Issue 21 Winter 2024

ISSN 2755-2756 (online)

eyes NEWS

The newsletter of the ESE Young Endocrinologists and Scientists

Building the foundations of endocrine research

European Society of Endocrinology

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Editor:
Juan Manuel Jiménez Vacas, UK

Deputy Editor:
Walter Vena, Italy

Editorial Board:
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Shamini Ramkumar Thirumalasetty, Germany
Victoria Withy, UK
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Sub-editor:
Caroline Brewser

Design:
Qube Design Associates

Website: www.ese-hormones.org

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ESE Young Endocrinologists and Scientists
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European Society of Endocrinology

Editorial


Juan Manuel Jiménez Vacas


Walter Vena


Settimio D'Andrea


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eyes
ESE young endocrinologists and scientists **looking forward**

It is both an honour and a privilege to step into the role of Editor-in-Chief of *EYES News*. Having served as Deputy Editor over the past year, I've had the incredible opportunity to learn from my esteemed friend and predecessor, Walter Vena. A heartfelt thank you to him for elevating our magazine's visibility and upholding the high standards set by previous Editors.

While I prefer to keep self-promotion to a minimum, I must acknowledge the brilliant team of clinicians and scientists on our Editorial Board. Their support will undoubtedly make this journey smoother, something that I've already had the pleasure of experiencing.

Now, let's dive into this issue's exciting content, as we delve deep into endocrinology, emphasising that, to make a clinical impact, we must first understand the biology of diseases. This is essential for successful translational research that can benefit patients and healthcare. We proudly feature articles from global leaders in various endocrine topics, showcasing significant advancements in both basic and clinical research.

Don't miss this issue's 'amazing career', featuring our **interview with Professor Cynthia Andoniadou**, a leading expert in endocrine stem cell biology. Additionally, we share highlights from the remarkable **EYES Annual Meeting in Helsinki, Finland** – and announce that the next one will take place in Milan, Italy! We also spotlight the **junior group of the Danish Society**, which is timely, as the forthcoming Joint Congress of ESE and ESPE (European Society for Paediatric Endocrinology) takes place in Copenhagen in May 2025.

There's much more to discover, so jump right in! I hope you enjoy reading this issue as much as we enjoyed putting it together.

Juan Manuel Jiménez Vacas
Editor, *EYES News*

You can flick through past and present issues of *EYES News* at **www.ese-hormones.org/eyesnews**

From your EYES Co-Chairs

This year's annual EYES Meeting in Finland was yet another resounding success!

Helsinki warmly welcomed early career endocrinologists and scientists from across Europe and beyond, with unseasonably pleasant weather (sunshine and warm temperatures) that made our 11th Meeting even more enjoyable.

What an incredible few days we had: the event was packed with amazing talks on cutting-edge basic and clinical science from world-renowned experts in endocrinology, as well as top-tier presentations by early career investigators. We also enjoyed lively discussions, a boat party with breathtaking views, coffee by the harbour, live Finnish music, and so much more. A huge thank you goes to the Local Organising Committee for their amazing work. Read the full story on **page 12.**

It will be hard, if not impossible, to match that meeting – that said, we are confident that the Italian organising team, led by Walter Vena, will rise to the challenge next year. We will gather in Milan for the **12th EYES Meeting** next September, and we're already looking forward to it!

Looking ahead, many exciting events and opportunities are on the horizon. In May, we will enjoy a **Joint Congress**, where ESE will meet with our colleagues from ESPE (the European Society for Paediatric Endocrinology). The 2025 programme for **ESE Summer School** is also already in preparation for Innsbruck, Austria, next June. And don't miss the new round of **EYES Observership Programme grants**. We strongly encourage all early career endocrinologists and scientists in our community to apply for this fantastic opportunity.

'Looking ahead, many exciting events and opportunities are on the horizon.'

EYES Committee members at the EYES Annual Meeting

There's so much more to come, so make sure you connect with us through social media to stay informed about the latest news and opportunities. In the meantime, your EYES Committee remains at your disposal, working hard to represent you and provide you with more exciting opportunities for growth and collaboration.

Juan Manuel Jiménez Vacas, UK
Walter Vena, Italy
EYES Committee Co-Chairs

Key dates for your diary

Keep up to date at **www.ese-hormones.org/events-deadlines** and watch your inbox for emails with details, Early Bird rates and grant information!

30 January–2 February 2025
Portuguese Congress of Endocrinology 2025
Porto, Portugal

3 February 2025
Joint Congress of ESPE and ESE 2025 Abstract submission deadline

6–7 February 2025
Dutch Endocrine Meeting 2025
Veldhoven, The Netherlands

6–7 February 2025
SIMBA Adrenal 2025
Birmingham, UK

20–23 February 2025
35th ESE Postgraduate Training Course
Bucharest, Romania/Online

28 February 2025
ESE Awards Nomination deadline

10 March 2025
EYES Observership (Exchange) Programme Grants Application deadline

10–12 March 2025
Society for Endocrinology BES 2025
Harrogate, UK

13–15 March 2025
11th Skeletal Endocrinology Meeting
Trento, Italy

24–26 March 2025
ESE Clinical Update on Aggressive Pituitary Tumours
Online

27 March 2025
Joint Congress of ESPE and ESE 2025 Early Bird registration deadline

29 March–1 April 2025
Joint Congress of the American Society of Andrology and the International Society of Andrology
Washington, DC, USA

8–10 April 2025
ESE Clinical Update on Management of Thyrotoxicosis
Online

24 April 2025
Joint Congress of ESPE and ESE 2025 Standard registration deadline

Connecting Endocrinology Across the Life Course

10–13 May 2025
Joint Congress of ESPE and ESE 2025
Copenhagen, Denmark

18–22 June 2025
17th International Thyroid Congress
Rio de Janeiro, Brazil

22–25 June 2025
ESE Summer School 2025
Innsbruck, Austria

9–12 July 2025
World Congress on Thyroid Cancer
Boston, MA, USA

26–28 September 2025
12th ESE Young Endocrinologists and Scientists (EYES) Meeting
Milan, Italy

Amazing careers:
Meet Cynthia Andoniadou

Cynthia Andoniadou is a principal investigator at the Centre for Craniofacial and Regenerative Biology, and the Associate Dean for Doctoral Studies at King's College London, UK, where she has just been promoted to Professor in Stem Cell Biology. She is also a member of the ESE Executive Committee. Her award-winning research focuses on endocrine stem cells. *EYES News* Editorial Board member Dorota Filipowicz recently had the opportunity to interview Cynthia, while undertaking a Research Observership in Cynthia's lab.

Cynthia Andoniadou

Could you tell us what you are currently working on?
I'm working with endocrine stem cells, specifically on the pituitary gland and adrenal medulla, but we're open to working with other endocrine organs as well. We're trying to understand the relationships between stem cells and other cells: in particular, how do they communicate and what governs what they do? We're looking at those mechanisms because they have implications for endocrine disease.

