Issue 13 Winter 2021

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Hormones in breast and prostate cancer:

Time to change the paradigm

Also in this issue

Learn more about EYES at ECE 2022, ESE's five year strategy and ENS T's 'HARMONISATION' initiative





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Cover Page: Multiplex immunofluorescence image, which shows prostate cancer cells in yellow and various types of immune cells surrounding and infiltrating the tumour that can be observed in red (T helper cells), green (T cytotoxic cells) and cyan (T regulatory cells).

Credits: Mateus Crespo, Bora Gurel, Ana Ferreira and Johann de Bono, Cancer Biomarkers Team, The Institute of Cancer Research.

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Editorial



















One might say that the most important things in life are subjective. We do not choose who we will truly love based on facts and data, and what we will find inspiring based on popularity or social acceptance. Sometimes, we find deeper meaning and connection by allowing ourselves to embrace the process, rather than just the result. This year was challenging, ruthless, and beautiful all in one, and we are so thankful for the support from ESE and our endocrine community which has inspired us to do more and be better.

In this issue, we celebrate great science and explore the role of hormones in breast and prostate cancer with four amazing feature articles while also remembering the patients and raising awareness about this incredibly important topic.

Also, you will meet Paddy Dempsey, our amazing scientist, hear more about ENSAT and its initiatives, including HARMONISATION, which aims to harmonise clinical care and research on adrenal tumours throughout Europe. We will hear about the exciting ESE strategy for the next five years and plans for ECE 2022 in Milano and EYES 2022 in Zagreb. We introduce the Spanish National Society and the CoMICs initiative from the UK.

Happy holidays and happy New Year to you from EYES Newsletter Editorial Board and thank you.

Happy reading!

Antoan Stefan Šojat, EYES Newsletter Editor



EYES Co-Chair Report

We're very excited to announce the first EYES Research Observership Programme (EYES R.O.P) to be launched. The new R.O.P is led by the Early Career Committee (EYES) of the European Society of Endocrinology (ESE) and allows Early Career Investigators (ECI) doing basic or translational research in Europe to grow and learn during a short, one-month stay in various European endocrinological centres.

We now have six distinguished centres across Europe that have confirmed their participation: Prof. Fassnacht (University of Würzburg), Dr Andoniadou (King's College London), Prof. McCabe (University of Birmingham), Dr Val (Université Clermont Auvergne), Prof. Migliaccio (University Foro Italico) and Prof. Biermasz (Leiden University Medical Center). The call is already open and we hope to receive your excellent applications to make this R.O.P. competitive and something to aim for! Successful candidates will be announced during the ECE in Milano in May 2022. The observerships will commence as soon as possible after this. Read more about the exciting event of the ECE and our EYES symposium during our congress on page 13.

We would like to thank all the EYES members who joined us in our special Christmas edition of the EYES Coffee Connection. We all enjoyed a jolly and light-hearted Christmas vibe with your favorite EYES Committee members in Christmas outfits and a fun and interactive Christmas quiz. We will be announcing many more activities to have fun together again! Stay tuned and follow us on our social media!

Last but not least, this issue is about awareness of prostate and breast cancer and the first edition with our new EYES News Editorial Board members Dr Settimio D'andrea (Italy) and Dr Karin Zibar (Croatia). We hope you enjoy this newsletter and see

you soon at one of our events! From the EYES Committee and EYES News Editorial Board we wish you all a happy New Year.

Eva Coopmans, The Netherlands EYES Co-Chair



Key Dates for your Diary

ESE's 2022 programme of events will be announced early January 2022! See www.ese-hormones.org/events-deadlines and watch your inbox for emails with details, early bird rates, free places and grant information!

7 - 19 Feb 2022

International Conference on Fatty Liver (ICFL 2022) Vienna, Austria

23 - 26 Mar 2022

45th Symposium on Hormones and Cell Regulation Mont Ste Odile, France

6 - 10 Apr 2022

Clinical Endocrinology 2022 Online

6 - 10 Apr 2022

International Liver Congress 2022 London, UK

21 - 24 May 2022

24th European Congress of Endocrinology, ECE 2022 Milan, Italy

7 - 10 August 2022

10th International Congress of Neuroendocrinology Glasgow, UK 2 – 4 September 2022 9th EYES Annual Meeting Zagreb, Croatia



Keep up to date with ESE events at Events & Deadlines | ESE (www.ese-hormones.org/events)

Oestrogen, progesterone, and breast cancer: a two-sided story

Ovarian function declines steadily towards menopause. Both oestrogen and progesterone levels change in the years prior to the final menstrual period. Thereafter, progesterone is almost undetectable, whereas oestrogen remains in low range mainly due to adipose tissue and aromatase activity which are the main sources of endogenous oestrogen synthesis in menopausal women. Oestrogen levels correlate strongly with body mass index (BMI) and BMI correlates strongly with breast cancer risk¹. Furthermore, most oestrogen receptor (ER+) positive breast cancer occurs after menopause.

Prior to the Women's Health Initiative (WHI) trial results in 2002, menopausal hormone therapy was generally accepted as appropriate and safe. However, the unexpected findings of breast cancer risk in women taking oral conjugated equine oestrogens (oCEE) and medroxyprogesterone acetate, led many women to stop taking, and many physicians to stop prescribing, menopausal hormone therapy. Further, in the general public, it led to overall misunderstanding that all menopausal hormone therapy modalities are the same and carry the same risks².

