Issue 19 Spring 2024

ISSN 2755-2756 (online)

Control Contro

Hormones and bone health

An insight into bone disease





In this issue

EYES News

- 03 From your EYES Co-Chairs, Diary dates
- **05** Digital milestone for EYES News
- 12 Harmonis@tion: supporting work on adrenal tumours across Europe
- 13 It's happening in Helsinki: the 11th EYES Annual Meeting!

Interview

04 Chris McCabe: meet an amazing scientist

EYES Selection

- 06 Bone disease in acromegaly
- 07 Hormones in bone development
- 07 Androgen deprivation therapy and bone
- 08 Parathyroid disorders and bone health
- 09 Early menopause and bone
- 09 New medications for osteoporosis
- 10 Ethnic differences in bone health
- 11 Research insights into bone disorders

At the Back...

- 14 The latest news from ESE
- 15 Meet the Brazilian Society of Endocrinology and Metabolism
- 16 Coming soon! ECE 2024 in Stockholm

Editor:

Walter Vena, Italy **Deputy Editor:** Juan Manuel Jiménez Vacas, UK

Editorial Board:

Settimio D'Andrea, Italy Stavroula (Lina) Paschou, Greece Antoan Stefan Šojat, Serbia Victoria Withy, UK Karin Zibar Tomšić, Croatia

Sub-editor: Caroline Brewser

Design: Qube Design Associates

Website: www.ese-hormones.org

©2024 European Society of Endocrinology The views expressed by the contributors are not necessarily those of ESE



DEYEScientists

fb.com/groups/eyes.endo

in european-society-of-endocrinology



We welcome contributions and suggestions for articles. Please contact EYES News at eyesnewsletter@gmail.com.

The addresses used to email this issue of EYES News were supplied by the members of ESE. If you do not wish to receive further mailings, you can update your mailing preferences in your Member Portal or email info@ese-hormones.org.

Cover image: 3D illustration of the structure of healthy bone. ©iStock/eranicle

















'Per aspera ad astra' (through hardship to the stars)...

The months between New Year and the coming of spring represent a time of rebirth for all of us, during which we review all that we have accomplished, and ambitiously look forward to the goals to come.

Similarly, our magazine plans new topics and innovative projects to interest you, the young doctors, biologists and researchers in endocrinology. As I complete my term as Editor and swap roles with our Deputy Editor Juan, I reflect on this period of collaboration with the Editorial Board: a team of bright young minds from across Europe. I am very proud of the journey that brought me here, and grateful for this magnificent opportunity for growth. This Editorial begins with heartfelt thanks to this beautiful team, who constantly innovate, always managing to distinguish themselves through the seriousness of their work and the ability to bring valuable content. Without even realising it, I've learned from them and our interaction every day, adding something to my knowledge.

May this year bring much satisfaction to everyone in the Editorial Board and to you, our all-important readers. May it keep alive our passion for medicine, research, and progress.

In this issue, you will find an insight into skeletal pathologies and their close correlation with endocrine disorders, including the perspectives of leading experts in the field. We have an interview with Professor Chris McCabe to inspire you in your journeys. We also have crucial information about the many forthcoming initiatives within ESE to support early career investigators.

I wish you all happy reading.

Walter Vena 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

We can't help but notice how 2024 is dotted with fantastic events and opportunities not to be missed!

This year's events began with the Early Career Update in Clinical Endocrinology in the historic centre of Rome in March. This was a joint event with our Italian friends from the Associazione Medici Endocrinologi (AME).

In just a few weeks' time, on 11–14 May, we will find ourselves in the Swedish capital, Stockholm, for the most significant event in the European endocrinology community's calendar: ECE 2024 [2]. See page 16 for more information about the EYES Symposium at ECE 2024 and our social event. It will be a great opportunity to get to know each other better, and to create connections and new friendships, as well as chances to collaborate.

In the blink of an eye, we'll meet again on 23–26 June in the splendid setting of Innsbruck, Austria, for the **ESE Summer School** C. This event also has a session entirely organised and co-ordinated by EYES. You're all invited to participate, for a chance to spend time together, focusing on ourselves, having fun, and enjoying the pure mountain air and a memorable starry sky.

Then there is just enough time for a summer vacation, before we meet again in Northern Europe. On 6–8 September, Helsinki will host the highlight of the year for our EYES community, the **11th EYES Annual Meeting** 2, in collaboration with the Finnish Society of Endocrinology. The Local Organising Committee is already putting in a tremendous effort, ensuring

'Another magnificent year is underway, and we can't wait to spend it with all of you!'



that this event will be a total success, and will once again prove the strength of our community in scientific terms and beyond.

As well as all the events, don't forget to apply for our **Clinical and Research Observership (Exchange) Programme** [2] and actively participate in the increasing range of EYES initiatives, which you can find out about through our social channels.

In short, another magnificent year is underway, and we can't wait to spend it with all of you!

Antoan Stefan Šojat Walter Vena 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, free places and grant information!

11-14 April 2024

WCO-IOF-ESCEO 2024: World Congress on Osteoporosis, Osteoarthritis and Musculoskeletal Diseases London, UK

18-20 April 2024 11th Baltic Congress of Endocrinology and ESE Postgraduate Course Tallinn, Estonia

22 April 2024 4th Regional Symposium of Young Endocrinologists Belgrade, Serbia

25 April 2024 ESE Spotlight on Science: Endocrine Disruptors Online

11-14 May 2024

ECE 2024 26th European Congress of Endocrinology

Stockholm, Sweden

23–25 May 2024 12th International DIP & FemTech Symposium on Innovative Perinatal Medicine Sorrento, Italy

1-4 June 2024 ENDO 2024 Boston, MA, USA

20 June 2024 ESE Spotlight on Science: Diagnostic and Therapeutic Advances in Thyroid Cancer Online

23–26 June 2024 ESE Summer School Innsbruck, Austria



Stockholm, Sweden, location of ECE 2024

26–28 June 2024 11th I-DSD Symposium Stockholm, Sweden

7-10 July 2024 ESHRE 40th Annual Meeting Amsterdam, The Netherlands

4–6 September 2024 13th European Congress of Andrology Stockholm, Sweden

6-8 September 2024 11th EYES Annual Meeting Helsinki, Finland

2-4 October 2024 23rd ENS@T and 3rd COST Harmonis@tion Meeting Palma de Mallorca, Spain

11–15 October 2024 36th Brazilian Congress of Endocrinology and Metabolism Recife, Brazil

17–20 October 2024 EndoBridge Antalya, Turkey

Amazing careers: Meet Chris McCabe

Chris McCabe is Professor of Molecular Endocrinology at the University of Birmingham, UK. He and his group investigate mechanisms underlying endocrine cancer, including tumours of the breast, thyroid, and head and neck. Here, he talks to Antoan Stefan Šojat about his career and future plans.



How did your journey in science begin?

I was interested in science relatively early, but I was also interested in literature, and eventually I ended up being a writer of fiction as well as a scientist. In the education system, of course, you have to choose at some point. Am I a scientist or am I an artist? I chose science at that time, and I was really interested in genetics.

During my PhD, which involved fruit flies, I was really interested in behavioural genetics. I then got interested in how hormones might turn genes on and off. So, I think that was the first step, which evolved into how those mechanisms get dysregulated in cancer. That really has taken me to where I am today.

What was your first publication?

It was on the subject of oviposition in *Drosophila melanogaster*.¹ I'm not sure anyone in the world has ever read it! I spent my PhD looking at how the fruit fly laid eggs in relation to single base genetic mutations. I was exploring an issue that kind of blew my mind at the time, that a single nucleotide change in *Drosophila*, with 300 million bases per genome, could change such a critical evolutionary behaviour as the ability to lay eggs and its timing.

It was only when I started my first post-doc in a completely different field that I went back to write the paper and publish it myself, because I was aware that it was critical to have a publication. And I think it's really important: you have written a paper and it is the start of the expansion of the universe of science.

'In science, I think there are times when people look at you and think you're succeeding, but you feel internally you're failing...'

Has the process of scientific publication changed?

One obvious thing is that the volume of data has increased exponentially. We now spend more time analysing our data than before. When I started, you would work all week on a Western blot, and when you submitted an article to a journal, you may only have had four or five panels of data. Recently, I noticed that a paper we had just published in *Cancer Research* had something like 116 separate panels of data, so there's a clear change.