As a basic researcher, why did you choose endocrinology?
By accident! Like so many things in science, we go down roads that we don't expect. I was particularly interested in neural stem cells and progenitors in embryology, and found myself asking, 'How does the brain form?' In my postdoc, I studied forebrain development and the genes involved, and found that many of those genes are also expressed in the pituitary gland. This led me to look at the pituitary which, for me, was entirely new – and I found it fascinating. So that's why I stayed in endocrinology.

Although it wasn't planned it has been very successful! What was the breakthrough moment?
We published a model of cell non-autonomous tumour formation, which means that the cells that sustain the mutation are not the cells that divide to give bulk to the tumour. They're the cells that tell other cells to divide and give the tumour mass. This is called paracrine signalling and is a main feature of the research that we're still doing.

'I think I possibly haven't encountered the biggest challenges yet.'

The key moment was when I was lineage tracing the cells with the mutation, using a genetic tool. Every cell that came from a mutated cell would be green, but I looked down the microscope and the tumour was not green – so I thought I'd done something wrong. But I looked more carefully at higher power, and saw pituitary crushed around the tumour, which was green. I knew then I hadn't made a mistake, and I thought, 'If it means what I think it means, that's big!' That to me was a defining moment.

Would you consider that as the biggest achievement in your whole career?
No, I think my biggest achievement is not scientific. I think it's training. If I look back when I retire and think, 'I've had a really good career', I will be remembering the people I have seen develop into independent scientists, and knowing that I contributed.

What has been the most challenging thing for you?
I think I possibly haven't encountered the biggest challenges yet. In a way, I have had it relatively easy, in that I have been very lucky to progress between jobs, going from one very good institute to another. When it was time for me to apply to become independent, that's when things started to get difficult. So putting in fellowship applications and getting rejections, sending papers out and then being turned down: that process, combined with the very hard work that was needed to get to that stage, was quite demoralising. I think that was a point when I could have quit. There are only so many positions and they're hard to get. So, in addition to working hard, which is essential, you have to be really lucky. Getting over the rejections still feels horrible, but you learn how to cope and say, OK, this is not personal, it's about the science. I need to do better in the science. That keep me going.

'In addition to working hard, which is essential, you have to be really lucky.'

What do you do to cope?
How do I cope with rejection? I think if I have a bad day then wine and a pizza is the best way to go! You need a little bit of time to wallow and cry on your own, to give yourself the time to process what's happening and then not take it personally. When you initially get reviewers' comments, you think, 'All of these people hate me, this is so unfair. I explained this so well.' And then, when you calm down, you look back at your grant application or your paper and maybe think, 'Actually, I haven't explained it well enough.' Then you look at it with a brand new set of eyes and improve.

What do you think is the biggest challenge for the young generation?
Nowadays things seem a lot tougher than when I was a postdoc. There are even fewer positions and the funding is more competitive. Equally, there are many alternative careers that are better known. Rather than just academia at the university, there is industry supporting basic and social science. It doesn't all have to be clinical research. There are also opportunities in science communication.

You need to be able to have someone investing in you and saying, 'OK, I trust that you're going to do a good job', and that's difficult to come by. Some people are lucky, but others are not lucky because they're not in the right environment. They may be in countries where they have to do a lot to get the same publications and the same opportunities.

What advice would you give young people?
You need to put things into context, to remind people where you're coming from. If you're coming from a big research institute that doesn't need to apply

‘That was a driving force for me: “I can get there. I can do this. I need to do it, for myself and for other women.” ’

for funding, then people should know that. And if you’re coming from a small university in a provincial town and you have very little in terms of resource, then remind people that you are doing a magnificent job compared to what you have. Be forthcoming. You need to explain what your background is, and people can place your work in context when they’re assessing you.

How can the EYES community have the biggest impact?
I think engaging more with the public is important in any sector, spreading accurate information rather than misinformation. Most of you are clinically trained, and you also have been trained in how to talk to the public, and to explain things simply. Also, if there’s something you need to advocate for in your careers, you can work together to do this, not wait for someone else to change it. You are the ones that should be active right now.

You inspire the younger generation, but who inspired you?
This is a tough one. There was never one person that inspired me. Because I got into endocrinology in a strange way, I didn’t have endocrinologists around me. What did inspire me was the lack of women in positions that were prominent and the lack of promotion of women who had achieved great things, and I felt that was a bit unfair.

So I didn’t see a lot of women in the Royal Society competition, for example, and when you look at Nobel Prize winners, you don’t see as many women as men. And even in my day-to-day encounters with big professors in talks, there were few women. But those women were extraordinary. And each and every one of them had something incredible to offer. I really felt at the time that we needed to change. That was a driving force for me: ‘I can get there. I can do this. I need to do it, for myself and for other women.’

One last question, if you could change one thing in your career, what would that be?
Like a magic genie? I would give more funding to whichever lab I was in, and all around me. Because if that big problem was taken away from us, we could do incredible things and it would accelerate everybody’s career. Being early in your career with a lot of funds, but knowing how to use them, would propel you to the next level. That’s what I would want for all of my trainees.

Watch **the full interview** and our other **Amazing Scientist interviews**

Let’s meet in Milan!

We are proud to announce that the EYES community will gather in Milan, Italy, for the 12th EYES Annual Meeting on 26–28 September 2025!

12th EYES Annual Meeting

26–28 September 2025
Register your interest now

Mark your calendars and don’t miss our next EYES Annual Meeting, which will be hosted at the Humanitas University Congress Centre, not far from the beautiful sights of Italy’s capital of fashion, Milan.

The 12th EYES Annual Meeting is sure to be a memorable event and a key gathering point for young endocrinologists, basic researchers, and other early career professionals who are interested in the world of endocrinology. Take advantage of the opportunity to present your clinical or research results to colleagues in this international, friendly setting, which welcomes constructive dialogue.

You can meet colleagues from other nations, exchange ideas about your experiences, and strengthen your professional networks. Above all, don’t miss the opportunity to share moments of relaxation and fun at the social events in Italy’s most vibrant city, surrounded by art, fashion and nightlife. Follow our social media for more updates to come … and join us in Milan!

Walter Vena
on behalf of the Local Organising Committee

EYEScientists eyescientists

Supported by science

Vital endocrine science provides the solid foundations for progress in clinical endocrinology and in healthcare for our patients.

Methodologies in pituitary research

Understanding the techniques that have underpinned important discoveries in pituitary research is vital for those hoping to make future breakthroughs.

Pituitary research is a critical area of endocrinology, focused on understanding the 'master gland' that regulates essential physiological processes through hormone secretion. Gaining insights at cellular and molecular levels into how this gland functions, and – more importantly – how it malfunctions, is crucial for identifying the causes of pituitary diseases, including tumours and hormonal imbalances.

Over the years, basic and clinical researchers have developed and refined many experimental techniques that have led to the discovery of new disease genes, pathways and biomarkers. This is also the case for translational research conducted in the pituitary realm. This article highlights some of these methodologies, specifically genetic and genomic approaches, showcasing how their application led to important discoveries (see the Figure).