The 2012 a WHI sub-analysis reviewed the risk of breast cancer diagnosis in the oCEE-alone study arm showing that with oestrogen use, there was a lower incidence of breast cancer compared with placebo, mortality per year from breast cancer was less than that seen in controls who did not use menopausal hormone therapy, and in fact, fewer women in the oestrogen-alone group than the control group died from any cause³. This led to the conclusion that adding a progestogen to menopausal hormone therapy increases the risk of breast cancer.

However, there are two sides to every story. Studies examining the breast cancer risk with respect to different progestogens showed that there is some risk with certain progestins, but not when natural (micronized) progesterone or dydrogesterone are used². In fact, the in vitro and in vivo studies of Jason Carroll's group (Cambridge, UK) show that progesterone has a protective role in breast tissue

'The benefits of menopausal hormone therapy outweigh the risks – we all agree on that. We also support the initiation of treatment for symptomatic women who are under the age of 60 or within 10 years of menopause and without contraindications.'



and antiproliferative role in ER+ breast cancer. Furthermore, they propose that the lack of progesterone in menopausal women allows unopposed oestrogen activity contributing to the increase in ER+ breast cancer incidence in a postmenopausal context².

The benefits of menopausal hormone therapy outweigh the risks – we all agree on that. We also support the initiation of treatment for symptomatic women who are under the age of 60 or within 10 years of menopause and without contraindications^{4,5,6}.

Ljiljana Marina, Serbia

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Breast cancer and bone health

Breast cancer represents the most common type of cancer in women, with an incidence that is continually increasing. On the other hand, survival has substantially improved during recent decades. These improvements are due to both the availability of better treatment options and the establishment of broader breast cancer screening programmes. The increasing number of breast cancer survivors creates inevitably new needs for their care and specifically for their bone health care.

Many of the available treatments, such as aromatase inhibitors (Als), suppress the production or counteract the effect of reproductive hormones, which are critical for the maintenance of normal bone remodelling. Tamoxifen is a selective oestrogen receptor modulator (SERM), which exerts oestrogen agonist effects in bone that are beneficial for post-menopausal women. However, chemotherapy-induced amenorrhea leads to negative bone effects in pre-menopausal women. Other chemotherapy regimens may induce premature ovarian insufficiency (POI). Bone health may also be compromised by the disease course, as there is a possibility of bone metastases.

Data regarding bone loss and increased fracture risk in breast cancer patients have resulted in recommendations by prominent scientific societies regarding bone health evaluation of all women with breast cancer. The goal is to identify women at high risk of fracture and to introduce anti-fracture interventions in those at higher risk. Bone mineral density (BMD) measurement should be performed in all women older than 65 years of age, independently of the next anti-cancer therapeutic steps, and in those who are going to be treated with Als before treatment initiation, even if they are younger than 65 years. Of course, premenopausal women who receive tamoxifen or any kind of chemotherapy and experience POI should be evaluated with BMD too.

Factors that increase the risk of fracture in these women are BMD T score < -2, treatment with Als, older age (especially >65 years), premenopausal women with POI, oral corticosteroid use for more than 6 months, low body mass index (BMI <20 kg/m2), personal or family history of hip fracture, as well as smoking habits. A detailed medical history will reveal all these factors and enable identification of an increased risk of fracture. FRAX score is a traditional fracture

'Breast cancer represents the most common type of cancer in women and survival has substantially improved during recent decades. The increasing number of breast cancer survivors creates inevitably new needs for their care and specifically for their bone health car.'



risk estimation tool for the general population. However, it does not include anti-cancer treatment as a specific risk factor and thus its value in women with breast cancer has not been evaluated. In case it is used, physicians should bear in mind that it may underestimate the fracture risk of these women, as a number of important parameters are not included in the algorithm.

After BMD measurement and baseline fracture risk assessment, all breast cancer survivors should be advised to follow lifestyle changes that favour bone health. More specifically, a diet rich in calcium is recommended along with appropriate supplementation, if needed, of both calcium (1,000 mg per day in total) and vitamin D to maintain 250HD levels of 30-40 ng/ml (2,000 iu per day in case of normal levels or 4.000 iu per day in case of deficiency). Breast cancer survivors should also follow a weekly exercise programme with weight-bearing exercise, which is essential for bone strength and bone quality improvement, although this is a general recommendation deriving from data of women without breast cancer. Alcohol consumption is suggested to be limited, while the need for smoking cessation should be emphasised.

On top of the above recommended lifestyle changes, some selected cases, those with T score <-2 or those with more than two risk factors present, need to also be treated with bone-directed, anti-resorptive therapies to manage low BMD, prevent rapid bone loss and decrease the risk of fracture. Indeed, some relevant efficacy and safety data are available for bisphosphonates and denosumab, while exogenous hormonal therapies (oestrogens or teriparatide) are not indicated in women with a history of breast cancer.

Stavroula A. Paschou, Greece

Amazing careers: Meet Paddy Dempsey

Paddy Dempsey is a multidisciplinary medical research scientist, with groundings in human physiology, sport and exercise science and public health. He is a National Health & Medical Research Council (NHMRC) Postdoctoral Fellow based within the Physical Activity Epidemiology programme, University of Cambridge, and the Leicester Diabetes Centre, University of Leicester. He continues close collaborations with several laboratories (Physical Activity, Behavioural Epidemiology and Metabolic/ Vascular Physiology) at the Baker Heart and Diabetes Institute and the Centre for Urban Transitions, Swinburne University of Technology (Melbourne, Australia).

