diagnosing GH deficiency and the use of ghrelin agonism in cancer cachexia and sarcopenia.

Further collaborations have also borne fruit. We found families with genes associated with predisposition to earlier pituitary adenoma onset. We hypothesised that shared genetic susceptibility may predispose a patient with a strong family history of malignancy (breast cancer) to an early-onset pituitary tumour (prolactinoma). We better understood the intriguing clinical presentation of polycythaemia/duodenal somatostatinoma with multiple paragangliomas, by discovering a mutation of the *HIF-2A* gene (Pacak–Zhuang syndrome). The phaeochromocytoma-paraganglioma-related gene panel is everexpanding; links with pituitary adenoma-predisposing mutations have been suggested.





John Wass Geoffrey Harris Award

My research has mainly centred around the pituitary gland, but I have also worked in the field of adrenal endocrinology and, earlier, worked on thyroid and osteoporosis genetics.

My objective has been, in significantly sized cohorts, to answer questions for which clinicians need to know the answer, but for which there is often no answer in the literature. For example, in the epidemiology of pituitary tumours, how often micro- and macro-adenomas enlarge in size when they are not treated over significant periods of time, and how

often they recur, based on the postoperative appearance in the pituitary fossa.

More recently, we have looked at headaches in acromegaly and their outcomes. We have studied a large cohort of giants from the acromegaly database I set up some 20 years ago, examined the prognosis for patients with acromegaly who have disparate growth hormone and IGF-I levels, and considered the frequency of cyclical Cushing's.





Ruben Nogueiras European Journal of Endocrinology Award

The obesity pandemic has a tremendous impact on economic and healthcare systems. Our group investigates molecular mechanisms involved in obesity and its associated diseases, such as type 2 diabetes and non-alcoholic fatty liver disease.

We are particularly interested in the mechanisms by which the central nervous system (more precisely the hypothalamus) controls energy homeostasis. We have provided evidence that gastrointestinal hormones (such as glucagon-like peptide-1, ghrelin or uroguanylin) act through the hypothalamus to modulate

not only food intake, but also peripheral metabolism. Furthermore, we have shown that neuropeptides (e.g. melanin-concentrating hormone) and neurotransmitters (e.g. dopamine) can differentially modulate systemic metabolism by acting on specific neuronal subsets.

The effects of peripheral and central signals are tightly controlled through the autonomic nervous system. The appropriate crosstalk between peripheral organs and the brain is essential to maintain fine-tuned regulation of energy balance. Understanding the complex and redundant metabolic networks is critical in finding new targets to fight against metabolic syndrome.



Rosario Pivonello Clinical Endocrinology Trust Award

Endogenous Cushing's syndrome is associated with several comorbidities, determining an impaired quality of life and increased mortality. Among these, metabolic syndrome contributes to increased risk of cardiovascular events. Immunosuppression causes susceptibility to infections, possibly complicated by sepsis. Neuropsychiatric disorders can be responsible for suicide attempts, while musculoskeletal disorders can impair patients' ability to conduct a normal life, and other comorbidities can further impair quality of life.

Treatment of patients not only aims to control hypercortisolism, but also to reverse the associated clinical picture, and to address and prevent chronic complications. The first line treatment for all types of Cushing's syndrome is surgery, but the role of medical treatment is increasing, with development of new drugs and more rational use of old ones. The availability of more drugs with different mechanisms of actions and safety profiles offers the chance to tailor the treatment of each patient. Eventually, the combination of drugs or use of different sequences of treatments may improve their efficacy and tolerability.



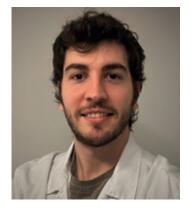
# Researchers and teachers in the face of COVID-19

In the last issue, we talked to four clinical endocrinologists about the impact that the COVID-19 pandemic has had on their lives during 2020. This time, it is the turn of researchers and teachers working in our field to reflect on their day-to-day experiences.



## Ulla Feldt-Rasmussen

Ulla is Professor and Senior Consultant in the Department of Medical Endocrinology and Metabolism at the Rigshospitalet, Copenhagen University, Denmark.



## Juan Manuel Jiménez Vacas

Juan has defended his PhD during the pandemic. He undertook his PhD at Maimonides Institute for Biomedical Research of Córdoba (IMIBIC), Spain, and is now at the Institute of Cancer Research in London, UK.

In January 2020, I was (as usual) on a dive vacation with my husband – and preparing for teaching, laboratory work and mentoring for the university term at all levels, from Bachelor and Masters, through PhD, to postdocs. The normal plans were made but, soon after returning from holiday, the coronavirus struck. We found ourselves in March with a close-down of Denmark.