Of course, there are many other basic methodologies that are preparatory or complementary to those discussed in this article, such as polymerase chain reaction (PCR), quantitative PCR, Western blotting and immunohistochemistry, but they are not covered here. Additionally, other 'omics' techniques are increasingly being used in pituitary research, both individually and in combination (a multi-omics approach). These include, among others, 3D genomics, epigenomics, single-cell and spatial transcriptomics, and proteomics. They could form the basis of a future article!

Sanger sequencing

Sanger sequencing, developed by the British biochemist Frederick Sanger in 1977, determines the nucleotide sequence of a DNA fragment by synthesising complementary strands and terminating the process with chain-terminating nucleotides. Of the first generation sequencing technologies, it is the most significant and most accurate, and is still widely used, although it is expensive. It also provided the foundation of some of the modern and most commonly used sequencing technologies. However, it suffers from being low throughput and hard to multiplex and scale up.

In pituitary research, Sanger sequencing was instrumental in identifying pathogenic variants

('mutations') in the gene *GNAS*, which is found in both a mosaic and a somatic state in McCune–Albright syndrome[1] and in sporadic pituitary somatotrophinomas.[2]

Next-generation sequencing

The most transformative technologies in research and clinical settings in the last decade include faster, higher-throughput and increasingly cheap sequencing technologies,

	Gene	Disease	Technique(s)	Reference(s)
1989	*GNAS*	GH-sec (sporadic)	Sanger	Landis *et al.*[2]
1991		MAS	Sanger	Weinstein *et al.*[1]
1998	*MEN1*	MEN1	Positional cloning, ddF	Chandrasekharappa *et al.*[7]
2000	*PRKAR1A*	CNC, ACTH-sec (sporadic)	DHPLC, Sanger	Kirschner *et al.*[8]
2006	*AIP*	FIPA (sporadic)	Linkage analysis, CMA	Vierimaa *et al.*[9]
	CDKN1B	MEN4	Linkage analysis, Sanger	Pellegata *et al.*[10]
2014	*GPR101*	X-LAG	CMA	Trivellin *et al.*[5]
2015	*USP8*	ACTH-sec (sporadic)	WES	Reincke *et al.*[3] Ma *et al.*[11]
	SDHx	3PAs	Sanger, MLPA, WES	Xekouki *et al.*[12] Dénes *et al.*[13]
2017	*CABLES1*	ACTH-sec (sporadic)	WES	Hernández-Ramírez *et al.*[14]
2018	*MAX*	3PAs	MLPA	Daly *et al.*[6]
2019	*TP53*	ACTH-sec (sporadic)	WES	Sbiera *et al.*[4]
2020	*SF3B1*	PRL-sec (sporadic)	WGS	Li *et al.*[15]
2024				

Timeline of significant discoveries of candidate disease genes in pituitary tumours (orange indicates genes with somatic mutations; green shows syndromes of multiple endocrine neoplasia (MEN)). 3PAs, pituitary adenoma and phaeochromocytoma/paraganglioma; ACTH-sec, adrenocorticotrophin-secreting tumour; CMA, chromosomal microarray analysis; CNC, Carney complex; ddF, dideoxy fingerprinting; DHPLC, denaturing high performance liquid chromatography; FIPA, familial isolated pituitary adenoma; GH-sec, growth hormone-secreting tumour; MAS, McCune–Albright syndrome; MLPA, multiplex ligation-dependent probe amplification; PRL-sec, prolactin-secreting tumour; WES, whole exome sequencing; WGS, whole genome sequencing; X-LAG, X-linked acrogigantism.

‘For young researchers entering the field, mastering these methods is essential in contributing to the next scientific breakthroughs in pituitary research!’

termed second generation or (more commonly) next generation sequencing (NGS). These methods allowed scientists to sequence entire genomes or specific gene regions, such as the exome (i.e. the aggregate sum of all exons), with unprecedented speed. NGS works by fragmenting genomic DNA into smaller pieces of about 200–400 nucleotides, amplifying and sequencing them in parallel. These DNA fragments, dubbed ‘reads’, are computationally assembled and compared with the human reference genome to identify single nucleotide variants (SNVs) or insertions/deletions (indels) that may be associated with specific diseases.

NGS, which has largely displaced Sanger sequencing in molecular diagnostics, has been instrumental in the identification of mutations in genes that contribute to pituitary diseases. Notable examples include somatic mutations in the *USP8*[3] and *TP53*[4] genes, identified by exome sequencing in corticotrophinomas.

Chromosomal microarray analysis

DNA microarrays contain a large assembly of DNA fragments (probes) spotted onto a solid surface (glass). Two main technologies are used:

1) Array comparative genomic hybridisation (aCGH), which measures the quantity of genomic DNA in a patient’s sample and compares it with that in a normal control.
2) Single nucleotide polymorphism arrays, which use DNA probes derived from regions in the genome that show differences between individuals at single sites (SNVs).

Since 2004, chromosomal microarray analysis technologies have been used in clinical practice to identify structural variants, including insertions, translocations, inversions and copy number variants (CNVs), which are large deletions, duplications or amplifications of the DNA.

Using high resolution aCGH, duplications in the X chromosome encompassing the *GPR101* gene were identified in patients with X-linked acrogigantism,[5] a rare condition characterised by early childhood-onset acrogigantism due to growth hormone excess.

Multiplex ligation-dependent probe amplification

Multiplex ligation-dependent probe amplification (MLPA) is a targeted technique for detecting CNVs in specific exons or entire genes. It involves using multiple fluorescently labelled probes (up to 60) that bind to adjacent DNA targets. After ligation, these probes are amplified simultaneously in a single reaction, allowing the detection of relative DNA copy number changes when analysed by capillary electrophoresis (the same instrument that is employed for Sanger sequencing).

MLPA has been instrumental in identifying single or multiple exon deletions in genes associated with pituitary tumours. For example, in 2018, MLPA was used to detect germline deletions in the *MAX* gene in patients with co-existing phaeochromocytomas and pituitary tumours (3PA syndrome). These deletions were missed by NGS panels and Sanger sequencing.[6]

Conclusion

Pituitary research is at the forefront of endocrinology, driven by a variety of experimental techniques that have been pivotal in uncovering the genetic basis of pituitary diseases. As these techniques continue to evolve, they will undoubtedly lead to new discoveries, offering hope for better diagnosis and treatment. For young researchers entering the field, mastering these methods is essential in contributing to the next scientific breakthroughs in pituitary research!

Giampaolo Trivellin, Italy

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Defining AVP deficiency

Distinguishing between AVP deficiency, AVP resistance and primary polydipsia is crucial, to avoid incorrect treatment and serious complications.

Disruption of the hypothalamic-pituitary axis – whether due to inflammation, tumours or head trauma – can lead to arginine vasopressin (AVP) deficiency; this was formerly known as central diabetes insipidus. It is a rare condition, affecting about 1 in 25,000 people, and is characterised by polyuria and polydipsia.[1,2]

Recent renaming

The terms 'mellitus' (honey sweet) and 'insipidus' (tasteless) were historically used to differentiate between the two types of diabetes, based on their clinical characteristics. However, the use of the term 'diabetes' in both has caused confusion, leading to severe outcomes and even death in patients with AVP deficiency.