Philosophically, I guess what has happened is that we have become more like curators and editors of the data than before. Previously, it was very simple; now it becomes more of a task of overseeing an incredible volume of data garnered by very different technologies, and trying to integrate all of that into a coherent story.

What have been some key moments in your career?

Science is 99% failure. We know this, right? Most experiments fail. Most grants get rejected. Most papers get rejected. So it's a career of just having a thick skin and pushing on and failing, and then failing better, and failing better, and coming back stronger. I think the only career highlights I would suggest are ones where we've had what I felt to be a really good paper accepted in a really good journal.

Interestingly, in science, I think there are times when people look at you and think you're succeeding, but you feel internally you're failing. And there are times when people look at you and think you're failing, while you are thinking, internally, 'Actually, I'm succeeding because I'm building something here.'

What challenges have you faced?

I'm a basic scientist in the UK, working in a fairly clinical translational research field, and I think that's a challenge every day. Funding is difficult. Getting funding for basic biomedical research is tough. The constant challenge is keeping a laboratory group going.

I've been lucky over the last 20 or 25 years to have a laboratory group of 8–10 people most of the time. I'm writing the next set of experiments and hoping that they will be funded. Some great ideas will never be funded and some terrible ideas do get funded. We mustn't overlook the contribution of luck to science and progress. Right time, right place. If we don't get the grant then, next time, I'm not going to give them an excuse to bounce the grant. Next time, it's going to be harder for them to say no.

What is the outlook like for early career researchers?

I'm very happy with the direction that early career development is taking. I feel that outreach is really important. I've been lucky to be involved with the Observership Programme. We had a terrifically keen and enthusiastic early career scientist come and join my lab for a few weeks from Italy.

What the EYES Committee within ESE is doing, in terms of observership and other activities, is critical. It's very easy to work by yourself in a laboratory in one country, in one city. However, until you come together with colleagues that you didn't know, until you go to a conference and meet hundreds of other early career scientists and clinicians, you can't start to understand where you fit in, and that there are other people suffering like you're suffering.

What advice do you have for people setting out in their career?

The best post-docs and early career scientists I've worked with are not the ones who come and say, 'OK, what experiment are we doing today?' Instead, they are the ones who look at their research question bit by bit, are critical of it, understand its weaknesses and start to think, 'Actually, why don't we move in this direction?' And then they go to their principal investigator or supervisor and say, 'I've really been thinking about this. There may be a better way to go.' And that's the secret to science, of course: always be thinking ahead of the immediate problem you're trying to solve.

Who have been your inspiration and role models?

Well, I suppose, scientifically, I came across people who embody terrific principles of integrity, of vision, of achievement, such as Paul Stewart, who was here at the University of Birmingham, Jayne Franklyn, who was my mentor, Shlomo Melmed, whom I worked for in UCLA in Los Angeles, people like that.

It would be rare to meet a mentor and think, 'I want to be part of it, I want to be you.' In science, you have to develop your own independent characteristics. But it's wonderful when you meet people who have some characteristics that you really aspire to. Away from science, I've always been inspired by great writers, great philosophers, people who write novels, such as Mark Twain and George Orwell. But really, within their novels, they are telling you about human nature.

The only people I am ever really impressed by and look up to are people who have had more adventures than me. This includes anyone whom I feel has lived a more interesting life, been more places, done more things, has tried more, or experienced more. Those are the people who really inspire me.

How do you divide your time in and outside of work?

Well, I'm mildly obsessive when it comes to exercise. I used to be a very serious person: I'm a serious runner and football player. These days, I do kickboxing. I enjoy martial arts a lot. I've just been to the Tour de France and cycled some of the mountain climbs there. For me, sport has been a really critical aspect, because, while it may seem a cliché, the mental side balances the physical side.

For me, the physical side of my life is every bit as important as the intellectual side of my life. One without the other just would not work for me. Perhaps it's always been that punishing my body physically soaks up the pain of my mental efforts. If you have the mental stamina to endure that, it's an obvious point to make. It's a career of endurance.

What are your future plans?

My short term goal is achieving a large funding grant to keep my research team going. I also take over as the Chief Operating Officer of the American Thyroid Association soon, which is a big job. One goal is to make a success of that and bring to it all I can. In terms of messages to the early career scientists who are reading this, it's just in addition to what we talked about in terms of thick skin endurance!

'...and there are times when people think you're failing, while you are thinking, "Actually, I'm succeeding because I'm building something here." '

And, finally, how did you reconcile your joint interests science and writing? When I became a post-doc, probably after about three years, I started to write. Writing a novel was just something I felt inherently that I would be able to do, and so I did it. I got my first book published and it sold very well in the UK and the rest of Europe. I had to change my name. I never wrote novels under the name I use in science, because of the obvious criticism that being a scientist who writes a novel might attract. I went on to publish nine novels in total. Some were very successful, others weren't.

I always tried to keep that discipline separate. The only time they really overlapped – in my second novel, which is terrible – was my attempt to write fiction seen through the eyes of a laboratory scientist. It wasn't a very successful experiment; it's probably the worst book of the nine!

For my later books, I actually used some of the science and wrote forensic thrillers, using what we were doing in the lab every day. What if you had a rogue scientist who started to manipulate forensics? What if you used forensic science for purposes other than just to catalogue what happened in the past?

I have currently stopped writing and haven't written a book for probably seven or eight years. It's something I may well go back to.

REFERENCE

1. McCabe & Birley 1998 Chronobiology International https://doi.org/10.3109/07420529808998677.

You can watch a video of this interview at www.ese-hormones.org/earlycareer

EYES News goes digital

We are thrilled that this issue of *EYES News* is the first to be published only in a digital format.

Since its inception in 2018, our magazine has played a pivotal role in keeping early career endocrinologists and scientists informed, engaged, and interconnected. It was founded by Ljiljana Marina and Ayse Zengin, who drew upon their extensive experience as representatives of the EYES community on the Editorial Board for what was then *ESE News*. Then, under the leadership of Antoan Stefan Šojat, the publication grew to its current format, spanning 16 pages of structured content. As well as covering essential news and diary dates, *EYES News* spotlights remarkable careers through our interviews, with the aim of inspiring the next generation of ESE investigators. Additionally, we proudly feature national endocrine societies and emerging young endocrine groups from diverse areas of the globe. *EYES News* also highlights topical themes in endocrinology and delves into research published in ESE journals, as well as sharing funding opportunities for early career endocrinologists and scientists.

The digital transition marks a new chapter for our magazine. Digital platforms offer cost-effectiveness, environmental sustainability and expanded reach, alongside the invaluable insights they provide into reader engagement and preferences. In keeping with the spirit of EYES, our magazine continues to adapt and innovate, and underscores our commitment to remaining at the forefront of scientific dissemination, connecting early career endocrinologists in an ever-changing world.



As we embark on this exciting journey, we invite you to join us in exploring the dynamic world of endocrinology through the digital pages of *EYES News*. Your continued readership and engagement are the heartbeat of our community, driving us to new heights of innovation and connectivity. Let's continue to shape the future of endocrinology together, one digital issue at a time!

Settimio D'Andrea Italy

5

Hormones and bone

Insights into the endocrinology of skeletal health and disease.

Bone disease in acromegaly

Assessing skeletal health in acromegaly and managing bone disease are not straightforward.