We were unable to perform basic research, since the laboratories at the Medical Faculty were completely inaccessible. Clinicians could continue clinical trials that had started and been approved, and which would have been unethical to discontinue; this saved some of the PhD students. However, we could not commence new trials – even those that had been in the pipeline before COVID-19. External mentors had no access to the hospital (it is still limited).

Additionally, research staff were signed up to assist in urgent COVID-related work. This included duties for doctors and nurses at the clinical units, and everyone (including research students and other personnel) at the virus test centres, which served both staff and the population at large. Most research funding was transferred to COVID-19 from endocrinology and other fields.

All staff were asked to work from home as much as possible, which made some scientific work possible, but not at the usual levels. Most internal and necessary tutor sessions had to be conducted virtually by means of media such as Skype, Zoom or Microsoft Teams. We had to limit the number of researchers showing up physically in the lab, in compliance with Government recommendations. In recent months, these have changed at short notice due to varying, unpredictable viral spread.

Teaching of medical students has mostly been virtual, in order not to delay their education. This has unfortunately been at the expense of the quality of the teaching. Even exams and PhD defences continue to be performed virtually.

The important activity of bringing students at all levels to international congresses in order to network has also been compromised, as physical meetings have been replaced by virtual ones: a possible but insufficient alternative.

I sincerely hope we'll not lose a generation of students and researchers due to our current limited ability to meet their rightful requirements for high quality personal mentoring and teaching. The current frail situation has, at least, reminded me of the immense importance of passing our personal, not just virtual, clinical experience on to our students. We are responsible for maintaining that.

The COVID-19 pandemic has altered our entire lives in the past months, at both a personal and a professional level. In my case, the situation drastically affected the last phase of my PhD, which was carried out in Spain: one of the countries most impacted by this pandemic so far.

Like many others, I had to undergo a strict lockdown. As a result, my plans and experiments were suddenly put on hold, just like my frozen cells, waiting to return to life soon. Nevertheless, I got to address all those new challenges, and I even made some progress in my PhD from home. Specifically, during lockdown, I planned the remaining experiments, wrote some sections of my papers and PhD dissertation, and even carried out the mandatory courses for my PhD that were still incomplete. Once back to the routine in the laboratory, I was finally able to finish my experiments in record time, with the help of my lab colleagues. Please believe me when I say that I had the opportunity to work with an astounding group of people!

Legend has it that all doctors will always remember the day of their PhD presentation. In my case, I will never forget it for two reasons. First of all, there was the meaning of this long-awaited day itself. Secondly and more significantly, however, was the fact that my PhD presentation and defence were quite different from usual because of the COVID-19 situation. The public attending had to take seats in a scattered manner, so that we could meet the social distancing rules. For that reason, many family members and friends were forced to follow the event online. Although I was honoured to have Professor Riccarda Granata as one of the committee members for my PhD, she was not allowed to attend onsite either. Therefore, we had our scientific discussion with a screen in between, to save all those thousands of kilometres. All in all, it was worth all the trouble: I really enjoyed that day!

I would like to encourage the students whose PhD has been also affected by the current situation to keep working and successfully overcome these tough times. We will get there.











Karim Meeran Karim is Professor of Endocrinology, Deputy Director of Medical Education and Lead Clinician for Endocrinology at Imperial College London, UK.



**Tejal Lathia** Tejal is a Consultant Endocrinologist at Apollo and Fortis Hospitals in Mumbai, India.

Conferences around the country and world were suddenly cancelled. The last endocrine conference I attended was on 12 March at the Royal Society of Medicine in London. Two speakers from Cambridge were unable to attend because of COVID concerns. It was then I realised how serious things were. Until that point, COVID-19 felt like a distant problem that was only in Italy and China.

On 13 March, we had annual national metabolic medicine registrar interviews and I went by train to Leicester. These were face-to-face interviews, but two candidates elected to use Skype. On 16 March, the Government announced that all unnecessary contact should cease. The annual endocrinology registrar interviews planned for 23 March clearly could not happen face-to-face. Could we do these on Zoom? Skype? Teams? The administrators were unhappy about the security of virtual interviews and they were cancelled. I wondered how we were going to get new endocrinology trainees.

I also work in acute and general medicine, and was on call towards the end of March. Until then, we had very little in the way of COVID-19, but I came in to a post-take ward round on 28 March where the night team had been overwhelmed in a way never seen before. Hypoxic patients were arriving in large numbers. It became clear that my hope of coping without major change would not be possible.