Paddy's research interests are currently focused on the role of physical activity, sedentary behaviour, and diet (including their interacting effects) in the prevention and management of chronic diseases – particularly type 2 diabetes and cardiovascular disease. His research on physical activity, sedentary behaviour and diabetes has appeared in a variety of high-impact medical and public health journals, has influenced international physical activity/exercise clinical guidelines for those with diabetes and hypertension, and has received international media attention. He has also been involved in physical activity guideline development for the American Diabetes Association and the World Health Organization.

What motivated you to choose endocrinology and how did your journey begin?

I have always had an inherent fascination with science and how the human body works. My research in the area of physiology and exercise physiology was initially motivated in part by my own athletic pursuits (undergraduate/Master years in Otago, New Zealand; where I am originally from), but evolved over time towards implementing Police physical fitness/competency testing and supporting elite level athletes in various disciplines (e.g. swimming, athletics, rowing, cycling).

'There is just so much potential to make a real impact, particularly in more vulnerable populations, through small and simple changes in the way we live our lives.'



Later, I became more interested in how I could apply the scientific principles I'd learnt to battle chronic disease (PhD, Baker Heart & Diabetes Institute, Australia; then postdoc in Cambridge). Physical inactivity is a key modifiable behaviour that is not only aberrant to human evolution (and thus a preventable affliction) but is also a major cause of illness in modern society. Despite this, we still have so much to figure out about why and how physical activity is beneficial, in whom, and most importantly, how to get more people to do more of it. This is where I felt I could make a bigger difference.

Much of the work I do is from a more applied perspective. I enjoy trying to better understand underlying physiological mechanisms and was really drawn to type 2 diabetes and cardiovascular disease because they are such big issues facing clinical and public health. There is just so much potential to make a real impact, particularly in more vulnerable populations, through small and simple changes in the way we live our lives. I have seen many patients (a family member included!) effectively 'reverse' their type 2 diabetes in this way without the need for any drugs. We need to do more to get these messages across, but vitally we also need to figure out ways to make more physical activity, less sitting, and other health-related behaviours (e.g., better diet, sleep, less stress) 'the easy choice'.

What do you see as a key moment of your career?

My work/career has spanned a few different areas so far (elite sport/ clinical exercise physiology, occupational physiology, metabolic and vascular physiology, and epidemiology), so it's hard to pick out 'key moments' as I have learnt valuable lessons along the way from these many different experiences/environments and the interactions between them. Most recently I have been involved in physical activity and sedentary behaviour guideline development for the American Diabetes Association and the World Health Organisation. I guess I think of these as 'key moments' so far (hopefully there are more to come!) as I was able to use my expertise to help make an 'impact' on a broader scale. It also made me more aware of the 'bigger picture' of what we are trying to achieve in my area of research, and the key challenges and research/ implementation gaps that we still need to bridge.

What were the greatest challenges you have encountered?

Science can be tough and frustrating at times for many reasons but is also a privilege and can be incredibly rewarding – you never stop learning. Key challenges/obstacles are probably similar to many other ECR's and tend to be related (ironically) less to the science itself, but more the systems within which we operate. To name a few: a paucity of funding or financial support, academic job market and career uncertainty, pressure to network and publish, emphasis on quantity over quality, competition and unclear targets (you never really know/feel as if you are doing 'enough' or what that bar even is), support and mentorship, work-life balance, time-management, bureaucratic burdens, coping with change, finding your place and trajectory... There are many things I'd like to change in the systems, but for the moment the flexibility, people, and the benefits of doing research I enjoy are currently outweighing the cons.

How do these compare with when you were starting out in your career? Has there been any progress?

There has been some progress, I think, but many fundamental issues remain and won't change without sufficient investment or change in policies. Social networking and technology have been important in increasing efficiency, engagement, and networking – which has been accelerated by COVID-19. Societies appear to be paying more attention to ECR members and their skills/ development/career pathways. There are also many opportunities for ECRs both inside and outside of academia with the right networks, guidance, and mentoring.

In which areas do you think EYES can have the greatest and most useful impact in the future?

Like most early career platforms/groups, I think that EYES can play an important role in fostering the interaction, capacity, and growth of early career professionals, identifying their training/career needs, and finding ways of training that suit those needs. EYES can also act as an important platform for awareness, networking, and finding mentors or colleagues with similar goals/interests/experiences. This could lead to the cultivation of new ideas/projects in a less intimidating environment, particularly to help bridge the gap between clinical and basic researchers, and even the more applied scientists or those working with big data (e.g., epidemiologists, bioinformaticians, etc).

Which endocrinologists did you find most inspirational when you were starting out, and why? Which have inspired you most since?

I have really enjoyed discussing ideas and learning from the amazing minds I have had the privilege of working alongside or bumping into over the years, and am continuously impressed and inspired by my colleagues, mentors, and collaborators. Most of the 'endocrinologists' I have come across have been more applied in the physical activity space, among other disciplines, to name just a few that spring to mind, in no particular order, and who's papers 'Remember, you are still a student – be willing to try things, make a few mistakes, and get outside of your comfort zone – that's when you really start learning. Do not assume anything and ask lots of questions. Expect setbacks and criticism, but stay positive, determined, and always persevere.'

I thought were cool, include: Mark Hargreaves, Bronwyn Kingwell, Frank Booth, John Hawley, Brendan Egan, Erik Richter, Bengt Saltin, George Brooks, Juleen Zierath, Darrell Neufer, Bente Pedersen, Mark Febbraio, John Thyfault, Barry Braun, Sheri Colberg, Ron Sigal, Michael Riddell, Audrey Bergouignan, John Holloszy. Many of these researchers have been pivotal in putting physical activity 'on the map' concerning mechanisms and physiology – but there are plenty of other physical activity researchers doing vital work in nonendocrinology areas.