An online survey of 1034 patients with AVP deficiency revealed that 85% preferred a renaming of the disease to avoid the term 'diabetes'.[3] Recently, following recommendations from an international working group, 'central diabetes insipidus' has been renamed 'AVP deficiency', while 'nephrogenic diabetes insipidus' is replaced by 'AVP resistance'.[4]

Diagnosis

The polyuria–polydipsia syndrome presents a significant diagnostic challenge, particularly in differentiating between AVP deficiency, AVP resistance, and primary polydipsia. Accurate diagnosis is crucial, as incorrect treatment can lead to serious complications.

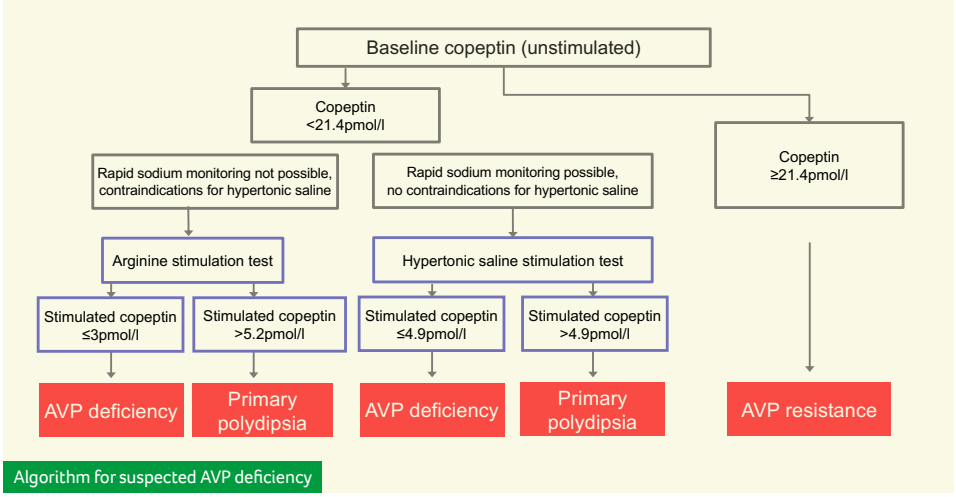
After confirming hypotonic polyuria, a baseline blood test can provide initial information as elevated plasma sodium (>147mmol/l) suggests AVP deficiency or resistance, while low sodium levels (<135mmol/l) indicate primary polydipsia. However, diagnosis is often not straightforward, requiring further evaluation.

For decades, the water deprivation test has been the gold standard. It measures endogenous AVP indirectly by assessing urinary concentration after prolonged water deprivation. While effective for diagnosing complete AVP deficiency or resistance, this test is less reliable for partial forms and primary polydipsia. The diagnostic cut-offs used are based on outdated data from a small study of only 36 patients, resulting in limited diagnostic accuracy of 70–77%.[5]

Direct AVP measurement is impractical due to its plasma instability. However, copeptin, a stable peptide that is co-released with AVP, has emerged as a reliable biomarker. A basal copeptin level of ≥21.4pmol/l indicates AVP resistance, while lower levels require further testing (see the Figure).[2,5]

Two main stimulation tests have been developed: the hypertonic saline test and the arginine infusion test. The hypertonic saline test, which elevates plasma sodium levels above 149mmol/l to stimulate copeptin release, offers a diagnostic accuracy of 96–97% with a copeptin cut-off of >4.9pmol/l.[2,5] This test is recommended if rapid sodium measurements and continuous monitoring are feasible and there are no contraindications, such as severe heart failure.

The arginine infusion test serves as a useful alternative when sodium monitoring is unavailable or contraindications for hypertonic saline exist. Although it is simpler, better tolerated, and generally preferred by patients, it has a lower diagnostic accuracy. This test uses copeptin cut-offs of ≤3.0pmol/l to indicate AVP deficiency and >5.2 pmol/l to suggest primary polydipsia.[5]



Algorithm for suspected AVP deficiency

Therapy

Desmopressin, a synthetic analogue of AVP, is the standard treatment for managing AVP deficiency. For long term therapy, oral preparations and nasal formulations are commonly used.

Dosage and frequency should be tailored to each patient's needs, often starting with a nighttime dose to reduce nocturia. Depending on the patient's symptoms, additional doses may be required in the morning or at midday.

Desmopressin escape method

One important side effect of desmopressin treatment is dilutional hyponatraemia. In a survey of 1034 patients with AVP deficiency, 22% reported experiencing outpatient hyponatraemia, while 26% had hyponatraemia leading to hospitalisation.[3] Postmarketing evidence suggests that the formulation of desmopressin can influence the risk of hyponatraemia, with nasal desmopressin being associated with a higher risk compared to other forms.

Educating patients about the risk and symptoms of hyponatraemia is essential. To reduce this risk during long term treatment, it is recommended that patients with AVP deficiency delay a desmopressin dose as often as several times per week or omit a dose once a week to allow aquaresis. This strategy is is known as the 'desmopressin escape method'.

Oxytocin deficiency

There is not only vasopressin, there is also oxytocin! Both hormones are produced in the hypothalamic supraoptic and paraventricular nuclei and they are structurally similar. Oxytocin is key in regulating complex socio-emotional and behavioural functioning.

Despite treatment, patients with AVP deficiency frequently report residual psychological symptoms, including reduced empathy, heightened anxiety, difficulties in social interaction, and decreased sexual desire, substantially affecting their quality of life.

Given the anatomical proximity, local disruptions of the AVP system could also disturb the oxytocin system, resulting in an additional oxytocin deficiency. A recent study utilised a novel stimulation test with MDMA (methylenedioxymethamphetamine) and revealed for the first time an additional oxytocin deficiency in patients with AVP deficiency. These findings may potentially explain the observed psychopathology in these patients.[6]

These results suggest that oxytocin replacement therapy in patients with AVP deficiency could be of great clinical importance to improve psychological symptoms.

Svenja Leibnitz and Julia Beck
Switzerland

Svenja and Julia are in the research group of Professor Mirjam Christ-Crain.

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Translational research in adrenocortical carcinoma

Martin Fassnacht shares his personal view of what we have learnt in this field over the last 25 years.

Adrenocortical carcinoma (ACC) is an exceedingly rare disease, with only approximately one new patient per one million inhabitants per year. Consequently, across Europe, only around 700 cases are identified annually. This low incidence rate hinders rapid improvement of clinical care, and also impedes basic and translational research (and the funding of this research).

Structures are important for research

The best strategy for overcoming these hurdles is undoubtedly collaboration. In this context, 2002 and 2003 were the most important years for research into ACC. In 2002, a group of enthusiastic adrenalists (Bruno Allolio, Xavier Bertagna, Massimo Mannelli, Franco Mantero, Pierre-Francois Plouin, Martin Reincke and Paul Stewart) founded the European Network for the Study of Adrenal Tumors (ENS@T).

It began as a small 'club of friends', united by a shared interest in exploring the fundamental aspects of adrenal tumours, through the exchange of biomaterials for basic and translational research. Over time, this initiative has grown to encompass a broader community of scientists from more than 100 institutions around the globe. These researchers have now collected clinical data and biomaterial from more than 5000 patients with ACC (and even more from patients with other adrenal tumours), making ENS@T *the* hub for adrenal tumour research.