All my endocrine colleagues have been trained in acute and general medicine, so the entire team of academic endocrinologists and clinical endocrinologists rapidly became experts at managing COVID-19 in patients who were not going to intensive care. Many of you will have had a similar experience. We were on the COVID frontline in April and May. I myself contracted COVID-19 and isolated for a week, and developed anosmia.1,2

In April and May, we diverted all our efforts into dealing with COVID-19. This was at the expense of almost everything else, and those in education have been badly affected, possibly with very long term implications. From mid-March, all patient-based teaching stopped. The final MBBS examinations, scheduled for 24-26 March, were cancelled. Undergraduate and postgraduate education rapidly moved to Zoom.

All laboratory and clinical research that was not directly relevant to COVID-19 was also stopped. Our own medically qualified PhD students were redeployed on COVID wards in April and May. The lockdown was extremely effective, and patient numbers rapidly fell. It became eerily quiet in June,<sup>3,4</sup> as patients were clearly anxious about coming to hospital. Most consultations were carried out via video or telephone.

Our annual Endocrine Masterclass on 27 April obviously had to be cancelled in its usual form but, by then, we had started using Zoom, so we tried a 2-hour session to replace the whole day of learning. This was very popular as all other education in endocrinology had either been cancelled or replaced with COVID teaching. Following this unexpected success, we have continued to run sessions on average every month. You can find recordings at www.imperialendo.com/metmed.

Zoom and Teams have now become part of life, and interviews since September have run on these platforms in a secure manner. With further lockdowns anticipated, they are likely to be in place for some time to come... When the pandemic hit India in March 2020, I had four or five projects with ethical approval underway, quantitative as well as qualitative. As a clinician-researcher, time opened up for me due to a fall in clinic attendance, but the projects hit several road-blocks.

Just before the pandemic and subsequent lockdown, I had obtained ethics committee approval for a study on the impact of lifestyle modifications instituted in early pregnancy on prevention of the subsequent development of gestational diabetes mellitus. The recruitment process depended on obstetricians, who were unable to recruit patients consistently. Also, regular follow-up visits have not been possible for the few who were recruited. Many trial subjects moved away to their home towns, in a bid to avoid the huge COVID-19 burden in Mumbai. Participants were unable to follow nutritional and exercise recommendations, due to limited access to fresh produce and the inability to leave home. Furthermore, the results generated in these conditions will not be easy to extrapolate to other times.

A qualitative project, entitled 'Communication in diabetes care', was shifted to a virtual medium during the pandemic, after successfully conducting in-person focus group discussions (FGDs). However, older people living with diabetes struggled with connectivity and technical issues during the virtual FGDs, and the project is currently at a standstill. Virtual and telephone focus groups are, at best, a compromise. Important cues like facial expression and body posture cannot be captured, compromising data quality.

However, we recognise that the pandemic is here to stay. We are slowing limping back to normality, by putting processes and systems in place to overcome the limitations placed on us.

## REFERENCES (KARIM MEERAN'S ARTICLE)

- 1. www.bmj.com/content/368/bmj.m1202/rr-2.
- 2. www.imperialendo.co.uk/Newskills/meeranONIONtest.mp4.
- 3. www.bmj.com/content/369/bmj.m1496/rr-2.
- 4. www.imperialendo.co.uk/Newskills/FiguresBMJ.htm.





# Cushing's syndrome and COVID-19

Since the end of 2019, the outbreak of COVID-19 infection has shaken the world. In particular, it has shown a more negative prognosis and a higher risk of death in patients already affected by concomitant comorbidities, including obesity, hypertension, diabetes mellitus, cardiovascular diseases and immunodeficiency syndromes. These may be easily recognised by clinical endocrinologists as complications of Cushing's syndrome.

Cushing's syndrome is characterised by excessive cortisol production by the adrenal glands, due either to increased pituitary adrenocorticotrophin stimulation of cortisol production or to autonomous adrenal hypersecretion. Therefore, we might speculate that patients with Cushing's syndrome could be at a higher risk of infection by SARS-CoV-2, or have a worse prognosis associated with COVID-19, as we discussed in a recent review.<sup>1</sup>

### The immune response

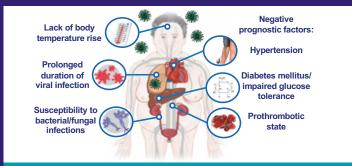
Glucocorticoids are well known immunomodulators, able to enhance the immune response at physiological levels in the early phase of infections, but also to reduce both the innate and the adaptive immune response in the case of prolonged exposure to excessive circulating levels. Therefore, patients with Cushing's syndrome are more prone to develop infections, in particular opportunistic infections, as well as to suffer a more prolonged and severe disease course during infectious diseases.

