Society for Endocrinology

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THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Close to the bone
HORMONES AND THE HUMAN SKELETON

Special features PAGES 7–14

A word from THE EDITOR...

Welcome to this issue of *The Endocrinologist*, which has the theme of bone–hormone interaction and bone health.

This is the penultimate issue with Craig Doig (Associate Editor) and myself at the helm – and, even if we do say so ourselves, it's a Christmas corker! One of the many highlights is an insight into bone health after bariatric surgery. Preeshila Behary and Alex Comninos discuss the relationship between **the different after-effects of bariatric surgery and their impact on bone function**, as well as the extent of our current understanding. We also bring you an interesting interview with Donna Rowe about **setting up a fracture liaison service**, and its role in clinical management and the patient experience. It's a fascinating read!

There is plenty of Society News for you to dig into. **A revamp of the Society Medals** brings name and category changes, to celebrate a broader range of member achievements. The processes for application and selection for these prestigious awards have been revised. The closing date for applications is fast-approaching, on 12 January 2025, so we encourage you to get nominating eligible potential recipients (perhaps including yourself).

In light of Craig and I stepping down, we are recruiting a replacement Editor at *The Endocrinologist* HQ. Our Editorial Board has recently expanded, and brings together a team of dynamic, engaged and supportive members, who are steered by our Managing Editor, Jane Shepley. This is a good time to join the Board, as the team will make any incoming Editor's job straightforward. We're looking forward to the applications coming through, so **please apply if you are interested**.

Wishing you a restful holiday and successful 2025.

KIM JONAS

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Become a contributor... Contact the Editorial office at **endocrinologist@endocrinology.org**

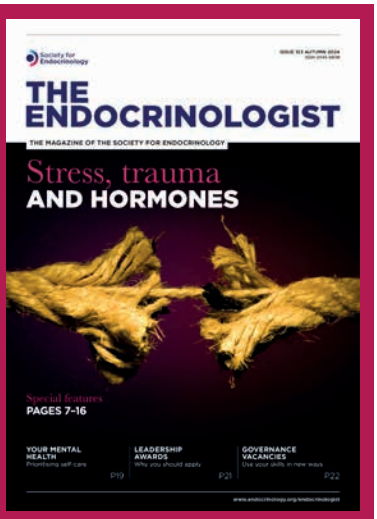
The Society welcomes news items, contributions, article suggestions and letters to the Editor. We would also like to hear your feedback on this issue of the magazine.

Deadline for news items for the SPRING 2025 issue: **13 January 2025**.

Front cover image ©Shutterstock

Season's greetings and a happy new year to all our readers!

COULD YOU BE THE NEXT EDITOR OF THIS MAGAZINE?



As a reader of *The Endocrinologist*, you know the importance of our member magazine for informing and connecting the endocrine community. Now you have the chance to guide the future of this publication.

We're seeking a visionary Editor to take the helm from March 2025. In this two-year role, you'll lead the Editorial Board, commission compelling articles and ensure that our magazine reflects the Society's strategy and diverse membership. This is a unique opportunity to refine your editorial and leadership skills, work with a supportive team of fellow members and shape the content for this key member resource.

Apply now and help us to showcase the best of endocrinology.

DISCOVER YOUR LEADERSHIP POTENTIAL

Applications are now open for the Society's Leadership and Development Awards Programme, which recognises and nurtures emerging talent in our field.

Over three years, participants will benefit from exclusive mentoring and networking with senior endocrine professionals, formal leadership training, and the chance to gain hands-on experience in the Society's governance.

This programme equips you with the skills and connections to step into future leadership roles in our community.

Apply by 30 April 2025

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ASPIRING RESEARCH LEADERS
Harrogate, UK

10–12 March 2025
SfE BES 2025
Harrogate, UK

20 June 2025
WOMEN'S HEALTH SUMMIT 2025
Birmingham, UK

Date: TBC
CLINICAL UPDATE 2025
Venue: TBC

Date: TBC
ENDOCRINE NURSE UPDATE 2025
Venue: TBC

www.endocrinology.org/events for full details

INSPIRE SCHOOL STUDENTS AT SfE BES 2025

Are you attending SfE BES 2025 and interested in public engagement? Join us on the final day of the conference for an exciting outreach event designed to inspire local secondary school students to explore the world of endocrinology.

You can participate in interactive table-top activities alongside fellow members, or contribute your career story to a workshop.

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Email **engagement@endocrinology.org** to get involved.