In acromegaly, late diagnosis of growth hormone (GH) hyperproduction by pituitary adenoma,¹ and consequent excess hepatic insulin-like growth factor-1 (IGF-1), causes acral enlargement, typical facial changes, systemic cardiometabolic complications,² and impaired quality of life and survival, often despite multimodal treatment, even when it apparently leads to biochemical control.3

Excess GH and IGF-1 have been demonstrated to increase bone turnover generally, with detrimental consequences for trabecular and also cortical bone. This, in turn, leads to increased vertebral fracture risk, which (after our seminal observation in 2006) has been consistently confirmed over the last almost two decades as one of the most relevant and studied co-morbidities of the disease.4-7

Predicting fracture risk

Unfortunately, assessing bone mineral density (BMD) with dual energy X-ray absorptiometry (DXA) does not reliably predict fracture risk in acromegaly, since lumbar spine (LS) BMD when measured by DXA may be overestimated (as in other pituitary-driven osteopathies) due to concomitant degenerative manifestations, such as osteophytes and facet joint hypertrophy in enlarged bones.⁴ Therefore, assessing BMD by DXA is not sufficient and may often be misleading in assessing skeletal health in acromegaly.⁵

In recent years, an important role has emerged for methods of assessing bone quality in acromegaly fracture risk prediction. Among these methods, the most widely available is trabecular bone score, a DXA-derived parameter which has been reported to be consistently decreased in acromegaly. Assessment of bone microarchitecture with cone beam computed tomography (CT), and particularly with high resolution peripheral quantitative CT, can also be of value, although it is still limited to research studies, due to its restricted availability and high cost.8 Finally, endocortical trabecularisation has been recently reported upon hip structure analysis, leading to the intriguing hypothesis that it could be involved in the increased fracture risk in controlled acromegaly, whereas altered trabecular architecture may lead to fractures in biochemically active acromegaly.9

Based initially on our studies, but subsequently on many others globally, detection of thoracic and LS vertebral fractures by means of vertebral morphometry, either with DXA or with spine X-rays (or, lately, opportunistically by thoracic X-rays) did become the method

of choice in assessment of bone status in acromegaly.¹⁰ In fact, prevalent morphometric fractures are seen in up to 60% of patients, with three- to eightfold increased risk versus the general population, and linked to disease activity, but not with DXA BMD.¹¹ Moreover, incident vertebral fractures are seen in up to 42% of subjects with acromegaly, not only in active but also in controlled disease.¹² In the latter, prevalent fractures, diabetes mellitus (another common co-morbidity of acromegaly, which can cause skeletal fragility) and hypogonadism are the main risk predictors.13

Recently, we reported that radiological thoracic vertebral fractures are a relatively early phenomenon in the natural history of acromegaly. They are highly prevalent in patients who are undergoing neurosurgery within one year of diagnosis and are associated with high presurgical GH levels.¹⁴ In this context, the known diagnostic delay of the disease may have a role, since it has been suggested to be a predictor of incident vertebral fractures.¹⁰ Therefore, all recent guidelines recommend that vertebral morphometry is performed at diagnosis in all patients with acromegaly, and repeated at follow-up, particularly in patients with active disease or with other concomitant risk factors (see above).2

Finally, a recent cohort prospective study from Korea of about 1700 patients with acromegaly, with a long follow-up of over eight years, found a significant (greater than twofold) increased risk of clinical vertebral and hip fractures versus age- and sex-matched controls.15

Management of acromegalic bone disease

Few data are available concerning prevention and treatment of bone disease in acromegaly. Particularly when treated with somatostatin receptor ligands (due to malabsorption of lipophilic molecules), active acromegaly appears to be burdened by a high prevalence of vitamin D deficiency, which is also widespread in many countries, and possibly by vitamin D resistance.¹⁶ Very recently, in a longitudinal retrospective study, patients with acromegaly who were supplemented with standard cholecalciferol doses for more than seven years showed fewer incident vertebral fractures than untreated patients.¹⁶ These findings suggest that an effective bone-protective approach should be to measure vitamin D in all patients with acromegaly (at least in countries where a lack of vitamin D is highly prevalent) and, if hypovitaminosis D is found, to start cholecalciferol supplementation.

Medical therapy is a key option for the first-line (octreotide or lanreotide LAR) or second-line (pasireotide LAR or pegvisomant) treatment of acromegaly.3 Cross-sectional17



and prospective studies¹⁸ suggest that achieving disease control with either type of treatment may decrease fracture risk, although it was recently reported that pasireotide decreased risk of incident vertebral fractures more efficiently than pegvisomant, independently of the impact on biochemical control.¹⁹ This suggests possible negative effects of high circulating GH on the skeleton.

In conclusion, bone disease is an emerging co-morbidity of acromegaly, with high epidemiological and clinical impact, which must be proactively diagnosed using techniques mainly devoted to exploring bone quality and resistance, such as vertebral morphometry. Optimal control of the disease, with use of cholecalciferol and pasireotide, provides clinical measures that can reduce fracture risk in acromegaly.

Andrea Giustina

Institute of Endocrine and Metabolic Sciences, San Raffaele Vita Salute University and IRCCS San Raffaele Hospital, Milan, Italy

REFERENCES

- 1. Melmed et al. 2022 Endocrine Reviews
- https://doi.org/10.1210/endrev/bnac010. Giustina et al. 2020 Journal of Clinical Endocrinology & Metabolism https://doi.org/10.1210/clinem/dgz096.
- Giustina et al. 2020 Reviews in Endocrine & Metabolic Disorders https://doi.org/10.1007/s11154-020-09588-z.
- 4. Mazziotti et al. 2018 Endocrine Review
- https://doi.org/10.1210/er.2018-00005
- 5. Giustina 2020 Trends in Endocrinology & Metabolism
- https://doi.org/10.1016/j.tem.2020.01.011. 6. Bonadonna et al. 2005 Journal of Bone & Mineral Research
- https://doi.org/10.1359/JBMR.050603. 7. Mazziotti et al. 2008 Journal of Clinical Endocrinology & Metabolism https://doi.org/10.1210/jc.2008-0791. 8. Uygur et al. 2023 Trends in Endocrinology & Metabolism
- https://doi.org/10.1016/j.tem.2023.01.006
- 9. Giustina 2023 Endocrinology & Metabolism
- https://doi.org/10.3803/EnM.2023.601.
- 10. Chiloiro et al. 2022 Pituitary https://doi.org/10.1007/s11102-022-01266-4.
- Mazziotti et al. 2015 Journal of Clinical Endocrinology & Metabolism https://doi.org/10.1210/jc.2014-2937.
- 12. Mazziotti et al. 2013 Journal of Clinical Endocrinology & Metabolism https://doi.org/10.1210/jc.2013-1460.
- 13. Mazziotti et al. 2011 Endocrine
- https://doi.org/10.1007/s12020-011-9486-x. 14. Frara et al. 2022 Journal of Clinical Endocrinology & Metabolism
- https://doi.org/10.1210/clinem/dgac183. 15. Kwon et al. 2023 Osteoporosis International
- https://doi.org/10.1007/s00198-023-06800-z. 16. Chiloiro et al. 2023 Journal of Clinical Endocrinology & Metabolism
- https://doi.org/10.1210/clinem/dgad493 17 Chiloiro et al 2018 Endocrine
- https://doi.org/10.1007/s12020-017-1391-5. 18. Chiloiro et al. 2018 Pituitary https://doi.org/10.1007/s11102-018-0873-7.
- 19. Chiloiro et al. 2020 Journal of Clinical Endocrinology & Metabolism https://doi.org/10.1210/clinem/dgz054.

Hormones in bone development

The hormonal regulation of bone development is a finely tuned process, crucial for achieving and maintaining skeletal integrity and overall health.

Despite popular belief, our bones undergo continuous remodelling throughout life, and hormones play a pivotal role in modulating the delicate balance between bone formation and resorption.¹ One of the key hormones involved in bone development is growth hormone (GH), which stimulates the production of insulinlike growth factor-1 (IGF-1) in the liver. IGF-1 promotes the proliferation and differentiation of osteoblasts, the cells responsible for bone formation. Consequently, GH deficiency can lead to impaired linear growth and skeletal abnormalities.²

Thyroid hormones, particularly thyroxine and tri-iodothyronine, also make a significant contribution. Indeed, these influence bone turnover by regulating osteoblast and osteoclast activity. Hypothyroidism results in decreased bone formation, while hyperthyroidism may lead to excessive bone resorption, both affecting bone density and structure.

During childhood and adult life, sex hormones, such as oestrogen and testosterone, exert profound effects on bone development and are crucial for maintenance of bone mass. They mainly have an anti-resorptive effect and hamper osteoclast-mediated resorption.¹ Reduced sex steroid levels are associated with a rapid increase in bone turnover and, ultimately, an increase in bone fragility, as clearly proven by clinical experience with hormonal-deprivation therapies to treat breast and prostate cancers.³

Parathyroid hormone (PTH) is also a pivotal regulator of calcium homeostasis, which can have a strong influence on bone metabolism. It



stimulates osteoclast activity, releasing calcium from bone into the bloodstream, ensuring a delicate equilibrium of calcium levels critical for bone mineralisation. Nevertheless, excess PTH production leads to acceleration of bone resorption and, eventually, to loss of both bone mass and microarchitecture.⁴

Lastly, vitamin D, although not a hormone in the traditional sense, plays an integral role in bone health. Synthesised in the skin or obtained from dietary sources, vitamin D is converted into its active form in the kidneys. This form enhances calcium absorption in the intestines and protects mineralisation in bones. A deficiency of vitamin D can lead to impaired bone mineralisation, resulting in conditions such as rickets in children and osteomalacia in adults.⁵

Bone development reflects how our hormonal balance deeply influences the physiological

health of another organ, involving various hormones working in concert. Imbalances in these hormonal signals can lead to a deterioration of bone health, and so the latter should be always addressed during endocrine disease management.