As a consequence, safety precautions, including social distancing, hand washing and face masks, should be strictly adopted by patients with Cushing's syndrome, to minimise the risk of contagion. Moreover, due to their susceptibility to opportunistic infections, empiric antibiotic prophylaxis should be considered in Cushing's syndrome patients with COVID-19 infection, as hospitalisation for COVID-19 infection has been associated with a higher risk of fungal and bacterial secondary and opportunistic infections, which may increase the risk of death.

## Inflammatory cytokine response

Fever is a clinical sign present in the great majority of COVID-19 patients, but it may be absent in patients with Cushing's syndrome, as they experience a blunted rise in pro-inflammatory cytokines that are responsible for increased body temperature during infections. Therefore, those suspecting COVID-19 infection in patients with Cushing's syndrome should rely on signs and symptoms other than fever, including dry cough, dysgeusia, anosmia and gastrointestinal disturbances.

COVID-19 infection is associated with a negative prognosis, in terms of both severity of disease course and mortality, in patients with some of the most common Cushing's syndrome comorbidities, such as visceral obesity, hypertension, diabetes mellitus and cardiovascular diseases. Therefore, patients with Cushing's syndrome may be considered at a high risk for COVID-19 infection. However, it should be noted that acute respiratory distress syndrome (ARDS, the final stage of COVID-19 pulmonary infection, which is associated with a strikingly higher mortality) usually develops as a consequence of the massive increase in pro-inflammatory cytokine levels induced by COVID-19 infection – the so-called 'cytokine storm'. As the cytokine rise in patients with Cushing's syndrome is usually blunted by chronic



Issues of clinical relevance in patients with Cushing's syndrome and COVID-19

hypercortisolism, it may also be speculated that, paradoxically, they may be at a lower risk for ARDS, and thereby experience a more favourable prognosis during COVID-19 infection.

Thromboembolic events are more frequent in patients with Cushing's syndrome, and they also represent one of the main causes of death in COVID-19 patients. This is particularly true in severe or critically ill patients, in which the rise of pro-inflammatory cytokines may lead to a hypercoagulable state. Therefore, thromboembolic prophylaxis should be considered in patients with Cushing's syndrome during the COVID-19 pandemic and in the case of COVID-19 infection, to potentially reduce the already increased risk for thromboembolic events.

## Management during the pandemic

Due to the lack of current evidence, a cautious approach is preferable in patients with Cushing's syndrome throughout the pandemic. First, the treatment of Cushing's syndrome comorbidities that are associated with a worse prognosis in COVID-19 infection should be optimised. Secondly, surgical treatment of Cushing's syndrome should be deferred, to reduce the potential related infective risk. Instead, transient medical therapy is favoured, to reduce cortisol levels and consequently improve Cushing's syndrome comorbidities, in order to ameliorate the prognosis of an eventual COVID-19 infection. Thirdly, patients with Cushing's syndrome in remission should be accurately monitored, as comorbidities usually improve after treatment, but do not always completely resolve, so carrying a higher risk for a worse COVID-19 infection disease course.

### **Rosario Pivonello**

Department of Clinical Medicine and Surgery, Section of Endocrinology, University Federico II, Naples, Italy

### REFERENCES AND FURTHER READING

- 1. Pivonello et al. 2020 Lancet Diabetes & Endocrinology 8 654-656.
- 2. Guarnotta et al. 2020 Reviews in Endocrine & Metabolic Disorders doi: 10.1007/s11154-020-09598-x.
- 3. Newell-Price *et al.* 2020 *European Journal of Endocrinology* **183** G1-G7. doi: 10.1530/EJE-20-0352.



# The thyroid and COVID-19

COVID-19 has been found to present a particular risk to those with underlying health conditions, and to affect a diverse range of organs within the human body. This article offers an insight into COVID-19's interaction with the thyroid gland and with pre-existing thyroid disease.

## COVID-19's impact on the thyroid

Patients with COVID-19 are frequently exposed to a cytokine storm that is associated with worse outcomes. Severe disease state and cytokine impact are expected to cause profound alterations to thyroid hormone metabolism and hypothalamic-pituitary function, such as those seen in classic non-thyroidal-illness (NTI).