BECOME A CONTENT EDITOR FOR YOU AND YOUR HORMONES

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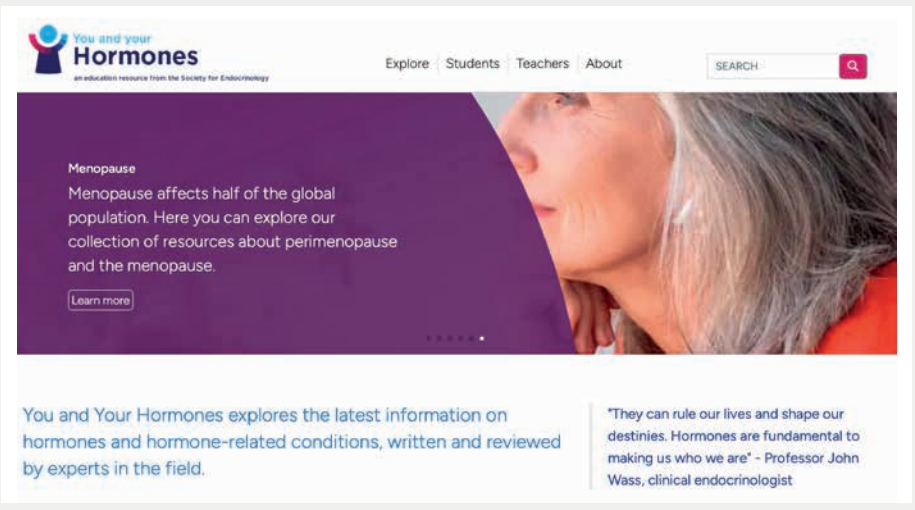


HOT TOPICS

Hot Topics is written by Victoria Chatzimavridou-Grigoriadou, Sophie Clarke, Craig Doig, Edouard Mills, Gareth Nye, Bhavna Sharma and Vincent Simpson

SOCIETY FOR ENDOCRINOLOGY OFFICIAL JOURNALS

Society members have free access to the current content of *Journal of Endocrinology*, *Journal of Molecular Endocrinology*, *Endocrine-Related Cancer* and *Clinical Endocrinology* via the **Members' Area of the Society website**. *Endocrine Connections*, *Endocrinology, Diabetes & Metabolism Case Reports* and *Endocrine Oncology* are open access and free to all. Publishing in *Endocrine Oncology* is currently free.

JOURNAL OF ENDOCRINOLOGY

Sex-specific islet hormone release by GHSR1a antagonist LEAP2

Regulation of energy balance is fundamental to homeostasis, and probably has sex-specific attributes. LEAP2 is a liver-derived ghrelin receptor (GHSR1a) antagonist that counteracts ghrelin's effects on appetite, but its influence on pancreatic islet hormone release is less understood.

Hewawasam *et al.* examined how acyl-ghrelin (AG) and LEAP2 regulate hormone secretion using isolated pancreatic islets from male and female mice. Using radioimmunoassay and quantitative PCR, they found that LEAP2 enhanced insulin secretion in males but not in females. Neither AG nor LEAP2 significantly affected glucagon release. Analysis showed no sex-based differences in *Ghsr1a*, *Ghrelin*, *Leap2*, *Mrap2*, *Mboat4* or *Sstr3* mRNA expression. However, MK4256, a somatostatin receptor antagonist, enhanced glucose-stimulated insulin secretion in males. In male islets without 17β-oestradiol (E2), AG reduced insulin secretion, an effect partially reversed by LEAP2. E2 pre-treatment abolished these responses. LEAP2 also suppressed AG-stimulated somatostatin release in untreated, but not in E2-treated, islets.

This study reveals that LEAP2 and AG modulate insulin and somatostatin release in a sex-dependent manner, with E2 influencing male responses. This suggests that somatostatin release modulation is critical to the role of GHSR1a in islet function and glucose regulation.