In 2003, David Schteingart organised the inaugural International Adrenal Cancer Symposium in Ann Arbor, USA. This landmark event facilitated enhanced networking between basic and clinical ACC researchers from all over the world. For me, it was also a milestone in my personal career, as it was there that I was introduced to the 'international ACC family'. This year saw the ninth symposium in Houston.

Both initiatives were driven by the spirit of collaboration and friendship, and were the prerequisites for all the successes described below – and many more. I will present a few highlights here, where research in the lab really made it to the patient, or will influence patient care in the future. A few additional use cases are illustrated in the Figure.

SF1 from the lab to the clinic

The first example is based on Hironobu Sasano's observation and hypothesis that transcription factor SF1 is likely to be a crucial factor for ACC cells. Indeed, our laboratory has demonstrated that virtually all ACCs express SF1.[1] Nowadays, SF1 is a globally established marker in the histopathological work-up of adrenal tumours. In the future, SF1 antagonists may even be evaluated for therapy.

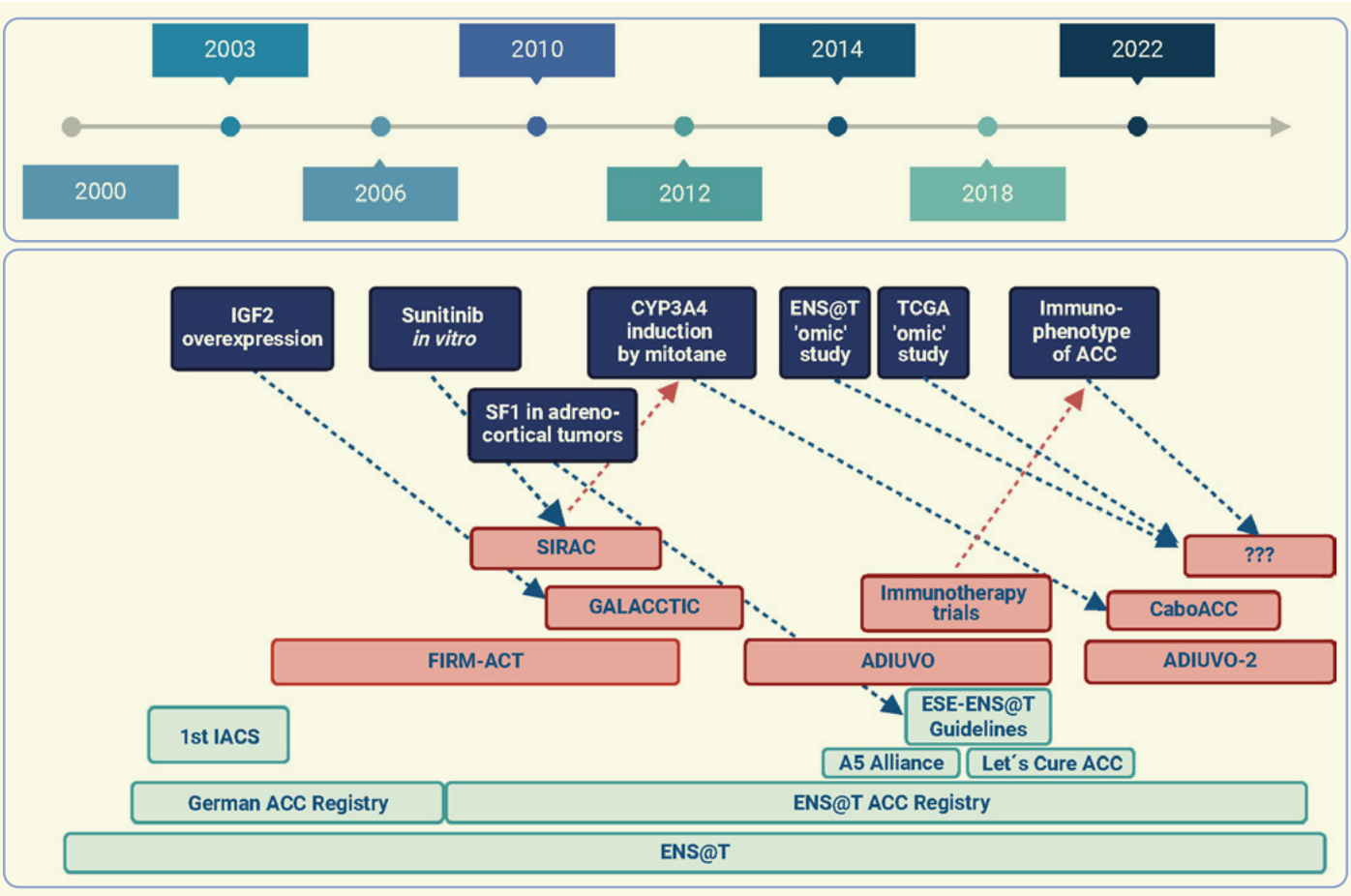
Elucidating the pathogenesis

About 15 years ago, 'omic' studies exploded onto the scene in tumour research. However, robust and reliable data require a relevant sample size. Consequently, 17 ENS@T centres joined forces and gathered over 120 ACC samples. Through their collaborative efforts, co-ordinated by Guillaume Assié, we not only gained insight into a previously 'unknown' gene, *ZNRF3*, which was identified as the most altered gene in ACC, but we were also able to delineate two main molecular subtypes.[2] In the meantime, it has been well established that *ZNRF3* is part of the β-catenin signalling pathway, and a key tumour suppressor gene in ACC.

Subsequently, ENS@T made a significant contribution to an even larger international study by the Cancer Genome Atlas (TCGA) consortium, expanding our knowledge about the genomic landscape of ACC and confirming three distinct molecular groups that predict clinical outcome.[3] Recently, we have employed more advanced methods, including single nuclei sequencing and spatial transcriptomics, to further elucidate the landscape and the heterogeneity of adrenal tumours.[4]

From bench to bedside

The following example illustrates that success in preclinical studies does not necessarily



Interaction of translational and clinical studies in the context of collaborative research structures in ACC research. Pale green boxes indicate research structures; dark blue boxes denote examples of translational research; red boxes show clinical trials. The arrows illustrate the mutual influences between the studies. The infrastructure presented provided the basis for almost all the translational and clinical studies mentioned. (Created using Biorender.com with the support of Laura Landwehr.)

‘While there have been successes and disappointments along the way, the most significant lesson I have learned is that international collaboration is essential for success.’

guarantee success in patients. Several research groups have demonstrated that overexpression of insulin-like growth factor-2 (IGF-2) is a characteristic feature of ACC. Studies in mice by Gary Hammer’s groups provided a strong rationale for drugs targeting the IGF-2/IGF-1R (IGF-1 receptor) signalling pathway. It was, therefore, particularly disappointing that, in a large randomised trial, most patients did not benefit from treatment with an IGF-1R antagonist.[5] However, I still believe that targeting this pathway is of value for a subset of patients, but we must do more translational research to identify the tumours that are susceptible to these drugs.