Accordingly, the same biochemical manifestations (low/normal free tri-iodothyronine, FT3; borderline high free thyroxine, FT4; partially suppressed thyrotrophin, TSH) have been reported in a number of cohorts of patients with COVID-19,<sup>1,2</sup> with FT3 decrease correlating with worse outcome.<sup>3</sup> Systematic analyses of the thyroid function tests in COVID-19 patients from intensive care units<sup>4,5</sup> interpreted these NTI-like alterations as a form of T4-thyrotoxicosis, resulting from an inflammatory thyroiditis without pain. However, this interpretation requires confirmation, due to the systematic administration of variable treatment protocols to COVID-19 patients, with drugs able to affect thyroid hormone metabolism or transiently suppress TSH (e.g. high doses of corticosteroids or hydroxychloroquine) or to interfere with free thyroid hormone measurement (e.g. heparin).

Nonetheless, the presence of SARS-CoV-2 receptor ACE-2 mRNA in thyroid cells makes them a potential target of the viral infection. Accordingly, classic painful subacute thyroiditis (SAT) has also been reported in several patients shortly after remission from acute COVID-19 manifestations. Euthyroidism was generally restored in these patients. These data indicate the need for monitoring of thyroid function in the early phases of COVID-19 remission, as well as a long term follow-up, particularly in subjects who developed SAT or positive anti-thyroid antibodies.

### COVID-19 in patients with thyroid disease

Thyroid diseases are frequent in the population and their diagnosis and management have been challenged by the COVID-19 pandemic and related lockdown.<sup>8</sup> Expert opinions on the management of thyroid diseases during the pandemic were recently published in *European Journal of Endocrinology*.<sup>9,10</sup>

So far there is no evidence that patients with autoimmune thyroid diseases are more susceptible to contracting viral illnesses, including infection with SARS-CoV-2, or that they are at risk of developing more severe COVID-19 disease. Similarly, there is no evidence that patients with poorly controlled thyroid disease are more likely to contract viral infections.

Hypothyroidism has been reported to have no impact on outcomes for 1379 American patients with COVID-19 disease. 11 However, it is plausible that patients with uncontrolled thyroid dysfunction, especially those with thyrotoxicosis, may be at higher risk of complications (e.g. thyroid storm or cardiac complications) if affected by COVID-19. Patients newly presenting with hyperthyroidism should be managed through video consultation or, if required, in person, at least initially. To reduce hospital access, monitoring of anti-thyroid drug treatments should be performed by teleconsultation as much as possible.

It may be possible to reduce the frequency of monitoring of patients on stable levothyroxine replacement. In pregnancy, women should be advised to augment their weekly levothyroxine dose by 30–50% as soon as possible after a positive pregnancy test, and to screen thyroid function every 4–8 weeks up to week 30 of gestation. They should reduce levothyroxine replacement to the pre-gestational dose after delivery.

In the case of a new Graves' diagnosis, a 'block and replace' approach is preferable, because it requires less strict monitoring of blood tests. Medical treatment should be prolonged beyond the usual duration (12–18 months) in patients with Graves' disease, and is also preferred in the case of toxic nodular goitre, in order to reduce the access to hospital care for surgical or radioiodine ablative treatment.

COVID-19-related conjunctivitis should be particularly feared in patients with thyroid-associated orbitopathy (TAO), because of the worsening of the underlying inflammation and the risk of viral transmission through the tears. Patients on immunosuppressive therapies for TAO are at increased risk of severe COVID-19 manifestations, although this assertion needs confirmation in patients receiving corticosteroids, as these drugs are now largely employed to minimise the excessive cytokine response during COVID-19 evolution.

Goitre monitoring and treatment should be postponed during the COVID-19 pandemic, unless there is a rapid progression of compressive symptoms.

Surgery for low and intermediate risk thyroid carcinomas can often be postponed for a period of time (up to 3–6 months). Most patients with differentiated thyroid carcinomas are not at an increased risk of developing a critical COVID-19 course. However, oncological patients in general suffer from a 3.5-fold higher risk of mechanical ventilation, intensive care unit admission or death compared with patients without cancer. Finally, thyroid carcinoma patients receiving multikinase inhibitors or chemotherapy are at an increased risk of developing adverse events, resulting in a higher probability of severe illness from SARS-CoV-2.