Read the full article in *Journal of Endocrinology* **263** e240135
https://doi.org/10.1530/JOE-24-0135

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Roles for RAMPs in obesity and diabetes

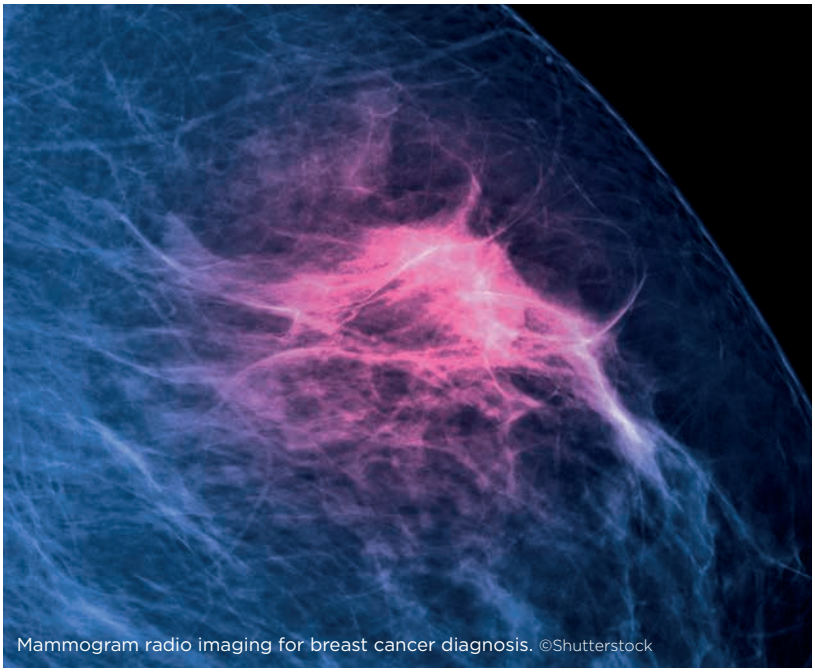
Receptor activity-modifying proteins (RAMPs) are involved in changing the activity of G protein-coupled receptors. A range of important physiological functions have been recognised, particularly around food intake and glucose homeostasis. Given the rise of obesity and related conditions, understanding the associated fundamental biology is of huge importance.

This review article by Malcharek *et al.* highlights this set of proteins and explains their potential to be targeted as novel therapeutics. The authors take readers through the importance and prevalence of G protein-coupled receptors, which constitute the largest receptor family in our body, before moving on to more novel findings regarding the role of RAMPs in modulating their activity.

The section on methods for studying these interactions is of particular note, giving readers all the tools and background to push forward with this methodology in their own labs. The authors' way of presenting novel approaches to the pathophysiology of both obesity and type 2 diabetes is one of the real benefits of this review, hopefully opening the door for new therapies to be developed.

Read the full article in *Journal of Molecular Endocrinology* **73** e240056
https://doi.org/10.1530/JME-24-0056

ENDOCRINE-RELATED CANCER


Mammogram radio imaging for breast cancer diagnosis. ©Shutterstock

Epigenetic insights: how diabetes drives breast cancer metastasis

Diabetes increases the risk of breast cancer, but the mechanisms behind this heightened risk, especially for metastasis, are still being uncovered.

In this recent study, Zhou *et al.* investigated the role of advanced glycation end products (AGEs), which are elevated in diabetic patients, in promoting breast cancer spread. Using a combination of *in vitro* cell culture studies and *in vivo* mouse models, the researchers demonstrated that AGEs interact with their receptor (RAGE) on breast cancer cells, leading to the demethylation of the *MMP-9* gene promoter, which is critical for tumour invasion and metastasis. Through detailed molecular experiments, they identified that this process is mediated by the GADD45α protein, which facilitates DNA demethylation through a base excision repair pathway.

This study underscores a novel epigenetic mechanism linking diabetes to cancer metastasis, and also shows how metabolic changes in diabetes can drive more aggressive cancer behaviour. It offers diabetologists valuable insights into the intersection of diabetes and cancer, and highlights how targeting the AGE–RAGE axis could be a new therapeutic strategy for treating cancer in patients with diabetes.

Read the full article in *Endocrine-Related Cancer* **31** e230330
https://doi.org/10.1530/ERC-23-0330

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CLINICAL ENDOCRINOLOGY

Untimed spot urine sampling in diagnosis of PHPT

Primary hyperparathyroidism (PHPT) is a common endocrinopathy referred to the endocrinology outpatient clinic. Distinguishing between PHPT and familial hypocalciuric hypercalcaemia (FHH) using a urinary calcium/creatinine clearance ratio (CCCR) is important, as FHH does not warrant surgical intervention. A urinary CCCR<0.01 favours FHH.

In this study, Sharma *et al.* describe 88 patients who were referred over a 4-year period with parathyroid hormone (PTH)-dependent hypercalcaemia. In total, 81 of the 88 patients completed diagnostic work-up, with 86% diagnosed with PHPT.