What advice would you give people starting out in endocrinology today?

I think some important things to ask yourself when starting out (e.g., considering a PhD) are:

- Will a PhD get me where I want to be? What skills do I hope to gain in the process?
- Will I enjoy the topic, and will it keep me interested for the next 3-4 years?
- Is the work important? How, why and to who?
- Is the laboratory a good fit for me? Will I like and get along with the supervisors and colleagues I will be working with? Do they provide inspiration and motivation?
- Can I work independently, but will I have plenty of support (e.g., funding, feedback, technical) along the way when I need it?

First explore all your potential options, then trust your gut. Remember, you are still a student – be willing to try things, make a few mistakes, and get outside of your comfort zone – that's when you really start learning. Do not assume anything and ask lots of questions. Expect setbacks and criticism, but stay positive, determined, and always persevere. Focus on the journey. Work Hard, Play Hard, Rest Hard, and take time for yourself, family, and friends. Have hobbies, take time off and do things you love outside of the work/PhD. Enjoy the privilege and flexibility of being paid to conduct research, travel, and more – many don't get this opportunity. Listen to everyone, but don't take everyone's advice - mine included! Talk to lots of people with different experiences, values, and beliefs.

Philip McBride,

UK

Endocrine therapy in advanced prostate cancer

Prostate cancer is the most diagnosed tumour pathology among men in more than 50% of countries worldwide and represents one of the leading causes of cancer-related death among the male population in developed countries. Importantly, when the cancer is diagnosed at an early stage, it usually represents a curable disease, due in part to the huge advances on surgery (radical prostatectomy) and radiotherapy during recent years. That is why it is so important for men to get themselves checked regularly! Unfortunately, these therapeutic strategies are not effective when we face advanced prostate cancers, clinically aggressive tumours that have spread to other sites of the body. In these cases, androgen deprivation therapy (ADT) as well as the blockade of the androgen receptor (AR) are the main standard-of-care therapeutic strategies.

But who discovered the anti-tumour effects of hormonal therapies in the context of prostate cancer? When? How? Let's start at the very beginning...

In 1941, Charles Huggins (who was awarded the Nobel Prize in Physiology or Medicine in 1966) and Clarence Hodges demonstrated the beneficial effect of surgical castration for men with metastatic prostate cancer. The next revolution in the field arose in 1971, when Andrew Schally, Roger Guillemin, and Rosalyn Yalow (winners of the Nobel Prize in Physiology or Medicine in 1977) found that chronic administration of LHRH agonists led to pituitary gonadotropin inhibition, thus reducing secretion of LH and FSH and resulting in a significant decrease of circulating testosterone. In 1989, the FDA approved flutamide, the first nonsteroidal anti-androgen for the treatment of advanced prostate cancer, which binds to the AR, thus effectively inhibiting the actions of androgens. Despite promising anti-cancer activity, some clinical limitations of flutamide led to the development of secondgeneration anti-androgens (e.g., enzalutamide). Remarkably, after all these advances in the field, the current endocrine therapies for men with advanced prostate cancer still comprise LHRH agonists, second-generation anti-androgens and abiraterone. Specifically, abiraterone was developed in the early 1990s and consists of a potent inhibitor of CYP17, an enzyme that is involved in the synthesis of androgens, which is expressed in testicular, prostate, and adrenal tissue.

'There is still a lot to be done to improve the outcome of patients with advanced prostate cancer, especially since the prevalence of this disease does not stop growing, but we are getting there, step by step.'



Although, as mentioned before, endocrine therapy represents the main standard of care for patients with advanced prostate cancer nowadays, these tumours will eventually become resistant to this strategy, ultimately representing a lethal disease. The rapid development in understating of the prostate cancer biology and the latest scientific advances (e.g., next-generation sequencing, single cell analysis) were key to discovering numerous mechanisms of resistance to the endocrine therapies, including AR overexpression, AR mutations, AR splicing or increased AR ligand availability, opening new therapeutic avenues for this subset of patients that should be validated in clinical trials in the near future.

In conclusion, there is still a lot to be done to improve the outcome of patients with advanced prostate cancer, especially since the prevalence of this disease does not stop growing, but we are getting there, step by step.

Juan Manuel Jiménez Vacas, UK

Filling the gap for sexual function after prostate cancer

Prostate cancer (PCa) is the second most common cancer in males and the fifth leading cause of cancer death in men. An estimated 1.3 million cases were diagnosed worldwide with prostate cancer in 2018, accounting for around 7% of all cancers diagnosed in both sexes and constituting a massive burden on healthcare systems worldwide. Thanks to the improvements in detection rates and management achieved in recent decades, PCa has the highest survival rates of all cancers, with growing percentages of early-stage diagnosis. On the other hand, men diagnosed earlier are dealing with the consequences of cancer and/or its treatments for a longer time¹.

Indeed, PCa treatment can negatively impact multiple areas of a patient's well-being, both psychological and physical. Nowadays, options for PCa include total prostatectomy, radiotherapy, androgen deprivation therapy (ADT), chemotherapy, and immunotherapy. All active treatments available have potential harmful effects on sexual function, varying by different specific treatments.

Radical prostatectomy involves the surgical removal of the prostate and surrounding tissue. Usually it provokes erectile dysfunction in 50-70 % of men, due to direct surgical damage to the nerves involved in penile erection located nearby the prostate gland. Furthermore, perception of penile length loss due to chronic loss of erections and decreased blood flow is often reported, as well as other functional impairments linked to extensive pelvic surgery: urinary incontinence and retrograde ejaculation². The choice of nerve-sparing surgical techniques, focused on safeguard of nerves, may result in an improved longterm recovery of erectile function; however, its feasibility largely depends on tumour location and aggressiveness. In most recent years, robot-assisted prostatectomy led to an improvement of erectile functioning in comparison to open radical prostatectomy.