Discovering reliable biomarkers that predict response to given therapies is a crucial objective in translational research in ACC. Unfortunately, we have to acknowledge that we have so far failed to identify strong predictors.

From bedside to bench

There are also examples in which clinical studies have been the foundation for important translational findings. In the period between 2007 and 2012, two phase 2 trials were the first to apply tyrosine kinase inhibitors in the treatment of ACC. Unfortunately, the results were once again disappointing. However, our exploratory studies clearly showed that one main reason for this failure was that most patients have been treated with mitotane. Initially, we hypothesised a synergistic effect, but subsequently discovered that mitotane is probably the most potent inducer of the key drug-metabolising enzyme in the liver.[6] This induction of CYP3A4 resulted in the rapid clearance of all tyrosine kinase inhibitors, thereby preventing any efficacy. Most importantly, this knowledge enables us now to avoid other harmful drug interactions in our patients.

Is immunotherapy possible in ACC?

Finally, I would like to discuss cancer immunotherapy. The remarkable success of checkpoint inhibitors in certain types of cancer has undoubtedly sparked interest in ACC. The results to date have been heterogeneous and largely disappointing.

Therefore, we analysed the immune cell infiltration and the expression of the different checkpoint inhibitor molecules in almost 150 ACC tumour samples, correlating these findings with clinical data.[7,8] A significant outcome of these studies has been the identification of a link between glucocorticoid excess and T cell depletion, which is associated with an unfavourable prognosis. To reactivate the immune system in ACC by immune checkpoint inhibitors, an inhibition of intratumoural steroidogenesis might be pivotal. However, this hypothesis requires testing in prospective studies.

Another therapeutic approach is currently being investigated in our laboratory, namely CAR-T cells. We are encouraged by the promising results we have seen *in vitro* and in mice. However, whether this can be translated to patients remains a vision of the future.

My personal conclusion

While the ACC community has achieved much over the past 25 years, the outcome for patients with this rare disease remains unsatisfactory. To achieve a turnaround here, it is evident that further basic and translational research is required. While there have been successes and disappointments along the way, the most significant lesson I have learned is that international collaboration is essential for success. Therefore, I encourage all readers to engage in such collaboration, as it not only yields superior scientific outcomes, but also fosters global friendships.

Martin Fassnacht
Germany

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Apply for an Observership in 2025

The EYES Observership (Exchange) Programme provides grants so that early career investigators can expand their experience and knowledge during a one-month stay in an endocrine centre of special interest (or a three-month stay for the Advanced Research Observership).

Submit your applications for the 2025 Observership grants by 10 March 2025. **Find out more** and make a decision that could transform your career.

Here's what previous recipients have to say!

MARIO DETOMAS, *Germany*

I express my heartfelt thanks for granting me this incredible opportunity. I am genuinely excited to begin my observership in the lab of Professor Márta Korbonits, a world leader in pituitary genetics. This experience, made possible through the EYES Advanced Research Observership Programme (AdROP), is a crucial milestone in my career as a clinician scientist, focusing on pituitary disorders and Cushing's syndrome.

My time in London will deepen my understanding of the genetic and molecular foundations of pituitary diseases, which are key to my clinical practice and my research. Working alongside Professor Korbonits and her team will allow me to learn state-of-the-art techniques, gain fresh insights and explore new research directions.

I am also eager to build lasting professional relationships and expand my connections in the international endocrinology community. This observership will enable me to make a greater impact in the field and put innovative strategies into practice at my home institution in Würzburg, Germany.

DOROTA FILIPOWICZ, *Poland*

Dorota Filipowicz (back row, centre) with colleagues in London

The EYES Research Observership Programme (ROP) allowed me to push my boundaries and explore a scientific path outside my clinical routine. As a physician, I have always been fascinated by the pituitary gland and stem cells, which led me to choose King's College London and the pituitary lab for my ROP experience. Meeting Professor Cynthia Andoniadou at ECE 2024 in Stockholm, Sweden, reaffirmed my choice. Her warm welcome, dedication and genuine interest in my goals provided invaluable support.

When I arrived, I was embraced by an international team of passionate young scientists who were keen to explain their work. Professor Andoniadou guided me through a translational project, where I conducted my own research. Outside the lab, we enjoyed lunches, networking, group activities and deep conversation.

Meanwhile, thanks to Professor Márta Korbonits, I connected with young endocrinologists, attended clinical meetings, and improved my skills in endocrinology consultations.

This 'bedside to bench' experience reignited my passion for scientific exploration. While I still identify more with the bedside, the ROP grant has opened the door for me to navigate both worlds confidently.

ZVEZDANA JEMUOVIC, *Serbia*

Zvezdana (left) with Annamaria Colao

The EYES Clinical Observership Programme (COP) was everything I expected, and more. During my time in Naples, Italy, I gained valuable personal and professional experience at the Centre of Special Interest for Neuroendocrine Tumours at Federico II University Hospital, under the mentorship of Professor Annamaria Colao. This opportunity allowed me to work with one of the leading teams in the field and to build international connections with colleagues, who soon became friends.

My working week was dynamic and engaging. On Mondays, I attended the acromegaly outpatient clinic; the adrenal clinic followed on Tuesdays. Wednesdays were dedicated to neuroendocrine tumours; Thursdays focused on the prolactinoma outpatient clinic, and Fridays saw the thyroid and adrenal insufficiency clinics. I observed a wide range of cases that deepened my clinical knowledge. At weekends, I enjoyed exploring beautiful Naples and the vibrant atmosphere.

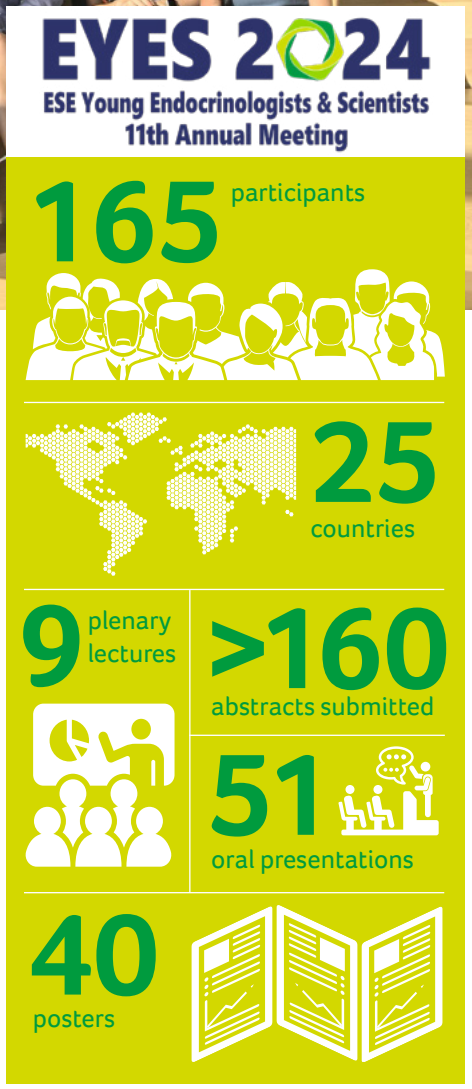
As well as enhancing my clinical skills, the connections I made were beyond rewarding, expanding my professional and social network.