In the series, 66 out of 70 patients with PHPT had untimed spot urine sampling. Of these, 56/66 had a positive urinary CCCR>0.01. Of the patients with a urinary CCCR<0.01, 7/10 were found to have a ratio >0.01 on subsequent 24-hour urine sampling.

Based on their findings, the authors demonstrate the clinical utility of untimed spot urine sampling in making a diagnosis of PHPT in 84% of patients in their series. This provides a quicker, more convenient and patient-friendly investigation in an outpatient setting. The authors also provide a proposed diagnostic algorithm for PTH-dependent hypercalcaemia, which includes untimed spot urine CCCR sampling.

Read the full article in *Clinical Endocrinology* 2024 **101** 203–205 https://doi.org/10.1111/cen.15116

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Unexpected hypocalcaemia: a rare presentation of breast cancer relapse

Hypocalcaemia affects around 10% of individuals with advanced cancer, usually caused by malabsorption, metastatic disease or treatment with bone anti-resorptive drugs. The prognosis is usually better than hypercalcaemia.

Darawshi *et al.* present the case of a 45-year-old woman with previously treated (left mastectomy, adjuvant chemotherapy and tamoxifen) metastatic breast cancer (T4b N0 M0 grade 2, oestrogen receptor-positive, progesterone receptor-negative and Ki-67=2%), who developed treatment-resistant hypocalcaemia. She had profound hypocalcaemia on admission (1.52mmol/l) with non-elevated parathyroid hormone (3.8pmol/l, reference range 1.6–6.8) and low 25-hydroxyvitamin D3 (27nmol/l). She was treated with i.v. calcium gluconate 10% and oral calcium carbonate (total average daily dose 11.2g). Her calcium remained low until she was treated with chlorambucil and leuprolide for a recurrence of her breast cancer confirmed on bone biopsy.

The case highlights the difficulties in managing individuals with calcium derangement in the context of cancer. However, it highlights that severe hypocalcaemia can sometimes be a presenting issue for metastatic recurrence.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* 2022 20-0222 https://doi.org/10.1530/EDM-20-0222

ENDOCRINE CONNECTIONS

AMH in inherited bone marrow failure

This article by Stratton and colleagues investigates low levels of anti-Müllerian hormone (AMH) in patients with an inherited bone marrow failure syndrome, such as Fanconi anaemia, dyskeratosis congenita-related telomere biology disorders or Diamond–Blackfan anaemia.

The authors highlight that, in males, AMH may be a direct marker of Sertoli cell function and an indirect marker of spermatogenesis. Their findings indicate a significant defect in the production of AMH in postpubertal males in the syndromes studied, with widespread implications for fertility potential. They call for action in further larger studies.

Read the full article in *Endocrine Connections* **13** e230510 https://doi.org/10.1530/EC-23-0510

ENDOCRINE HIGHLIGHTS

A summary of papers from around the endocrine community that have got you talking.

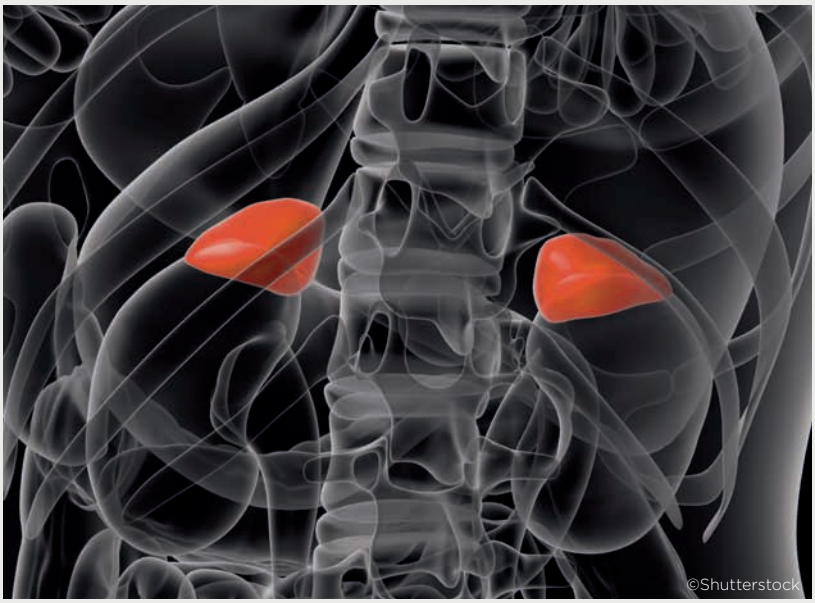
Phase 3 trial of crinecerfont in adult CAH

Congenital adrenal hyperplasia (CAH) requires administration of supraphysiologial doses of steroids to reduce adrenal androgen production, increasing the likelihood of glucocorticoid-related complications. Treatment strategies that result in a reduction in steroid dose therefore have significant potential. Crinecerfont is an oral antagonist for the corticotrophin-releasing factor 1 receptor and has been demonstrated to reduce androstenedione production.