Although often necessary, surgery is not the only option. Radiotherapy for PCa consists of two techniques: external radiotherapy, in which radiation beams are targeted at the prostate; and brachytherapy, in which radioactive seeds are implanted into the prostate. Usually, the sexual side effects of radiotherapy are lower and with gradual onset, but they can worsen over time. Although ejaculation mechanism is preserved, radiation treatment can decrease the semen volume and therefore contribute to psychological distress of patients. Moreover, external radiotherapy beams may damage the rectum, causing gastro-intestinal complications potentially leading to severe negative impact on sexual intercourse.

In addition, ADT could be used in association with other treatments or independently, especially for patients with metastatic disease. ADT can be reached with bilateral orchiectomy or using medications such as anti-androgens or most commonly with luteinizing hormone-realising hormone agonists or antagonists. ADT is inevitably causing erectile dysfunction, reduced libido, and decreased semen volume, due to hypogonadism. Moreover, other side effects, such as gynecomastia, altered body composition, asthenia, and body hair loss, may also negatively impact sexual life³.

In this context, medical interventions are focused on penile rehabilitation, aimed to restore erectile function, and prevent penile changes that worsen the psychological impact of disease. Phosphodiesterase-5 inhibitors (PDE5i) are the most widely used treatment for penile rehabilitation in PCa men, particularly efficacious on erectile dysfunction and penile length loss. Second-line medical treatments involve intra-urethral or intra-cavernosal administration of vasoactive medications (e.g. alprostadil, papaverine). Despite the large number of studies so far conducted involving both animal and human models, no univocal agreement has been reached to define a "standard protocol" for penile rehabilitation. In this view, other non-medical and non-surgical treatments have been proposed (e.g. vacuum erection devices, and low-intensity extracorporeal shockwaves) to be used independently or in conjunction with PDE5i. However, the evidence for their applications remains too poor to propose them universally⁴. Penile prosthesis implant is usually limited to young men with no response to either first or second-line treatments.

In conclusion, a great improvement of management of sexual life after prostate cancer has been achieved during recent decades, but no univocal and curative treatment is yet available, therefore further efforts are needed to fill the gap and protect this crucial aspect of male health.

Settimio D'Andrea & Walter Vena, Italy

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EJE CoMICs

A medical student / junior doctor-led initiative to share the latest scientific research to a wider scientific and clinical community in <2 min

The practice of evidence-based medicine requires healthcare professionals to stay up to date with an ever-growing body of medical literature. This volume of information can be overwhelming and may deter medical students and junior doctors from engaging with the latest research¹. Studies have shown that information presented visually is processed more quickly than words alone and allows students to remember up to 6.5x more information than simple text in books or online². As such, the Concise Medical Information Cines (CoMICs) team developed an innovative solution to tackle this issue: European Journal of Endocrinology (EJE) CoMICs.

CoMICs, a medical education initiative, conceptualised by medical students and junior doctors, produces bite-sized videos consisting of illustrations and infographics. Each video depicts a specific disease or medical condition, from presentation and investigations to stepwise management and follow-up options. Building on the success of CoMICs, the team has collaborated with the EJE to produce short videos presenting selected articles published in the EJE.

Each EJE CoMIC takes approximately one month to produce. The editorial team selects a peer reviewed article which is of particular interest to the wider medical and scientific community. The CoMICs team create the videos and the CoMICs are released biweekly on the EJE YouTube channel, summarising the latest research in the field of endocrinology in under 2 minutes!

During the current pandemic, the issue of accessibility has been at the forefront for many educators. EJE CoMICs have several advantages over traditional media used to disseminate scientific











Emily Warming









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content. These 2-minute videos are useful for clinicians and academics to engage with the latest research despite their busy schedules. With the CoMICs being created by medical students, who are in turn mentored by early career researchers, end user satisfaction is at the core of EJE CoMICs, ensuring the content and presentation is concise and simplified to maximise engagement. Furthermore, the videos are freely available worldwide on YouTube, ensuring easy access. EJE CoMICs also provide publicity for new research articles on social media, thus helping to increase the profile of both the research and the researchers who made it happen.

The medical students involved in creating EJE CoMICs have greatly benefited from being part of this initiative. They get to study the latest research before it becomes available to the wider scientific community and engage with authors to understand the science behind the articles. Engaging with authors of these research articles further helps improve scientific writing skills.

All current and past EJE CoMICs are available on the European Society of Endocrinology YouTube channel. For more information about CoMICs, please visit our webpage <bit.ly/SimbaComics> or follow us on social media: YouTube SIMBA Simulation, Twitter @SimbaComics, and Instagram @simba.comics.

The EJE CoMICs Team

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10

Stronger together!

The European Network for the Study of Adrenal Tumours, ENS@T, was founded in 2002. National adrenal networks from France, Germany, and Italy alongside adrenal teams from United Kingdom joined forces in order to work towards a common aim: improve the understanding of the genetics, tumourigenesis, and hypersecretion in patients with adrenal tumours and associated familial syndromes.