Walter Vena Italy

REFERENCES

- 1. Mills et al. 2021 Endocrine Reviews
- https://doi.org/10.1210/endrev/bnab015. 2. Mazziotti et al. 2022 Nature Reviews Endocrinology
- https://doi.org/10.1038/s41574-022-00649-8. 3. Mazziotti et al. 2022 Journal of Bone Oncology https://doi.org/10.1016/j.jbo.2022.100421.
- https://doi.org/10.1016/j.jbo.2022.100421. 4. Rejnmark *et al.* 2020 *Current Osteoporosis Reports*
- https://doi.org/10.1007/s11914-020-00574-7. 5. Lips et al. 2019 European Journal of Endocrinology https://doi.org/10.1530/EJE-18-0736.

Androgen deprivation therapy and bone

Prostate cancer is the second most prevalent cancer among men worldwide, with rising global morbidity and mortality rates, mainly due to an ageing population and the pervasive adoption of Western lifestyles.

At the heart of prostate cancer lies its dependence on androgens, which bind the androgen receptor (AR) to fuel uncontrolled proliferation. In combating this dependency androgen deprivation therapy (ADT) emerged in 1941, when Charles Huggins, Clarence Hodges and their colleagues revealed the beneficial effect of ADT for men with metastatic prostate cancer via castration or oestrogenic therapy. ADT, through the reduction of testosterone levels via pharmacological or surgical means, has extended the lives of countless men with prostate cancer; yet, it comes at a cost to quality of life.¹ Muscle loss, increased body fat, metabolic changes and erectile dysfunction are among its adverse effects. However, one of its most profound impacts is on bone health.

Testosterone and oestradiol (converted from testosterone via aromatase activity) play pivotal roles in bone metabolism, maintaining bone density and strength by preventing osteoblast apoptosis and decreasing osteoclastogenesis.² Consequently, ADT disrupts this balance, leading to increased bone fragility in patients with metastatic prostate cancer. Indeed, research efforts have resulted in the approval by the US Food and Drug Administration of zoledronic acid and denosumab for the prevention of metastasisrelated skeletal-related events in this vulnerable population.

However, it is imperative to recognise that bone fragility can also manifest in individuals without documented metastases. Notably, patients undergoing ADT for non-metastatic prostate cancer exhibit a substantial cumulative loss of bone mineral density, predisposing them to fractures. This risk is underscored by findings from studies examining bone complications in patients with prostate cancer, both metastatic and non-metastatic, who are subjected to ADT.

Moreover, the duration of ADT appears to exacerbate its adverse effects on bone health.

Specifically, studies have indicated that patients receiving prolonged ADT regimens (exceeding one year) exhibit elevated fracture rates and bone medication use.³

In conclusion, as we navigate the complex landscape of prostate cancer management, addressing the bone challenges of ADT is of critical importance in enhancing the quality of life of these patients. Let's safeguard bone health in the fight against prostate cancer!

Juan M Jiménez Vacas UK

REFERENCES

1. Westaby et al. 2022 Annual Review of Pharmacology & Toxicology https://doi.org/10.1146/annurev-pharmtox-052220-015912.

- Clarke & Khosla 2009 Steroids https://doi.org/10.1016/j.steroids.2008.10.003.
 Hussain et al. 2021 Prostate Cancer & Prostatic Diseases
- Hussain et al. 2021 Prostate Cancer & Prostatic Disease https://doi.org/10.1038/s41391-020-00296-y.

Parathyroid disorders and bone health

Primary hyperparathyroidism (PHPT) and chronic hypoparathyroidism in adults (HypoPT) are the most important bone diseases in the endocrine clinic.

The main function of parathyroid hormone (PTH) is to regulate calcium and phosphate metabolism. The Figure shows the impact of these notable disorders on this regulation: (A) in PHPT and (B) in HypoPT.¹

Calcium levels are closely (within minutes) regulated by the action of PTH on tubular reabsorption of calcium, at the expense of phosphate. Moreover, PTH activates vitamin D, thereby increasing absorption of calcium from the intestine (over a period of hours). More delayed is the PTH-driven release of calcium from bone by osteocytes and by increasing bone turnover.² In adults, bone turnover mirrors the bone remodelling process, ensuring biomechanical competence.

Primary hyperparathyroidism

PHPT is the most common parathyroid disorder, with a prevalence as high as 2–5% in periand postmenopausal women. The disease is described as a set-point error in the parathyroid gland followed by a stable hypercalcaemia over a period of years, with an inappropriately high PTH in relation to calcium levels. The most common form, and most controversial for therapy, is asymptomatic, mild PHPT.

Panel A of the Figure shows increased bone turnover in PHPT, with a negative balance inducing a progressive bone loss. Based on histomorphometry, this bone loss is reversible, i.e. it can be restored by treatment (parathyroidectomy; PTX). The reversibility has primarily been described in trabecular bone, with a paradoxical thinning of the cortical bone (endocortical trabecularisation). Accordingly, long term observational studies by dual energy X-ray absorptiometry (DXA) indicated a progressive bone loss, primarily in cortical sites, following PTX.¹

A long term randomised controlled trial of operation versus observation in mild PHPT was recently published.³ The 10-year data show a significant treatment effect of PTX on bone mineral density (BMD) for all compartments, including both sites in the proximal forearm. For the PTX group, a positive long term effect (T score) was demonstrated for the lumbar spine, but not for other compartments. Conversely, a significant loss of bone (T scores) was found in both sites in the forearm. For the observation group, a pronounced and significant loss of bone was found for all compartments.³

Fracture rate is increased in PHPT, including mild PHPT, based on several register and observational studies.¹ For years, the controversy has concerned whether PTX would impact low-energy fractures. Based on detailed morphometry analyses, the previously mentioned long term randomised controlled trial could not demonstrate a beneficial effect of PTX on vertebral fractures over a 10-year perspective,³ or for any fracture.⁴ As patients with PHPT might fracture at a higher BMD level than other patients,² the lack of effect might be ascribed to a type 2 error.

Chronic hypoparathyroidism in adults

HypoPT is an orphan disease, in adults most often secondary to previous neck surgery.^{1,2} Panel B of the Figure shows HypoPT as a two-hormone deficiency disease, with reductions in PTH and active vitamin D. Thereby, bone turnover is low, where all phases of the remodelling process are increased with a potential positive bone balance, at the DXA level leading to increased BMD.^{1,2} The implication for bone strength is, however, unclear, even though case-control studies have indicated an increased fracture rate for idiopathic HypoPT on conventional therapy, whereas the risk of fracture in postsurgical HypoPT so far is ambiguous.^{1,2}

The management of HypoPT has mostly been conventional, i.e. focusing on symptomatic treatment with active vitamin D in combination with calcium and native vitamin D supplement, to minimise symptoms and keep the calcium level in the lower normal range. This strategy does not improve bone metabolism and strength.¹

PTH and PTH analogues are now available and expected to be implemented in the clinic in the coming years. PTH(1-84) was approved for treatment of HypoPT in 2015, as a single daily injection. Due to pharmacokinetics, this is not a truly physiological replacement therapy, as PTH rises quickly in the circulation after injection, with an effect in target tissues for some hours. Accordingly, long term open studies of PTH(1-84) in patients with HypoPT showed an increase in indices of bone remodelling in all envelopes, with some even exceeding normal values (an anabolic effect). As expected, bone mass by DXA decreased in most compartments (normalisation?) and, after several years, a new steady state seemed to be established.⁵

PTH(1-84) will leave the market by the end of 2024. However, new PTH analogues are already close to being approved internationally, and will hopefully be ready for patients in due time. These analogues have a prolonged pharmacokinetic profile, potentially normalising bone metabolism.⁶

Summary

PTH is an osteoanabolic hormone regulating bone remodelling. In PHPT, bone turnover is high, followed by low BMD for all compartments. In mild PHPT, PTX normalises BMD in the lumbar spine only; however, PTX was clearly superior to observation for BMD levels in all other areas (10-year randomised controlled trial), where the effect of PTX on fracture rate was equivocal. Hormone replacement therapy is still not standard management for HypoPT. PTH treatment will increase bone turnover potentially to a new steady-state close to normalisation after several years. The effect on fracture risk is not clear.