Auchus *et al.* report this phase 3 trial, where 182 patients with classical CAH were randomised to receive either crinecerfont or placebo for 24 weeks. Glucocorticoid treatment was reduced and optimised alongside crinecerfont, to ensure androstenedione was either ≤120% of the baseline value or within reference range. Co-administration of crinecerfont to patients with CAH resulted in a greater decrease in glucocorticoid dose compared with placebo, along with reduction in androstenedione.

Given that CAH requires lifelong treatment with glucocorticoids, crinecerfont offers an exciting potential therapeutic strategy to reduce the burden of glucocorticoid-related complications.

Read the full article in *New England Journal of Medicine* **391** 504–514 https://doi.org/10.1056/NEJMoa2404656



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BONE HEALTH AND BARIATRIC SURGERY: SHRINKING BONES?

WRITTEN BY PREESHILA BEHARY AND ALEX COMNINOS

Weight loss through calorie restriction, anti-obesity medications or bariatric surgery (BS) drives multiple health benefits. However, it has long been known that accelerated weight loss is linked to bone loss and resultant fractures. In the 'Look AHEAD' study, participants randomised to intensive lifestyle intervention experienced an average weight loss of 6% over a median time of 9.6 years. This degree of weight loss was associated with 39% increased risk of fragility fractures spanning 11 years, compared with a control group who only lost 3.9%.[1]

The Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are the most common procedures in the UK and result in superior weight loss compared with lifestyle intervention and/or anti-obesity medications, typically between 20 and 35%. It is therefore not surprising that BS appears to have a substantial negative impact on bone health.

CURRENT UNDERSTANDING OF THE IMPACT OF BS ON BONE

In a study where participants were followed for 5 years after RYGB, there was a significant fall in bone mineral density (BMD) at both the spine (>5%) and the hip (>10%), with the greatest loss occurring within 2 years of surgery.[2] However, of particular concern was the ongoing progressive fall in BMD at these sites beyond 2 years, despite stabilisation of weight.

Markers of bone resorption (serum levels of CTX (C-terminal telopeptide of type 1 collagen)) are increased within days after BS; they peak at around 1–2 years, with increases of between 50 and 300%, and remain elevated years after surgery. Bone formation markers (P1NP (procollagen type 1 N-terminal propeptide)) are also elevated, but to a lesser extent than CTX, resulting in net bone loss.

Furthermore, measures of bone microarchitecture (such as cortical porosity), which are important additional determinants of bone strength, are negatively impacted after BS.[2]

Collectively these detrimental impacts result in up to a twofold increase in fracture risk.[3]