### Luca Persani

Istituto Auxologico Italiano IRCCS and Department of Biotechnology and Translational Medicine, University of Milan, Italy

## Kristien Boelaert

Institute of Applied Health Research, University of Birmingham, UK

### **REFERENCES**

- 1. Chen et al. 2020 Thyroid doi: 10.1089/thy.2020.0363.
- 2. Zou et al. 2020 Frontiers in Endocrinology 11 566439.
- 3. Chen et al. 2020 BMJ 368 m1091.
- 4. Lania et al. 2020 European Journal of Endocrinology 183 381-387.
- 5. Muller et al. 2020 Lancet Diabetes & Endocrinology  ${\bf 8}$  739–741.
- 6. Rotondi et al. 2020 Journal of Endocrinological Investigation **6** 1–6.
- Brancatella et al. 2020 Journal of Clinical Endocrinology & Metabolism 105 dgaa537.
- 8. Caron 2020 Annales d'Endocrinologie 81 507-510.
- 9. Boelaert et al. 2020 European Journal of Endocrinology 183 G33-G39.
- 10. Vrachimis et al. 2020 European Journal of Endocrinology 183 G41-G48.
- 11. van Gerwen et al. 2020 Frontiers in Endocrinology 11 565.





# What's in a method? Supporting your research





During the challenging COVID-19 pandemic, ESE has recognised the dedication of endocrinologists worldwide, as they strive to continue their research, support their patients, and develop new care pathways. The Society has supported the education of its members, especially early career endocrinologists, with online educational webinars and courses.

In this context, and in the absence of the usual schools, a series of six articles on research methodology has been published in *European Journal of Endocrinology*, with a seventh recently accepted, and more planned. You can find them at https://eje.bioscientifica.com/page/methodology. We highlight four of them here, to give a flavour of their importance and value.

## Who is afraid of non-normal data?

Le Cessie, Goeman & Dekkers

This article discusses parametric and non-parametric statistical methods. When comparing outcomes between two groups (for example, hormone levels between groups or at different points in time), researchers have to decide whether to use parametric methods, such as the t-test, or non-parametric methods, such as the Mann-Whitney test. The authors explain that non-parametric tests have drawbacks in medical research and that they are often not necessary; standard t-tests have a much easier interpretation.

## Measurement error in clinical research, yes it matters Groenwold & Dekkers<sup>2</sup>

By considering various aspects of measurement error in clinical research, the authors argue that an in-depth discussion is often needed to appropriately assess the quality of a study and the impact of measurement error. Indeed, the validity of any biomedical study is potentially affected by measurement error or misclassification. This can impact different variables included in a statistical analysis, such as the exposure, the outcome and confounders, and can result in an overestimation or an underestimation of the relationship under investigation.

'A series of six articles on research methodology has been published, with a seventh recently accepted, and more planned'

## Missing data: the impact of what is not there

Groenwold & Dekkers3

This explains why missing data may lead to bias, and discusses a commonly used classification of missing data. Any variable measured in a study can have missing values, including the exposure, the outcome and confounders. When missing values are ignored in the analysis, only those subjects with complete records will be included. This may lead to biased results and loss of power. Researchers should be aware of the impact and how to handle it.

## Study design: what's in a name?

Dekkers & Groenwold⁴

The name of the study design should reflect the actual method of conduct and analysis. This article provides guidance on proper naming. The first distinction is between a trial (an intervention given to patients to study its effect) and an observational study. In the case of observational studies, it should be decided whether it is cross-sectional or whether follow-up time is taken into account (a cohort or case-control study). The authors emphasise that the distinction between prospective and retrospective is not always helpful. There are two disadvantages: prospective is often seen as marker of higher quality, which is not necessarily true, and there is no unifying definition that makes a proper distinction between retrospective and prospective possible.

The other articles that have been published so far are:
Why not to (over)emphasise statistical significance Dekkers<sup>5</sup>
Basic aspects of confounding adjustment Groenwold & Dekkers<sup>6</sup>
When observational studies can give wrong answers: the potential of immortal time bias Dekkers & Groenwold<sup>7</sup>

Further items on diagnostic accuracy studies, genetic studies and multiple testing are in preparation.

This series of articles is really useful for junior researchers, and also for all academics, independent of age or experience. Moreover, even clinicians who do not perform research themselves can benefit, as the papers make them more capable of deeply reading studies and interpreting results for the good of their patients. Such initiatives are really important especially during these COVID-19 times, in the absence of other resources and in-person training for improvement of skills in research methodology.