Jens Bollerslev

Professor Emeritus, Faculty of Medicine, University of Oslo, Norway

This article is based on original presentations by the author during workshops for the PARAT Programme [2] in 2018–2022, and subsequent publications thereafter.^{1,2} PARAT is an ESE initiative, aiming to identify unmet scientific and educational needs regarding parathyroid disorders. A taskforce of more than 100 European experts met through a series of workshops over five years, leading to consensus reports, workshop reports and further educational material. At present, the programme aims to continue its work through biannual workshops associated with ECE.

REFERENCES

- Bollerslev et al. 2019 European Journal of Endocrinology https://doi.org/10.1530/EJE-19-0316.
- Bollerslev et al. 2022 European Journal of Endocrinology https://doi.org/10.1530/EJE-21-1044.
- 3. Lundstam et al. 2023 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.4763.
- 4. Pretorius et al. 2022 Annals of Internal Medicine
- https://doi.org/10.7326/M21-4416. 5. Agarwal et al. 2023 Journal of Bone & Mineral Research
- Agarwal et al. 2023 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.4780.
 Khan et al. 2023 Journal of Bone & Mineral Research
- 6. Khan et al. 2023 Journal of Bone & Mineral Resea https://doi.org/10.1002/jbmr.4726.



Calcium homeostasis and bone metabolism in (A) PHPT and (B) chronic HypoPT. Reproduced under CC BY 4.0 licence (https://creativecommons.org/licenses/by/4.0) rom Bollerslev et al.¹ https://doi.org/10.1530/EJE-19-0316 ©2019 ESE PARAT Workshop Group.

Early menopause and bone

A major issue regarding menopause and its health consequences is bone health. The tight connection between sex steroid levels and bone is of fundamental importance.

According to the classic definition, menopause is a period in woman's life which starts 12 months after her final menstrual period. However, experts in the field agree that there is a need for a new, broader and more inclusive definition, with respect to early menstrual cycle regularity, symptoms, surgical procedures and, finally, health consequences.

The median menopausal age depends on race and ethnicity. For Western countries, it is around 50-51 years. About 10% of women will reach menopause between the ages of 40 and 45; this is defined as an early menopause.

The path to the final menstrual period is not the same for all women. Some will not feel significant changes, yet the majority will experience complaints of different characteristics and individual intensity, such as vasomotor symptoms, insomnia, mood roller coasters and urogenital problems.

The impact of menopause on bone health is a result of the close relationship between sex steroid levels and bone. Oestrogens are essential for proper bone formation and peak bone mass. Insufficient oestrogen levels lead to accelerated bone resorption that exceeds bone formation.

For women entering natural menopause, these changes are seen from the onset of the menopause transition and peak at about two years after the final menstrual period. However, for women with early menopause, this happens even sooner. Early menopause is a risk factor for osteoporosis, with evidence showing that it leads to greater bone loss than natural menopause.¹



In their meta-analysis, which included more than 462,000 menopausal women, Anagnostis et al. showed that there is an association between menopausal age and fracture risk, and that women with early menopause have a higher fracture risk compared with women of normal age at menopause.2

Women with early menopause need close follow-up of bone health and fracture risk. with the aim of achieving early and timely bone loss protection and, if needed, starting the appropriate anti-osteoporosis treatment. Menopausal hormone therapy is highly relevant for these women, not only in the context of

treating menopausal symptoms, but also because of its beneficial effect on the maintenance of skeletal health and fracture risk reduction, which has been well established.³

Ljiljana Marina Serbia

REFERENCES

- 1. Francucci et al. 2008 Maturitas https://doi.org/10.1016/j.maturitas.2008.03.008. 2. Anagnostis et al. 2019 Endocrine
- https://doi.org/10.1007/s12020-018-1746-6. 3. Rozenberg et al. 2020 Osteoporosis International https://doi.org/10.1007/s00198-020-05497-8.

New medications for osteoporosis

While we await new drugs, treatment must rely on combined and sequential strategies using established therapeutics.

Osteoporosis is a chronic, systemic bone disease caused by an imbalance between bone formation and resorption. This disease is characterised by the loss of bone mass and an increased risk of bone fractures. It is a global public health problem that will become increasingly important in the coming years.

The pharmacological treatment of osteoporosis began more than 70 years ago with oestrogens for the treatment of postmenopausal osteoporosis. After that, bisphosphonates were prescribed for the treatment and prevention of osteoporosis. To date, other pharmacological agents have been approved for treatment, such as denosumab as a strong anti-resorptive drug, teriparatide and abaloparatide as bone anabolics, and the novel agent romosozumab, which has a dual anabolic/anti-resorptive mechanism of action.

As the duration of therapy is limited to two years for the bone anabolics and one year for romosozumab, and discontinuation of denosumab is associated with rapid bone turnover and an increased risk of multiple vertebral fractures, bisphosphonates remain the most commonly used therapy for osteoporosis worldwide. However, as osteoporosis is a life-long disease that often requires sequential treatment with different drugs, there is a constant need for the development of new therapeutics.1

Today, the Wnt signalling pathway, as a stimulator of osteoblast function, and its key inhibitors sclerostin and Dickkopf-1 (DKK-1) have become targets of interest for the treatment of osteoporosis. In addition to romosozumab, other sclerostin inhibitors, such as blosozumab, are in development.² There is increasing evidence that non-coding RNA can regulate bone metabolism by interacting with the Wnt signalling pathway, and may be an important therapeutic target.³ Additional methods, including stem cell transplantation and exosome therapy, have also been proposed.⁴ Another interesting area of research is the use of nanotechnology for targeted treatment of osteoporosis, either by introducing anti-resorptive drugs or by

incorporating molecules for gene regulation.5 However, most of these studies involved in vitro models and should be verified by additional clinical studies.

Although there is a lot of interest in a novel osteoporosis drug, we have to wait for the trial results. Until then, we can adopt combined and sequential strategies using drugs that have already been approved.

Lana Šambula Croatia

REFERENCES

- 1. Adami et al. 2022 Therapeutic Advances in Musculoskeletal
- Disease https://doi.org/10.1177/1759720X221083541. 2. Recker et al. 2015 Journal of Bone & Mineral Research
- https://doi.org/10.1002/jbmr.2351.
- 3. Gao et al. 2023 Biomolecules
- https://doi.org/10.3390/biom13030483.
- 4. He et al. 2023 Stem Cell Research & Therapy https://doi.org/10.1186/s13287-023-03317-4.
- 5. Salamanna et al. 2021 Nanomaterials
- https://doi.org/10.3390/nano11020530

Ethnic differences in bone health

There are differences in fracture risk between ethnic groups around the globe, in both men and women.¹ To determine strategies for prevention of osteoporosis and bone fragility in an ever-changing environment, we must understand the phenotype underlying these differences.

Most studies report ethnic differences in areal bone mineral density (aBMD) measured by dual energy X-ray absorptiometry (DXA), which do not consistently parallel ethnic patterns in fracture rates. Variations in body size and composition are likely to contribute to reported differences. More recently, three-dimensional bone-imaging modalities, including quantitative computed tomography (QCT), peripheral QCT (pQCT) and high resolution pQCT (HRpQCT), have enabled the measurement of volumetric bone mineral density (vBMD), structural dimensions and internal organisation of cortical and trabecular bone. As a result, more and more studies are now focusing on bone microarchitecture and how this influences fracture risk in different ethnic groups.