I thank ESE and its EYES Committee for their support, and Professor Annamaria Colao for her selfless mentorship. And to all early career investigators out there – you don't want to miss this opportunity!

Find out more about the **Bilateral Observership Programme (BOP)**, and how you could engage in an Observership in a leading Brazilian centre in 2025!

Júnia ROL Schweizer (BOP Ambassador) with Paulo Miranda (President of the Brazilian Society) and Nathália Lisboa (Co-Chair of the Brazilian Young Committee)

EYES in Helsinki



Helsinki hosted the 11th EYES Annual Meeting on 6–8 September 2024 in a weekend of sunshine, networking, inspirational speakers and exciting presentations by participants, with a fun social programme.

The EYES Meeting is a unique forum for early career clinicians and scientists, where participants get a chance to present their research and network at an international level.

A thought-provoking lecture on the treatment of obesity from Professor Kirsi Pietiläinen (Finland) was followed by participants' presentations on obesity, metabolism, environmental endocrinology, the pituitary and neuroendocrinology. The first evening saw dinner and dancing on a party boat cruise in the Helsinki archipelago: one of the true gems among the sights of the city.

Diabetes was the theme for the start of the second day. Jonna Männistö (Finland) gave a great talk on classification of diabetes, followed by an entertaining workshop on differentiating diabetes types by Jarno Kettunen (Finland), a member of the Local Organising Committee (LOC). We welcomed more oral presentations and poster pitch talks by participants. State-of-the-art plenary lectures followed, with Carla Pieterman (The Netherlands) covering MEN1 syndrome and Mikkel Andreassen (Denmark) on follow up of non-functioning pituitary adenomas.

Dinner, followed by a live band and DJ set, kept people on the dance floor until 2am! The evening was spiced up by an endocrinology-themed quiz and a 'seating lottery' to help delegates meet new colleagues.

The final day featured an enlightening session with Professor Anna Keski-Rahkonen (Finland), giving lots of practical tips on how to tell a compelling scientific story, as well as a magnificent lecture by Elisabeth Nowak (Germany) on cyclic Cushing's syndrome. The LOC's Aino Latva-Rasku (Finland) and EYES Committee's Barbara Altieri (Germany) drew the meeting to a close with valuable talks on positron emission tomography and adrenocortical carcinoma respectively.

We thank everyone who helped make this great weekend a dream come true!

Liisa Kullamaa
LOC Chair, on behalf of the Local Organising Committee


Award winner Marc Philipp Schauer


Local Organising Committee members

‘The meeting was well organised, with very good plenaries by important experts. Also, it was nice that almost every participant had the opportunity to talk.’

Evening boat cruise in the Helsinki archipelago

‘The organising committee, speakers and participants were all incredibly friendly and approachable, making socialising an effortless experience.’

Popular presentations

Speaker Jonna Männistö

On the dance floor

‘One of the best conferences I have been to so far.’

Packed poster viewing

‘The highlight of the conference was the diverse range of topics, covering various aspects of endocrinology through insightful case reports and engaging lecture slides.’

Speaker Carla Pieterman

‘A global stage for exchange of ideas, with such perfection in event co-ordination.’

Enjoying the evening cruise

Some of the best moments from the meeting were captured by our colleague and photographer Jyrki Mustonen.

Award recipients

MARC PHILIPP SCHAUER
(Germany)
Overall winner

ANA RITA LEITE
(Portugal)
Overall runner up

MARTYNA BOROWCZYK
(Poland)

LEONARDO DALLA VALENTINA
(Italy)

NIKLAS GEIGER
(Germany)

SANAS MIR-BASHIRI
(Germany)

You can view all the abstracts in ***Endocrine Abstracts***

Joint Congress of ESPE and ESE 2025 Register now!

For the first time, ESE will be coming together with ESPE (the European Society for Paediatric Endocrinology), at our Joint Congress entitled 'Connecting Endocrinology Across the Life Course'. It will take place on 10–13 May 2025 in the spectacular Danish capital, Copenhagen.

Don't miss this opportunity to meet new colleagues and develop more collaborations. **Submit your abstracts** by 3 February 2025 and take advantage of **Early Bird registration** before 27 March 2025.

Connecting Endocrinology Across the Life Course
Joint Congress of ESPE and ESE 2025
Copenhagen, Denmark. 10-13 May 2025

Key deadlines

Abstract submissions:
3 February 2025

Early Bird registration:
27 March 2025

Standard registration:
24 April 2025

www.espe-ese-congress2025.org

World Hormone Day 2025

Building on the great success of European Hormone Day, the annual awareness day with a focus on endocrine health will become **World Hormone Day** from 2025. It will take place each year on 24 April. Watch out for more details about the 2025 campaign!

World Hormone Day
Because Hormones Matter
24 April 2025

New ESE Curriculum

ESE and UEMS (the European Union of Medical Specialists) have worked jointly to produce a new **ESE Curriculum and European Training Recommendation in Endocrinology**.
The initiative involved input from many ESE members, including the EYES Committee.
It includes an updated list of the necessary areas of knowledge, experience and training in endocrinology, as well as recommendations for the duration and structure of training.
Find out more

It's time to renew

Don't miss out on all the benefits of ESE membership in 2025. **Renew now online**.
Did you know, you can now set up an annual direct debit for your renewal?
Find out more

Have your say: State of Endocrinology 2025

There is a growing shortfall in healthcare workers across Europe, and we need to ensure that we are informed and ready to support our field. In the words of ESE President Jérôme Bertherat, 'ESE is launching a Europe-wide "fitness test" to assess how the discipline of endocrinology is equipped for the future.' Part of the fitness test will be a comprehensive survey in early 2025. Look out for it and make sure you send your feedback.

Early Career Clinical Endocrinologists meeting

The **8th Early Career Clinical Endocrinologists (ECCE) meeting** took place in October in Antalya, Turkey, during EndoBridge 2024. Discussion centred on 'Imaging in endocrinology', and Evangelos Chartampilas gave the keynote lecture.

Organised by **ECAS** (the ESE Council of Affiliated Societies), the event was attended by 23 early-career participants from 17 countries. EYES Committee member Julia Beck talked on 'Supporting early career endocrinologists at the European level', and Roman Králik and Bilel Ben Amor presented national perspectives from Slovakia and Tunisia respectively.

The 9th ECCE meeting will take place next October during **EndoBridge 2025**. The main topic will be 'Nuclear medicine and endocrinology'.

Watch the video
Attendees at the 8th ECCE meeting

Time to meet the...

Danish Society of Young Endocrinologists

The **Danish Society of Young Endocrinologists**, or Foreningen af Yngre Endokrinologer (FYEN), consists of medical students and younger physicians with a special interest in endocrinology. We are a self-governing association, officially part of the Danish Endocrine Society, but we operate independently.

Our members range from medical students to physicians in the early stages of their careers in endocrinology, with most being young physicians in clinical specialist training or pursuing PhDs and postdoc positions.

What does the FYEN do?