## Stavroula A Paschou

ESE Science Committee EYES Committee

## REFERENCES

- 1. Le Cessie et al. 2020 European Journal of Endocrinology 182 E1-E3.
- 2. Groenwold & Dekkers 2020 European Journal of Endocrinology 183 E3-E5.
- 3. Groenwold & Dekkers 2020 European Journal of Endocrinology 183 E7-E9.
- 4. Dekkers & Groenwold 2020 European Journal of Endocrinology 183 E11-E13.
- 5. Dekkers 2019 European Journal of Endocrinology 181 E1–E2.
- 6. Groenwold & Dekkers 2020 European Journal of Endocrinology 182 E5–E7.
- 7. Dekkers & Groenwold 2021 European Journal of Endocrinology 184 E1–E4.

# Endocrinologists are experienced 'pandemicologists'

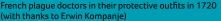
The COVID-19 pandemic is having a major impact on worldwide economic and social activities, including scientific conferences, such as ECE 2020. In many countries, clinicians (including endocrinologists and endocrine nurses) have been intensely involved in COVID-19 care. Morbidity and mortality data are monitored and COVID-19 hotspots identified. This situation may have taken the world by surprise but, as we know, endocrinologists are no strangers to tackling global threats to human health.

Historically, pandemics caused by infectious diseases have played a major role in impairing daily life and activities, disrupting societies and causing tremendous mortality rates. The plague or 'Black Death' in the 14th century killed between 30 and 60% of Europe's population (40-70 million people). More recently, between spring 1918 and winter 1919, Spanish 'flu swept across the globe, killing an estimated 50-100 million people. To date, 35 million have died from AIDS and 12 000 perished in the 2014-2016 Ebola epidemic.

It is quite logical for the general public to rely on infectiologists, virologists and epidemiologists as THE experts to tackle this new viral pandemic. However, humble endocrinologists should not forgot their important role in very recent pandemic history. Indeed, we were dealing with at least three large pandemics, long before COVID-19 popped up in China.

First, consider diabetes: in 2011, Nigel Unwin wrote a chapter entitled 'The world pandemic of diabetes' for the Oxford Textbook of Endocrinology and Diabetes.1 An estimated 463 million people (roughly 9% of the world's adult population) have been diagnosed with diabetes.2 In 2019, it is estimated to have led to around 1.9 million deaths among those aged 60 years and younger.







Secondly, we are faced with an ongoing pandemic of obesity: in 2016, over 650 million adults were obese. According to the World Health Organization, 2.8 million people die each year as a result of being overweight or obese.

Last, but not least, the pandemic of endocrine disruptors is of growing concern. This is particularly the case because we do not yet know the impact of the multitude of effects endocrinedisrupting compounds have on our health and, especially, on our endocrine system.

For years, endocrinologists have warned governments and world leaders about the effects of a high sugar content in foods and drinks, the tremendous health impact of obesity and the potential future risks of microplastics. We see now some world leaders and governments largely downplaying the health impact of COVID-19. How striking is the similarity with them ignoring the scientific data regarding diabetes and obesity?

In diabetes and obesity, major changes in social habits, behaviour and activities are required. Similarly, social behaviour during the COVID-19 pandemic definitely had to change. Again, certain governments, world leaders and some political groups have tended to ignore, or fight, these recommendations.

Furthermore, the public expect the medical world and pharmaceutical industries to develop medication to prevent or cure diabetes and overweight. In the same way, the hope is that effective medical (preventive) treatments for COVID-19 will be developed, so there will be no need to change our regular habits in the long term.

It is only with regard to plastics that people in general seem convinced that their use should be reduced - but progress is still slow.

Of course, endocrinologists continue to make our scientific contribution in the face of COVID-19. We have long reported on the effects of specific infections on the endocrine system, such as the relationship between mumps or other viruses and diabetes mellitus. Now, we report on COVID-19's role in the pathogenesis of specific endocrine disorders, and new guidelines instruct us on dealing with COVID-19 infections in patients with endocrine

conditions. The synthetic steroid dexamethasone was first made in 1957 by Philip Showalter Hench and approved for medical use in 1961. Some 60 years later, it has been revived as a 'new' life-saving drug in COVID-19 patients.

There also seems to be a clear link between the recent and new pandemics. People with obesity and/or diabetes seem to be at higher risk of developing more severe COVID-related disease.

So, we endocrinologists should reflect on our experience as 'pandemicologists' at this time. The major difference between the endocrine pandemics and COVID-19 is that endocrinologists usually don't quarantine their patients with diabetes and obesity.