The literature has shown that the lowest fracture rates are in populations with African ancestry,² with a greater than 10-fold variation in age-standardised hip fracture risk among 63 countries,² demonstrating the variation in fracture risk between ethnic groups. Large population studies have used aBMD measured by DXA as a marker for bone health and fracture risk to study ethnic differences in bone health. The third National Health and Nutrition Examination Survey (NHANES III) has shown that African Americans have the highest mean femoral neck and total hip aBMD levels compared with Caucasian men, who had the lowest levels.³

One of the largest multi-ethnic studies, the National Osteoporosis Risk Assessment (NORA), showed that African American women had the highest aBMD and that Asians had the lowest.⁴ Even after adjusting for body weight and other risk factors, the greater aBMD in African American women persisted. However, Asian women had similar values to Caucasian women.⁴ This study led to the suggestion that there may be other components of bone health that need to be considered: namely bone geometry, size and microarchitecture.

The Osteoporotic Fractures in Men Study (MrOS) used OCT and showed that African American and Asian men have increased bone strength compared with White men, due to greater vBMD and thicker cortices of the femoral neck.⁵ In the UK, data from the European Male Ageing Study (EMAS) were compared with a group of Afro-Caribbean and South Asian men.6 Afro-Caribbean men had higher aBMD compared with White and South Asian men, and these differences were independent of weight and height. In contrast, differences in aBMD between White and South Asian men were attenuated by correcting for body size.⁶ With the exception of cortical vBMD, which was lower in White men compared with both Afro-Caribbean and South Asian men, the differences in vBMD were far fewer than in DXA outcomes where Afro-Caribbean men did not differ from White or South Asian men. Rather, the geometry of bone differed between the groups and mostly at the diaphyseal sites, and hip axis length was longer in White men.⁶ At the radius and tibia diaphysis, Afro-Caribbean men had more cortical bone within a slightly larger periosteal envelope, and consequently greater bending strength than the other two groups.6

Fracture and bone mineral density data in Aboriginal and Torres Strait Islander people of Australia are sparse.⁷ Aboriginal and Torres Strait Islander men and women were 50% and 26% more likely to have a hip fracture compared with non-Indigenous men and women respectively. Hip fractures occur at a much younger age in Aboriginal and Torres Strait Islander people (in men, 65 compared with 81 years; in women, 74 compared with 83 years).8 Between 1999 and 2009, a study reported a significantly disproportionate increase in minimal trauma hip fracture rates among Aboriginal and Torres Strait Islander people aged ≥40 years,9 in contrast to declining agerelated rates of hip fracture in non-Indigenous Australians.¹⁰ Use of 3D-imaging modalities



in future studies will help shed light on why fracture rates are higher among Aboriginal and Torres Strait Islander people.¹¹

Studies are now beginning to demonstrate that bone geometry and microarchitecture are different in ethnic groups, and these variations are likely to contribute to the ethnic differences in fracture rates. Chinese American women have smaller bones; however, they have higher cortical vBMD12 and better trabecular microarchitecture, with more plate-like structures, when compared with Caucasian American women.¹³ African American women have a high aBMD which contributes greatly to a reduced fracture risk; however, thicker cortices and better trabecular microarchitecture also contribute to decreasing fracture risk when compared with Caucasian women,¹⁴ suggesting that cortical and trabecular bone together contribute to bone strength.

The Study of Women's Health Across the Nation (SWAN) reported no differences in aBMD between Chinese, Japanese and Caucasian women, but that bone geometry varied greatly.¹⁵ Femoral neck cross-sectional area and section modulus of the hip, measured by DXA, were higher in Japanese compared with Caucasian women.¹⁵ Thus, Japanese women have better resistance to axial compressive and bending stresses due to greater bone area, which conferred a larger section modulus. HRpQCT has been used to explain the structural basis of bone fragility, but is somewhat limited today. A study in premenopausal Chinese American women showed that the trabecular microarchitecture of Eastern Asian women appears to have a structural advantage when compared with White Caucasian women, with more plate-like and larger trabeculae, and greater plate-rod junction density - a parameter indicating trabecular network connections.13

There is a need to go beyond aBMD and assess skeletal parameters contributing to a healthy bone phenotype, i.e. bone shape, mineralisation and distribution, to ultimately decrease the burden of osteoporosis worldwide and to highlight that a 'one-size fits all approach' is not appropriate.

Ayse Zengin, Australia

REFERENCES

- 1. Zengin et al. 2015 Frontiers in Endocrinology
- https://doi.org/10.3389/fendo.2015.00024. 2. Kanis et al. 2012 Osteoporosis International
- https://doi.org/10.1007/s00198-012-1964-3. 3. Looker et al. 1998 Osteoporosis International
- Looker et al. 1998 Usteoporosis international https://doi.org/10.1007/s001980050093.
 Barrett-Connor et al. 2005 Journal of Bone & Mineral Research
- Barrett-Connor et al. 2005 Journal of Bone & Mineral Research https://doi.org/10.1359/JBMR.041007.
 Marshall et al. 2008 Journal of Bone & Mineral Research
- Marshall et al. 2008 Journal of Bone & Mineral Research https://doi.org/10.1359/jbmr.070908.
- Zengin et al. 2016 Bone https://doi.org/10.1016/j.bone.2016.07.018.
- https://doi.org/10.1016/j.bone.2016.07.018.
 Zengin et al. 2018 Archives of Osteoporosis https://doi.org/10.1007/s11657-018-0493-x.
- https://doi.org/10.1007/s11657-018-0493-x. 8. Australian Institute of Health & Welfare 2010 The Problem of Osteoporotic Hip Fracture in Australia https://www.aihw.gov.au/reports/chronic-musculoskeletal-
- conditions/osteoporotic-hip-fracture-in-australia/summary. 9. Wong et al. 2013 Internal Medicine Journal
- https://doi.org/10.1111/imj.12040. 10. Crisp et al. 2012 Archives of Osteoporosis
- Crisp et al. 2012 Archives of Osteoporosis https://doi.org/10.1007/s11657-012-0095-y.
 Zengin et al. 2022 BMJ Open
- https://doi.org/10.1136/bmjopen-2021-056589.
 12. Walker et al. 2011 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.352.
- https://doi.org/10.1002/jbmr.352. 13. Liu et al. 2011 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.378.
- Putman et al. 2013 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.1953.
- Danielson et al. 2013 Journal of Bone & Mineral Research https://doi.org/10.1002/jbmr.1781.

Research insights into... Endocrine disorders of bone

We bring you some topical highlights from the world of research, selected from ESE's co-owned, open access journal *Endocrine Connections* by Settimio D'Andrea.

Age-dependent sex differences in calcium and phosphate homeostasis

As sex differences in calcium and phosphate have been observed, Koek *et al.* collected laboratory values of serum calcium, phosphate and albumin in the years 2005, 2010 and 2014 from the Erasmus Medical Centre, The Netherlands, for this observational study.

The samples were divided into three age groups: 1–17, 18–44 and ≥45 years. There was a significant sex×age interaction for serum calcium and phosphate, with levels significantly higher in women compared with men above 45 years. No sex differences in the younger age groups were found.

In men, serum calcium and phosphate levels were highest in the youngest age group compared with the groups aged 18–44 and ≥45 years. In women, serum calcium levels were significantly higher in the groups aged 1–17 and ≥45 years compared with the 18–44 year group. In women, serum phosphate differed between the three age groups, with the highest level in the group aged 1–17 years and the lowest in the group aged 18–44 years.

In conclusion, serum calcium and phosphate differed between age groups and between genders.

See Endocrine Connections 2021 https://doi.org/10.1530/EC-20-0509

Clinical phenotypes of PHPT in patients undergoing parathyroidectomy

Yanevskaya *et al.* undertook an observational study to investigate the distribution of the clinical manifestations and biochemical features of primary hyperparathyroidism (PHPT) in patients who underwent parathyroidectomy.

The records of 449 patients (median age 60 years) were collected from three medical centres in Russia. No difference in age was found between symptomatic and asymptomatic patients. The serum level of parathyroid hormone (PTH) was higher in symptomatic patients. Serum 25(OH)D level negatively correlated with PTH, ionised calcium and total calcium. Cardiovascular diseases were observed in 67.7% of cases, both in symptomatic and asymptomatic patients (*P*=0.076).

The authors concluded that a symptomatic phenotype is still the most common form of PHPT.

See Endocrine Connections 2021 https://doi.org/10.1530/EC-20-0515

Impaired bone quality in men with type 1 diabetes

This cross-sectional study by Syversen *et al.* explored the relationship between type 1 diabetes mellitus and bone mineral density (femoral neck, total hip, lumbar spine, whole body), spine trabecular bone score (measured using dual X-ray absorptiometry), and bone material strength index (measured by *in vivo* impact microindentation).