The FYEN organises a variety of activities to support educational, networking and professional opportunities for our members. These include specialised courses and annual meetings.

We also represent our members' interests on various educational and professional committees. The FYEN has appointed representatives on the board of the Danish Endocrine Society, the steering committee for the Danish Endocrine Guideline Group, the Danish Endocrine Educational Group, the Specialist Training Hiring Committee, and the inspection programme that evaluates the training environment in endocrinology departments.

As well as providing educational opportunities, our role is to create a strong sense of community among our members and to secure the best possible specialist training in endocrinology in Denmark.

What educational programmes do we develop?

Our flagship event is the FYEN Annual Meeting, which takes place every autumn. This gathers our members together for two days filled with educational presentations by both young and senior speakers, which are designed to provide knowledge that is directly applicable to clinical practice. It is both a learning experience and an opportunity to network with peers.

In addition to the Annual Meeting, we organise an annual one-day course that focuses on a specific area of endocrinology. This is often conducted as a joint venture with another junior medical society. It focuses on the complexities of clinical patient management in interdisciplinary fields (e.g. between endocrinology and nephrology).

We are also actively involved in securing the best possible training programmes. While the overall structure is determined by Danish health authorities, we work to ensure the best educational conditions within the given frameworks at the endocrinology departments where our members are employed during their specialist training.

Some of the members of the FYEN Board: (L–R) Mads Bengtsen, Mette Riis-Vestergaard, Stina Willemoes Borresen, Fredrik Mellbye and Andreas Ebbehøj

Delegates at the 2023 FYEN Annual Meeting

What are the biggest challenges for young endocrinologists?

Achieving a work–life balance is an important challenge. While there are many educational and academic opportunities, the demands of the medical profession are high, and a clinical workday is often very busy. For many of our members, the years they spend as endocrinologists in training are also the years when they are starting a family, and when they have to find a good balance between their professional and private lives.

Another significant challenge is balancing clinical practice with research and education. In Denmark, many people pursue PhDs during or before their specialist training. They often work part-time in research positions alongside clinical positions, in order to continue their research while progressing towards specialist certification.

How does the FYEN help in these situations?

Our networking events and meetings foster collaboration and mentorship, allowing members to learn from and support each other. The FYEN strives to build networks where members can safely exchange experiences and support one another. When rotating through various departments during specialist training, it makes a big difference to already know some of the other trainees at the department from the start.

Additionally, we advocate for our members' interests at the national level, ensuring that the young voices are heard in important discussions about the future of our specialty.

We look forward to welcoming you all to Copenhagen for the Joint Congress of ESPE and ESE in May 2025.

Stina Willemoes Borresen
Chair, FYEN

FYEN
Foreningen af Yngre Endokrinologer

ESE Summer School

- Learn
- Cutting-edge science
- Network
- New technologies
- Grow

ESE Summer School 2025 will take place on 22–25 June in Innsbruck, Austria. Delegates from 2024 tell you what you can look forward to – so save the date now!

What is ESE Summer School?

ESE Summer School is organised by the ESE Science Committee, and has a focus on basic science, though it also covers some translational topics. You can enjoy lectures from leading endocrine researchers and group breakout sessions to discuss scientific challenges in detail. Delegates will benefit from expert education across the broad field of endocrinology: it is a great way to develop as an endocrine scientist. Networking opportunities, including the social programme and sports activities, mean you will also make friends across Europe in the field of endocrinology.

What delegates thought in 2024

Alexandra Zueva, UK

Attending the ESE Summer School 2024 was an incredibly enriching experience, filled with inspiration and professional growth. Set in the beautiful Tyrolean Alps, it perfectly combined learning, networking and relaxation.

Guided by European experts and emerging scientists, we explored diverse areas such as neuroendocrinology, adrenal disorders, environmental endocrinology, reproduction and all aspects of thyroid function – from embryonic development to rare clinical challenges. Among the many impactful lectures, the presentation by Professor Allan Herbison on kisspeptin research particularly stood out, highlighting the crucial role of translational medicine in connecting basic research to clinical practice.

Beyond the academic side, meeting professionals from various countries broadened my cultural perspectives and created a sense of global community. The friendships I made added a personal touch, complemented by memories from social activities. The stunning natural surroundings also offered a chance to relax and recharge, providing extra inspiration and motivation for my research.

Dragana Vlahović & Ivona Gizdović, Serbia

Unforgettable – that's the 2024 ESE Summer School in a word. Imagine the perfect mixture of learning and fun, set against the breathtaking Alps.

We engaged in interactive lectures and workshops on the latest research topics, with friendly lecturers and attendees generously sharing their knowledge. As first year PhD students from the same department, this was our first experience of its kind, which inspired us and boosted our confidence in our scientific journey. We met amazing people from all over the world, each bringing unique perspectives and experiences.

A huge shoutout is due to the organising committee for their warm welcome and support, which made everything run smoothly and added so much to the experience! It's unfair not to mention the social activities. Football and volleyball were epic team-building events. The lake trip was pure refreshment. And the karaoke nights? We sang our hearts out together and uncovered hidden talents! The ESE Summer School was a unique chance to learn, laugh and make amazing friends. We can't wait for the next one.

Petros Papalexis, Greece

It was a great pleasure to participate in the 2024 ESE Summer School. It was an exciting experience in the wonderful natural landscape of the Tyrolean Education Institute Grillhof in Austria. Here we gained new knowledge of endocrinology, met new colleagues and friends from all over the world, and talked with remarkable researchers, professors and scientists from different regions of Europe.

This year, the main focus was on the thyroid. The programme also included neuroendocrinology, developments in endocrine research and diagnostics, developmental endocrinology and female reproduction. Every participant could present their own scientific poster in any field of endocrinology.

I thank the ESE Team members for their friendly welcome and assistance and, of course, all the members of the ESE Science and EYES Committees for planning the programme. It was the ideal environment to enable discussion, and combine sports activities, social events, making new friends, exchanging ideas and having fun with the scientific education provided. I highly recommend this Summer School experience to any interested colleague.

A rewarding experience

It is incredible how much inspiration can be generated in a productive setting with no boundaries to communication, when scientists and physicians are put outside their regular work environment.

One problem in conferences can be the lack of natural communication. The lecturer's dominance over the knowledge of attendees sometimes leaves younger scientists in fear of asking a redundant question.

However, the ESE Summer School is a bastion of successful scientific discussion. The repeated stimulation, in-depth lecture style and presence of the speaker for the entirety of the programme makes it a perfect example of how knowledge exchange should work.

For me, it has been a great pleasure and honour to be an organiser of activities at the ESE Summer School and other events for the EYES community for the past three years. Along the way, we gave space to some incredible lectures and ideas. We met some amazing people and brought them together to create an atmosphere of true scientific exchange, resulting in novel projects and life-changing professional opportunities.

We are all indebted to the ESE Science Committee, Professor Josef Köhrle, the ESE Team and all the incredible lecturers, who made these occasions truly spectacular and warm for all.

The ESE Summer School should remain a fascinating playing field for true creation and freedom of expression, and I hope to see the results of our work shine for years to come.

Antoan Stefan Šojat, Serbia