The founding Executive Committee Members were Bruno Allolio (Würzburg, Germany), Xavier-Yves Bertagna (Paris, France), Massimo Manelli (Florence, Italy), Franco Mantero (Padua, Italy), Pierre-Francois Plouin (Paris, France), Paul M. Stewart (Leeds, UK), and Martin Reincke (Munich, Germany). Since then, many great endocrinologists from the adrenal world gave their best to ENS@T and created an open and warm Pan-European network.

Every year ENS T organises the annual scientific meeting. This is an opportunity for people to meet the greatest adrenal endocrinologists in one place in a friendly and informal atmosphere. Also, you can join many of the ongoing and upcoming ENS T studies and projects. These collaborations are a great opportunity for young clinicians and researchers as you get to learn from and work with the best in the sector. The results of these multicentric studies are presented in big meetings and published in high impact journals.

One of the biggest ENS@T studies was published last year in Lancet Diabetes & Endocrinology: Urine steroid metabolomics for the differential diagnosis of adrenal incidentalomas in the EURINE-ACT study: a prospective test validation study by Irina Bancos, Angela Taylor, et al. This truly Pan-European interdisciplinary project, led

by Wiebke Arlt (Birmingham, UK) took 10 years from conception to publication. It prospectively recruited 2017 patients and compared the accuracy of urine steroid metabolomics and imaging in detecting the adrenocortical cancer (ACC) patients with newly diagnosed adrenal masses. It has shown that unenhanced CT tumour attenuation cut-off of 20 HU should replace that of 10 HU for exclusion of ACC and a triple test strategy of tumour diameter, imaging characteristics, and urine steroid metabolomics showed to improve detection of ACC, which could shorten time to surgery for patients with ACC and help to avoid unnecessary surgery in patients with benign tumours.

Another great European project was just launched in September 2021. In the context of quite heterogeneous management of adrenal tumours, which leads to substantial inequality in patient care throughout Europe, the leading members of ENS₂T created HARMONISATION. The goal of this COST Action is to constitute a multidisciplinary network to harmonise clinical care and research on adrenal tumours throughout Europe. HARMONISATION is chaired by Darko Kastelan (Zagreb, Croatia) and co-chaired by Guillaume Assie (Paris, France) who is also the president of ENS₂T.



The originality of HARMONISATION is that it gathers participants from different geographical sub-groups. Another innovation is that it involves experts in artificial intelligence, databases, data protection, and legal and ethical issues, in addition to researchers and clinicians. However, one of the cornerstones of HARMONISATION is the inclusion of Early Career Investigators (ECIs) in all its activities. They will be engaged by internationally renowned researchers, and this will promote their careers by helping them acquire new skills, running original research, and building/expanding their international networks. ECIs will be specifically targeted through master classes, training schools, and short stays.

With ENS[®]T and HARMONISATON, this is an amazing time to be an ECI in the Adrenal field! So, use the opportunity to get involved with some of the many exciting and promising European collaborations!

Ljiljana Marina, Serbia

Croatian Young Endocrinologists Section welcome the EYES Annual Meeting in 2022!

The 'Young Endocrinologists Section' is a subdivision of the Croatian Society of Endocrinology and Diabetology, Croatian Medical Chamber. The aim of the Section is to bring together and network young specialists and residents in endocrinology and diabetology in Croatia and the surrounding region.

The active work of our section began during the COVID-19 pandemic, so we have shifted our activities to the digital domain:

- We have organised various lectures on endocrine cases.
- On our YouTube channel we have a project called "How do I?", where our experts teach interesting topics within endocrinology.
- We create written educational materials and conduct training for emergency medicine colleagues.
- We are also active on Facebook and Twitter (@croendoyoung).
- Our last event was "The Second Online Regional Meeting of Young Endocrinologists" with the theme "Endocrinopathies in Pregnancy". Six countries were actively involved: Serbia, Slovenia, Bosnia and Hercegovina, Macedonia, Montenegro, and Croatia.

Welcoming EYES to Croatia in 2022!

We are delighted to be hosting the 9th EYES Congress next year, which will be held in Zagreb, Croatia, from 2 - 4 September 2022.

Zagreb is the capital and largest city of Croatia and is located in the northwest of the country. It is becoming increasingly popular and attracts tourists from all over the world due to its many historical sites, interesting museums, and events. Accommodation and lectures will be provided in the centre of Zagreb. We have already been working on the plans for the three-day meeting, which will start early Friday afternoon and end early Sunday afternoon.





Young Endocrinologists Section of the Croatian Society of and Diabetology and LOC of EYES 2022 Annual Meeting



Young Endocrinologists Section of the Croatian Society of Endocrinolog and Diabetology and LOC of EYES 2022 Annual Meeting

The scientific programme will include:

- 4 plenary lectures
- 2 workshops (clinical and scientific)
- and 6 oral sessions (adrenal and neuroendocrine tumours, thyroid, calcium& bone, diabetes, obesity& metabolism, reproductive endocrinology, and pituitary& neuroendocrinology).
- The social programme will include two conference dinners with live music, a pub quiz, and a city tour. Registration and abstract submission will be open in spring 2022.

We invite you to come to Zagreb, explore our city, educate yourself, share experiences, and enjoy our social events.

Anja Barač Nekić, Croatia **Karin Zibar Tomšić,** Croatia EYES 2022 Local Organising Committee



The most important Endocrinology Congress in Europe will be in Milan in May 2022! We'll be there - will you?

24th European Congress of Endocrinology (ECE), 21-24 May 2022 heads to Milan, Italy!

It is with great pleasure that I and the rest of the Local Organising Committee for ECE 2022, invite you to join us in the beautiful city of Milan in Italy in May for the first face-to-face ECE since 2019. The Chair of the ECE 2022 LOC and ESE's immediate Past President Andrea Giustina has stated that this will be "the 'renaissance event' of world endocrinology!", and we both look forward to welcoming you to Milan.