The authors found that men with type 1 diabetes showed compromised bone material in terms of strength and microarchitecture. They concluded that diabetes mellitus should be recognised as a risk factor for bone health.

See Endocrine Connections 2021 https://doi.org/10.1530/EC-21-0193

Global differences in vitamin D status and dietary intake

For the Endocrine Connections collection of papers marking '100 years of vitamin D', Cashman conducted this narrative review, aiming to provide a summary and assessment of vitamin D nutritional status data globally.

The limited data suggest a relatively low overall prevalence of vitamin D deficiency in South America, Oceania and North America, whereas there is a more moderate prevalence in Europe, Asia, and Africa. Despite the intakes of vitamin D varying by world region, there are very high levels of inadequacy of vitamin D intake.

See Endocrine Connections 2022 https://doi.org/10.1530/EC-21-0282



Members of ESE receive a 40% discount on Open Access publishing in *Endocrine Connections*. Find out more at https://ec.bioscientifica.com



'As the incoming Editor-in-Chief, I believe we need to build on the word "connections", whether that be connections with other sciences, connections between the different clinical professions within endocrinology, connections between the bench and the lab, connections between centres, or connections between datasets.'

Faisal Ahmed

Editor-in-Chief, Endocrine Connections

Preoperative inflammatory markers of parathyroid carcinoma

In this retrospective study, Ohkuwa and coworkers investigated the main preoperative features of 36 cases of parathyroid carcinoma and 50 of parathyroid adenoma.

.....

All enrolled patients with carcinoma had significantly higher preoperative levels of intact parathyroid hormone and serum calcium, and greater gland diameter, than patients with parathyroid adenoma. The multivariate analysis showed that lymphocyte-to-monocyte ratio (LMR) and tumour length diameter were independent predictors for parathyroid cancer. In the receiver operating characteristic (ROC) analysis, the cut-off value for LMR was 4.85 and that for tumour length was 28mm. Moreover, the ability to predict carcinoma improved when the two selected factors were stratified by the number of evaluated factors.

See Endocrine Connections 2022 https://doi.org/10.1530/EC-22-0062

Addressing adrenal tumours

The Harmonis ation COST Action aims to create a multidisciplinary network, harmonising clinical care and research on adrenal tumours throughout Europe.

As an early career clinician scientist, I am thrilled to update you on this dynamic initiative, which is wide open to early career investigators, recognising their vital role as the driving force of innovation. It is supported by COST, an EU programme that enables researchers to establish networks.

The wide variability of adrenal tumour management results in substantial inequalities in patient care across Europe. The Harmonis ation initiative focuses on COST Inclusiveness Target Countries, aiming to create a modern framework for real-time and real-life randomised clinical trials, which are federated and registry-based. Harmonis@tion is organised into five working groups, which cover key aspects, including clinical practice, research, technology, ethics, legal frameworks and communication. Success hinges on collaboration



across diverse fields, including artificial intelligence, data science, data protection, legal and ethical issues, and patient representatives.

There is no better way to exchange insights, build connections and collectively advance understanding than through in-person events. So far, Harmonis@tion and ENS@T (the European Network for the Study of Adrenal Tumors) have jointly conducted two highly successful meetings (Warsaw 2022 and Dubrovnik 2023). The next, highly anticipated event is the joint

Harmonis@tion

23rd ENS@T and 3rd COST Harmonis@tion Meeting, in the beautiful Palma de Mallorca, Spain, on 2-4 October 2024. It will be one of the most exciting, state-of-the-art meetings in adrenal endocrinology.

If you are an early career investigator, interested in adrenal endocrinology and eager to learn and connect, Harmonis@tion is the right place for you. Find out how to join at www.goharmonisation.com or follow Harmonis@tion on X 12 to stay updated, engage in discussions, and be part of the vibrant community. Harmonis@tion is also dedicated to organising exceptional online educational events.

As we embark on the path ahead in endocrinology, our way is illuminated by initiatives such as this, encapsulating the spirit of innovation and our collective commitment to advancing patient care and research.

Kristina Saravinovska Serbia

Gaining experience abroad

Antoan Stefan Šojat reflects on the experience he gained while working in Paris, supported by the Harmonis@tion initiative.

In an age of growing gaps in research and funding, and various socioeconomic divisions, grants and opportunities such as the COST Harmonis Tion Short Term Scientific Missions **C** stand out as valuable opportunities for early career development in endocrinology.

Since my first day as a medical student, I have observed the world as a vast field of academic mobility. I feel that practising medicine should not be limited to a certain region or country, and that it is almost imperative for young practising researchers and clinicians to gain experience abroad, so they can truly expand their scientific thought.

I am fortunate enough to have a mentor who is almost as devoted to the true art of mentorship, selfless support and making endocrinology better as she is dedicated to scientific and clinical work. True mentors are now rarer than ever, and the warm Parisian days





and nights were my perfect introduction to how meaningful this can really be.

Feeling at home

I like to refer to my stay in Paris and my work at the Cochin Institute and Institut Imagine Paris as life-changing in many ways. Not only was I welcomed as if I was at home by some of the greatest minds in contemporary endocrinology, I was also embraced by the entire team and immediately assimilated into the daily rhythms of the lab.

I worked each day on several projects; some concerned the IT, legal and technical aspects of the adrenal tumour data collection, while others focused on new target genes for pituitary neuroendocrine tumours. I spent my days collaborating intensively with amazing and vibrant minds, learning new things and writing essentially beautiful science. I dived deep into French culture, which always fascinated me, and spent my evenings and nights having inspiring conversations about life with old friends and many new people I met along the way.

New perspectives

The ether of Paris raised many questions and challenged many of my previous views on life and science. The more I worked with the team, the more I found myself progressing through new challenges with ease. Just like the contrast between the hectic art of Basquiat and Warhol and the gentle, subtle light in Impressionist paintings, I drifted between new knowledge and techniques and new people whom I was learning from.

The visit to Cochin Institute brought me personal and professional growth. Moreover, from Paris, I carry with me many arrondissements, flavours, knowledge and memories. I am very grateful to Guillaume Assie for this whole experience, as well as Jérôme Bertherat, Anita Burgun, Anne Juinot, Ciarra Villa and the entire Cochin and Imagine teams for taking me in as one of them.

Antoan Stefan Šojat Serbia

EYES NEWS

Get ready for Helsinki



ESE Young Endocrinologists & Scientists Annual Meeting 6.-8.9.2024 Helsinki, Finland

The 11th Annual EYES Meeting takes place in Helsinki, Finland, on 6–8 September 2024. Prepare yourself for a warm welcome!

The three days of the meeting will include experts covering topics such as classification and genetics of diabetes, PET imaging and the syndrome of multiple endocrine neoplasia type 1 (MEN1). You can also hear presentations by participants through oral communications and guided poster tours.

We eagerly encourage you to submit your abstracts on original scientific work or patient cases. Abstract submissions open on 1 May 2024 and abstracts will span the following categories:

- Adrenal and Cardiovascular Endocrinology
- Calcium and Bone
- Diabetes, Obesity and Metabolism
- Environment, Society and Governance
- Interdisciplinary Endocrinology
- Pituitary and Neuroendocrinology
- Reproductive Endocrinology
- Thyroid.

An essential part of any EYES Meeting is getting to know fellow clinicians and researchers from across Europe. Two exciting evening programmes will make sure that you will get plenty of opportunity to network.

Registration for the meeting, including accommodation, meals and the social programme, is just €150.

Liisa Kullamaa

on behalf of the Local Organising Committee

Register your interest now 🚺 to stay informed about

- Programme information
- Registration dates
- Abstract submissions



Follow the EYES Annual Meeting...Image: State of the example of t

ESE's digital transformation

After two years of detailed planning and development, ESE's new digital infrastructure has gone live.

A new member management system is now in place, providing improved analysis of ESE's data, so that we can better understand your needs as our members, and support you and your career.

Two new ESE journals!

ESE is delighted to be launching two new journals this year.