### Wouter de Herder

Professor of Endocrine Oncology, Erasmus MC. Rotterdam. The Netherlands

## REFERENCES

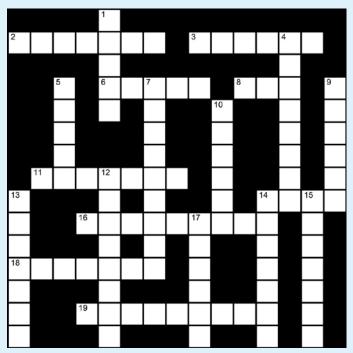
- 1. Unwin 2011 In Oxford Textbook of Endocrinology and Diabetes, edn 2, Eds Wass et al. Oxford: Oxford University Press.
- 2. International Diabetes Federation 2019 IDF Diabetes Atlas www.diabetesatlas.org.



# 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.



## **Solution**

Answers to the puzzle in issue 42

## Across

- 1. Flu, 2. Death, 6. Black,
- 7. Russia, 9. Yersinia,
- 11. Polio, 12. Salk,
- 17. Antonine, 18. Smallpox

### Down

- 1. Fever, 3. Ebola, 4. Half,
- 5. Cocoliztli, 8. Spanish,
- 9. Yellow, 10. Roosevelt,
- 11. Pestis, 13. Theiler,
- 14. Jonas, 15. Zika, 16. Max

### Across

- 2 Haemorrhagic fever virus identified in Germany in 1967 (7)
- 3 Viral infection of the nervous system, generally fatal once symptomatic (6)
- 6 'Virus-like' infectious agent that triggers abnormal protein folding (5)
- 8 Lentivirus leading to progressive immune system failure (abbr.) (3)
- 11 Asian coronavirus outbreak of 2003 (abbr.) (4-3)
- **14** First to use 'informed consent' forms, in his studies of mosquito-borne yellow fever (4)
- 16 Self-assembling structural unit of a virus (9)
- 18 Won Nobel Prize for virus protein studies (7)
- 19 'Vomiting bug' causing 200 000 deaths globally per annum (9)

### Down

- 1 Viral infection typically featuring parotitis (5)
- 4 Membrane surrounding 9 down (8)
- 5 West African viral fever spread by rats (5)
- 7 Russian microbiologist considered to have first discovered a virus (9)
- 9 Protein shell enclosing the viral genome (6)
- **10** Mosquito-borne viral disease leading to hospitalisation of 500 000 people per annum (6)
- 12 Infection last seen in Bangladesh in 1975 (8)
- **13** Camels are a host of this virus, identified in Saudi Arabia in 2012 (abbr.) (4-3)
- **14** \_\_\_\_\_ transcriptase: enzyme transcribing DNA from RNA (7)
- 15 Part of antigen recognised by antibody (7)
- 17 Tobacco \_\_\_\_\_: first virus to be identified (6)

# Save the date

All ESE educational events will be held virtually for the first 6 months of 2021, in as comprehensive a programme as possible. Details will follow soon. The latest ESE event information can be found at www.ese-hormones.org.

# **eECE 2021**

23rd European Congress of Endocrinology

22-26 May 2021

www.ece2021.org

45th Symposium on Hormones and Cell Regulation

6-9 October 2021

Mont Ste Odile, France

# **Deadlines**

15 January 2021

ESE COVID-19 Research Grant

Application deadline

28 February 2021

## ESE Awards 2021:

- Geoffrey Harris Award
- European Journal of Endocrinology Award
- Clinical Endocrinology Trust Award
- European Hormone Medal
- Jens Sandahl Christiansen Award

Nomination deadline

# Did you know?



# Influenza virus infection in obesity

Some 250 000-500 000 people die of influenza infection annually, worldwide. The 1918 Spanish 'flu pandemic caused 50-100 million deaths. However, at that time, undernutrition was more of an issue in society than obesity.

After the 2009 influenza A (H1N1) pandemic, obesity was found to be an independent risk factor for increased morbidity and mortality. Using rodent models, studies examined why obesity is a risk factor for influenza infection. Increased leptin levels in obesity may promote infection by lowering antiviral type 1 interferon (IFN). Furthermore, the lungs of infected obese mice showed diminished NK cell cytotoxicity, lower expression of IFNa/ $\beta$  and delayed expression

of pro-inflammatory cytokines, as well as changes in monocytes, lymphocytes and antigen presentation by dendritic cells associated with an impaired immune response. In contrast, adipose tissue showed increased inflammatory cell infiltration and cytokine levels, which are associated with complications such as insulin resistance.

In people, obesity appears to delay clearance of the viral load and to prolong shedding. Obese individuals infected with H1N1 virus were twofold more likely to be admitted to intensive care.

Read more in Bhattacharya et al. 2020 Frontiers in Endocrinology doi: 10.3389/fendo.2020.556962