When you read this, I hope that you will have already submitted your abstract as the deadline is 31 January 2022, and registered. If not, do it now as we are looking forward to seeing you at the EYES Symposia on Sunday 22 May - this year dedicated to the theme of Artificial Intelligence use in the field of Assisted Reproduction Technology, a virtuous example of the application of advanced technologies to the field of endocrinology and healthcare.

This will be followed by the Informal Networking event which the EYES Committee are organising (it's going to be one to remember!) that evening and also for the Young Investigator Awards session on Monday 23 May. In between we will see you at the sessions, in the

ECE 2022 24th European Congress of Endocrinology

21-24 MAY 2022, Milan, Italy

ABSTRACT DEADLINE: MONDAY 31 JANUARY 2022

European Society of Endocrinology 'The Chair of the ECE 2022 LOC and ESE's immediate Past President Andrea Giustina has stated that this will be "the 'renaissance event' of world endocrinology!", and we all look forward to welcoming you to Milan'

halls between them, meet for coffee in the exhibition hall or in front of one of your posters – the best thing about it is we will see each other!

But if you can't travel to Milan, you can still experience it via ESE Home – live streamed sessions, networking tool and the rest on ESE On Demand. You can still join us!

If you are able to come to Milan, please bear in mind that you can apply for an ESE grant to help you with travel and accommodation costs (opens in February 2022).

All information is available at www.ese-hormones.org/ece-2022 and you will be receiving lots of updates and information about ECE 2022 in the lead up to May.

Non aspettare, registrati ora! Non vediamo l'ora di vederti a Milano! (Don't wait - register now and we can't wait to see you in Milano!).

Walter Vena, Italy EYES Representative on ECE 2022 LOC

European Women in Endocrinology (EUWIN) – launching soon

The ESE Office Team is delighted to announce that we are working with the founders of a new group, 'European Women in Endocrinology' (EUWIN) to improve opportunities and diversity for women in European endocrinology and within ESE.

This group has been founded by Cynthia Andoniadou, Wiebke Arlt, and Jenny Visser and has the primary aim to enhance networking and collaboration between European women in endocrinology.

One of the key aims of this new ESE Community is the development of specific mentoring and support for career advancement of young female trainees and investigators. We are currently working with Cynthia, Wiebke and Jenny to ascertain how the group can best support them and will be reaching out to our early career EYES members to ask for feedback, ideas and commentary as well as involvement. An official launch is being planned at ECE 2022 in Milan. Watch this space!

Victoria Withy, UK

ESE Sales & Marketing Manager



Martin Reincke – Introducing our ESE strategy for 2022-26

As I reported within the last Endocrine Views, ESE is in the process of reviewing its strategy for the next strategic period of 2022-26 and I am keen to involve all early career EYES members of ESE as we are developing the Society to support your futures! I remember well the last strategic review which I was personally fully involved with - which was for the 2012-16 strategic plan and was developed in 2011 at a workshop at Schloss Hohenkammer in Munich. How the world has changed since then - as has ESE.

We have now gone through the process of development of our new strategic goals with the Executive Committee and the EYES Co-Chairs were involved in this, representing you all. We have also consulted with all members (I hope many of you will have completed the survey during this consultation period as your voice is vital) and adjusted following this feedback. The over-riding aim is to continue to support our vision to shape the future of endocrinology to improve science, knowledge, and health.

I am pleased to announce our goals for the next five years:

- To UNITE and REPRESENT the European endocrine community and be acknowledged as the reference point for endocrine science, knowledge, and health
- To SUPPORT our members in education, clinical practice, and research
- To ADVANCE the science and standards of endocrinology
- And our internal goal to develop ESE as a SUSTAINABLE ORGANISATION which is trusted, valued, and referred to as bestin-class by its stakeholders

These five-year goals will be supported by strategies and tactics which are planned over the next two-year time period.

To provide accountability and provide a solid overview I am also launching a Strategic Review Committee with a diverse membership who will have the responsibility to make sure we are on track!

A key objective of my Presidency was to stay true to our values and improve the level of equality and diversity within ESE. This is now captured in our 'The Way that We Work' statement:

We aspire to be visionary, inspiring, engaging and supportive. We are open, transparent, and inclusive in everything that we do and work towards diversity across our activities.

I look forward to working with you all in line with our strategy – your support and engagement makes it possible. We take the responsibility of continuing to develop ESE to support your during your whole career very much to heart as you are the future leaders of ESE and of our discipline. Thank you.



Martin Reincke, Germany ESE President

Meet the Spanish Society of Endocrinology and Nutrition

The Spanish Society of Endocrinology and Nutrition (SEEN) is a non-profit organisation which aims to organise activities, publish scientific articles, as well as establish collaborations with teaching and research centres, bolstering its ultimate goal of 'promoting the research in the field of Endocrinology and Nutrition'.

Specifically, SEEN is comprised of endocrinologists, biochemists, biologists, and other professionals working in the field of Endocrinology, Nutrition and Metabolism. SEEN supports their members throughout their career with programmes and activities for continuing medical education and certification, while granting them the privilege of being at the forefront of the news related to the field. A great example of this is the monthly journal "Endocrinología, Diabetes y Nutrición", wherein the readers can find all the key dates and information about the society. In addition, SEEN organises numerous events, such as education courses, discussion forums, working groups, as well as the Annual Congress of the Spanish Society of Endocrinology and Nutrition.