Obesity and Endocrinology is an interdisciplinary, open access, online journal for high quality clinical and translational research and reviews on all aspects of obesity. Its content will span the complexity of obesity as an endocrine disease, and obesity's biology, diagnostics, treatment and relationship with other endocrine and metabolic diseases, as well as the interplay between the microbiome and the exposome, and the sociological, political and global implications of this complex area.

Environmental Endocrinology is dedicated to all aspects of environmental impacts on hormone systems in humans and living systems, incorporating the One Health perspective. It, too, is an interdisciplinary, open access, online journal, dedicated to publishing high quality clinical, translational, and basic research. It will welcome submissions from many research disciplines, including epidemiology, climate research, toxicological sciences, endocrinology and developmental biology. You are likely to have also noticed our new website, which launched in December. An integrated learning management system will form the final component, and will be launched soon. These valuable changes provide a solid foundation for our future plans and independence, and support ESE's strategy for 2022–2026.

Help raise hormone awareness

You can help increase public awareness of hormones' vital role in health and disease when European Hormone Day returns on Wednesday 24 April 2024.

To help you spread the word, ESE is providing a public outreach toolkit with social media materials covering endocrine-disrupting chemicals, cancer, obesity and rare endocrine diseases. You can choose whatever themes and activities are most relevant to your community. There will be translations in 13 languages.

We have also updated the *Because Hormones Matter* leaflet and awareness days calendar that we published in 2023.

More information can be found at www.europeanhormoneday.org. We hope you'll join us again to raise awareness of endocrine health #BecauseHormonesMatter.



New Editorin-Chief

We welcome Felix Beuschlein as the new Editor-in-Chief of *European Journal of Endocrinology* from May 2024. Felix is Professor of Internal Medicine/Endocrinology and Director of the Clinic for Endocrinology, Diabetology and Clinical Nutrition at the University Hospital Zurich, Switzerland. He will take the role over from the current Editor, Wiebke Arlt, who became ESE's President-Elect in 2023.





Challenges in the lab

'Challenges for endocrinologists in the hormone laboratory' was the focus of the 7th Early Career Clinical Endocrinologists (ECCE) Meeting, on 19 October 2023 in Antalya, Turkey, during EndoBridge 2023.

This annual event is organised by the ESE Council of Affiliated Societies (ECAS) and was led by Anton Luger, Bulent Yildiz, Djuro Macut and Dimitrios Goulis. A total of 30 early career participants attended from 19 countries. Sabina Baumgartner-Parzer gave the keynote lecture.



Members of the EYES community played an active part, with EYES Committee Co-Chair Walter Vena speaking on 'Supporting early career endocrinologists at the European level', and national perspectives from Riikka Sane ('Greetings from the north: endocrinology training in Finland') and Nazi Tchelidze ('The Georgian Association of Endocrinology and Metabolism as an example of a successful initiative for early career endocrinologists').

The 8th ECCE Meeting will focus on 'Imaging in endocrinology' and will take place during EndoBridge 2024 (www.endobridge.org).

Time to meet the... Brazilian Society of Endocrinology and Metabolism

With over 4000 members from 22 regional offices in Brazil, this society truly represents the breadth of expertise and backgrounds in our field.

Established more than 70 years ago, the Brazilian Society of Endocrinology and Metabolism (Sociedade Brasileira de Endocrinologia e Metabologia, SBEM (2) has become one the five largest endocrine societies in the world, and is a long-standing partner of ESE. Its inclusivity, respect for diversity and commitment to excellence have been instrumental in its success. The Society fosters a vibrant community of endocrinologists who share a passion for the progress of science and improvement in patient care.

The Board of Directors comprises colleagues with a forward-thinking mindset and an unwavering dedication to excellence, such as the current President, Paulo Augusto Carvalho de Miranda, and his predecessor, César Luiz Boguszewski. Among the membership, one can find world-renowned scientists and clinicians who make substantial contributions to the global body of knowledge in endocrinology.

Publishing and education

In its mission to disseminate knowledge and promote the exchange of ideas, SBEM boasts its own journal, *Archives of Endocrinology & Metabolism*, which serves as a vital online, free-to-access platform for the publication of ground-breaking research and clinical insights. The journal not only enhances the visibility of Brazilian endocrinology but also contributes significantly to the international body of scientific literature.

SBEM's commitment to education is exemplary. The Society organises a wide range of courses and conferences, covering various areas of expertise for endocrinologists at different levels of their careers. These events provide a platform for professionals to deepen their knowledge, exchange experience, and forge collaborations. Through such strategic initiatives, SBEM consistently raises the bar for the quality of care provided for endocrine and metabolic disorders, benefiting its members in Brazil as well as expanding its horizons across the globe.



Sociedade Brasileira de Endocrinologia e Metabologia







SBEM President Paulo Augusto Carvalho de Miranda evaluating the posters at CBEM 202

One of SBEM's critical responsibilities is the co-ordination of the board of certification for endocrinologists in Brazil. This crucial role ensures that medical professionals specialising in endocrinology and metabolism meet rigorous standards, maintaining the highest quality of care for patients.

Meetings and collaboration

SBEM usually hosts its annual meeting in a breathtaking location, allowing its members not only to take part in a successful conference but also to bask in the natural beauty of Brazil! This exemplifies SBEM's commitment to creating a holistic experience for the participants. Many international colleagues have also had the privilege of enjoying this uplifting opportunity.

Additionally, numerous Brazilians residing abroad have actively engaged in ESE activities. The formal collaboration between SBEM and ESE, cementing their official partnership, is a source of immense pride and pleasure. In 2024, during the 36th Brazilian Congress of Endocrinology and Metabolism in Recife, we will celebrate 10 consecutive years of SBEM–ESE workshops at our annual meeting. This is a testament to the synergy that can be achieved when two prominent societies join forces to advance the field of endocrinology.

Júnia ROL Schweizer Brazil/Germany ECE 2024

ECE 2024

11–14 May 2024 Stockholm, Sweden

> Reduced registration rates for Early Career Members of ESE

deadline 22 April 2024

EYES in the spotlight at ECE 2024 A great program

Get ready for the ultimate fusion of knowledge and fun at the 2024 EYES Symposium. It'll be stealing the spotlight during ECE 2024, the 26th European Congress of Endocrinology, in the heart of Stockholm!

ECE 2024 isn't just any conference – it's the largest endocrine event in Europe, and is taking place on 11–14 May in the Swedish capital.

During the Congress, the EYES community can look forward to a sensational session for all young investigators who want the lowdown on neuroendocrine tumours. In fact, the 2024 EYES Symposium on 12 May will be your backstage pass to the latest and greatest in neuroendocrine tumour research. There'll be no boring lectures here – we've got top-notch experts centre stage, sharing ground-breaking discoveries, funky therapies, and what's sizzling in the trends department.

But it's not just about the big names; it's about you too. Share your research mojo through cool oral presentations and poster sessions. Let's face it; science should be anything but snoozy. Networking is the name of the game at the 2024 EYES Symposium. But this ain't your grandma's stuffy networking – it's more like a knowledge carnival. Rub shoulders with your scientific heroes, connect with fellow brainiacs, and maybe even strike up a convo with that cool industry leader. Who says science can't be a party?

And, speaking of parties, brace yourself for the EYES social event on 13 May – a headline act at ECE 2024. Picture this: you and your new-found pals, on a stunning terrace against a backdrop of the Stockholm skyline, with the city lights twinkling, the vibe relaxed, and the science chat flowing freely. It's not just about business, it's about building lasting connections and soaking in the charm of Scandinavian nights.

The 2024 EYES Symposium isn't just a sideshow – it'll be centre stage at ECE 2024. So, get set for an unforgettable mix of science, connections, and good times. Because when it comes to neuroendocrine tumours, this is the hottest gig in town!

Walter Vena

Programme Organising Committee, ECE 2024

A great programme – created especially for you!

- \bullet Grow your knowledge through the EYES Symposium at ECE 2024 on Sunday 12 May
- Network with peers at the EYES social event on Monday 13 May
- Discover the latest trends at the New Scientific Approaches sessions
- Hear from leaders in our field at the Award and Plenary Lectures, and the Meet the Expert sessions
- Take part in lively discussions on cutting-edge topics during the debate sessions
- Discover the latest research in the Oral, Rapid and Poster sessions
- Interact with industry in the satellite symposia, mini-satellites and ECE Hub sessions.

For the latest details see www.ese-hormones.org/ece2024