In summary, SEEN offers to their members the opportunity of networking and establishing collaborations as well as being part of a fully committed group of basic and clinical researchers focused on



Sociedad Española de Endocrinología y Nutrición

generating new knowledge and transferring it to the clinical care to improve the diagnosis, treatment, and clinical management of the patients suffering from diseases affecting the endocrine system.

Javier Escalada, Spain President of the SEEN

EYES experience at the 62nd Congress of the Spanish Society of Endocrinology and Nutrition

I would like to start by thanking (on behalf of all the EYES community) the Organising Committee of the 62nd Congress of the Spanish Society of Endocrinology and Nutrition for the invitation to participate in this event, which took place from 13 to 15 October in Seville, Spain.

This opportunity allowed me to get to know SEEN better. I can tell that this prestigious Spanish Society is fully committed to its younger members, supporting the development of their career by promoting their training and developing activities for them specifically. Regarding the congress, I would like to highlight the excellence of the scientific programme, comprising both basic and clinical studies, with high-quality speakers, including not only Spanish experts in the Endocrinology field but also international guests, such as Dr. Albert Beckers, Dr. Maria Chiara Zatelli, and Dr. Monica Gadelha.

I had the pleasure of representing EYES in the ENDO-Young session, where I had time to explain our activities and main programmes, which caught the attention of many young members of the SEEN.



The EYES Committee is very grateful for this opportunity to share ESE's early career programmes and activities this congress and we are really looking forward to collaborating in the near future with the early career group of the Spanish Society of Endocrinology and Nutrition.

Juan Manuel Jiménez Vacas, UK

Latest research

Cardiovascular risk profile in growth hormone-treated adults with craniopharyngioma compared to non-functioning pituitary adenoma: a national cohort study.

More frequent presence of hypothalamic metabolic disruption in people with craniopharyngioma may lead to differing cardiovascular risk profiles when compared to non-functioning pituitary adenoma for patients being treated with growth hormone. This was a sub-analysis of the Dutch National Registry of Growth Hormone Treatment in Adults, in which baseline and longterm follow-up cardiovascular risk profiles and morbidity were assessed in over 1,000 patients with either craniopharyngioma or non-functioning pituitary adenoma. Craniopharyngioma patients had overall poorer cardiovascular profiles, including higher BMI measurements, and men in this group also had higher waist circumference measurements and lower levels of HDL.

Verweij, Tim *et al.* "Cardiovascular risk profile in growth hormonetreated adults with craniopharyngioma compared to nonfunctioning pituitary adenoma: a national cohort study." *European Journal of Endocrinology* **vol. 185**,6 793-801. 21 Oct. 2021, doi:10.1530/EJE-21-0419.

Metformin as an anti-inflammatory agent: a short review.

Despite its widespread use, particularly in the treatment of type 2 diabetes, the mechanisms of action of metformin are not fully understood. This review by Kristófi and Eriksson describe the current status of knowledge around the mechanisms by which metformin impacts inflammatory pathways and to highlight the existing evidence discussing metformin as an anti-inflammatory drug. The review discusses metformin's consistent exhibition of anti-inflammatory actions and relates these to modulation of mitochondrial function and subsequent increase in intracellular

AMP levels and activation on AMPK. The review concludes with a recommendation for prospective, randomised clinical trials with large cohorts to establish the effects that metformin has on classical inflammatory diseases.

Kristófi, Robin, and Jan W Eriksson. "Metformin as an antiinflammatory agent: a short review." *The Journal of Endocrinology* **vol. 251**,2 R11-R22. 28 Sep. 2021, doi:10.1530/JOE-21-0194

The characteristics of intestinal flora in overweight pregnant women and the correlation with gestational diabetes mellitus.

This study aimed to investigate the characteristic of intestinal flora in overweight pregnant women and to highlight any correlations with gestational diabetes mellitus. Study researchers split 122 women into four groups based on BMI (above or below 24) and presence or absence of gestational diabetes mellitus. Composition of intestinal flora was found to be significantly different in women with a BMI of at least 24 kg/m2 with gestational diabetes mellitus compared to the other three groups. Specifically, this imbalance intestinal flora presented in the form of increased Bacteroidetes and decreased Firmicutes. The authors posit that this imbalance could play an important role in the onset and development of gestational diabetes in women with a high pre-pregnancy BMI.

Su, Yao *et al.* "The characteristics of intestinal flora in overweight pregnant women and the correlation with gestational diabetes mellitus." *Endocrine connections* **vol. 10**,11 1366–1376. 19 Oct. 2021, doi:10.1530/EC-21-0433.

Pituitary surgery as alternative to dopamine agonists treatment for microprolactinomas: a cohort study.

Typically, treatment for microprolactinomas comes in the form of dopamine agonists. However, treatment with pituitary surgery is growing, and this study sought to evaluate the efficacy and safety of surgical treatments for microprolactinoma patients. The study followed-up on 114 consecutive patients treated by surgery between 2008 and 2020. From this cohort involved, 12% were not cured by the surgery that was undertaken; this included ten early surgical failures and four late relapses after surgery. However, the majority of patients responded positively and the study team conclude by highlighting that in well-selected microprolactinoma patients, pituitary surgery performed by an expert neurosurgical team can be an effective first-line treatment used as an alternative to dopamine agonists.

Baussart, Bertrand *et al.* "Pituitary surgery as alternative to dopamine agonists treatment for microprolactinomas: a cohort study." *European Journal of Endocrinology* **vol. 185**,6 783-791.21 Oct. 2021, doi:10.1530/EJE-21-0293.