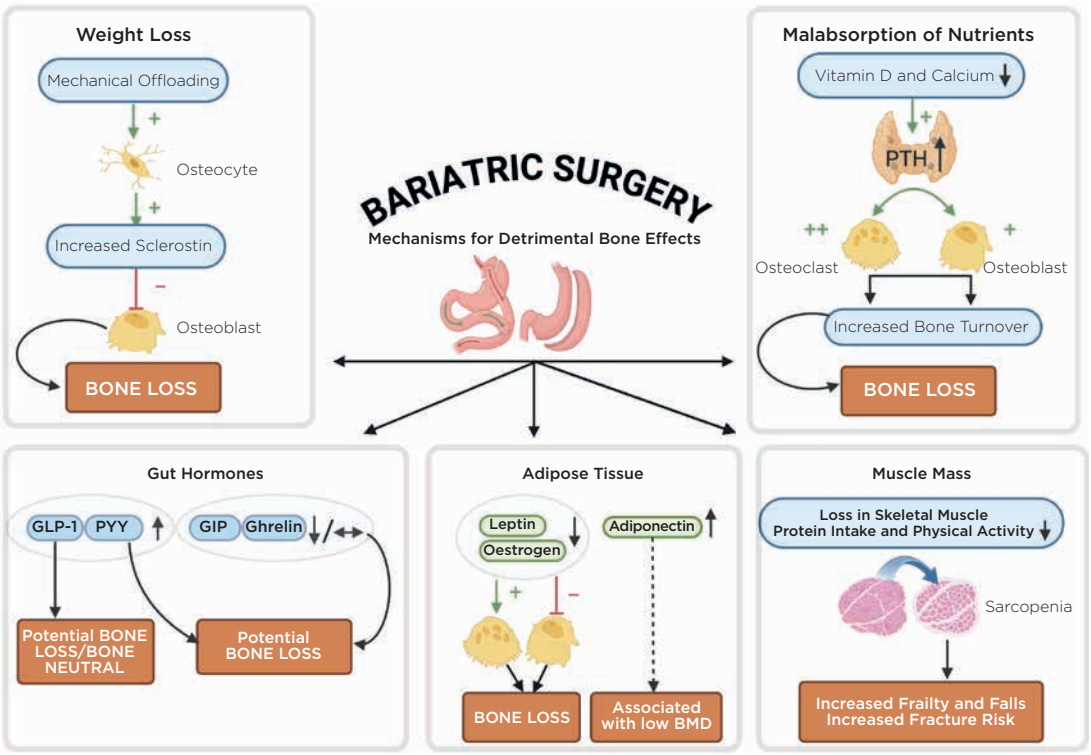
NOT ALL THE BONE EFFECTS OF BS ARE EQUAL

Current data suggest that different types of BS impact bone health to varying degrees. Although SG leads to significant increases in CTX and P1NP, coupled with clinically significant drops in BMD, these changes are greater after RYGB.[4]

Consistent with this, an increased risk of major osteoporotic fractures (hazard ratio 1.7 over controls with obesity) has been observed after RYGB, but not after SG or gastric banding (GB), in a large, population-based, French study of over 80,000 participants, followed over 5 years.[3]

The jury is still out on whether the newer and most performed form of BS in the UK – the SG – leads to increased fracture risk. What is becoming clear is that fracture risk is increased following malabsorptive procedures, and this risk seems to emerge as early as 2 years postoperatively.[5]

Figure. Possible theories to explain bone loss after bariatric surgery. PTH, parathyroid surgery; +, stimulate; –, inhibit. Created using BioRender



POSSIBLE THEORIES TO EXPLAIN BONE LOSS AFTER BS

The Figure illustrates potential mechanisms for detrimental bone effects.

The notion of mechanical 'offloading' of the skeleton, with weight loss resulting in bone loss, is a popular concept. Astronauts, for example, can lose up to 2% in BMD per month while in space.[6] A positive correlation between weight loss and bone loss was observed in some but not all studies. Interestingly bone loss at the hip tends to be more extensive than at the spine. This is probably due to the weight-bearing hip bone being more susceptible to the detrimental effects of offloading. However, gradual bone loss continues beyond 2 years, despite

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stabilisation in weight loss or even a slight weight regain in some. This infers that other mechanisms are at play.

RYGB is associated with malabsorption of nutrients that are key for bone health. Vitamin D levels are generally suboptimal in members of the population who have obesity, and vitamin D deficiency/insufficiency can be further exacerbated after surgery due to malabsorption. In addition, calcium absorption is impaired after both SG and RYGB.[7] In the latter, this relates to the bypassed proximal gut and reduced gastric acid production. The ensuing secondary hyperparathyroidism results in increased bone turnover, primarily bone resorption. Indeed, secondary hyperparathyroidism is highly prevalent, affecting approximately 50% of the population that has undergone BS at ≥5 years.[8]

The direct impact of gut hormones on bone is also important and an emerging area of study. Post-prandial levels of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) are substantially elevated after RYGB and SG, but not after GB. PYY has been shown to have negative effects on bone in rodent studies, primarily through suppression of osteoblastic activity.[9]

The impact of GLP-1 on human bone is less clear, especially when given at supraphysiological levels. A neutral effect on bone has been suggested but, worryingly, two recent trials reported reductions in hip/spine BMD at 1 year in participants with obesity but not diabetes, who were treated with semaglutide and liraglutide.[10,11] The post-bariatric hormonal milieu is complex, with other notable changes in ghrelin, glucose-dependent insulinotropic polypeptide (GIP), adiponectin and leptin, all capable of exerting distinct effects on bone.

WHAT CAN WE DO?

Bariatric surgery is increasingly being recognised as a risk factor for bone health. The current British Obesity and Metabolic Surgery Society guidelines advocate for higher daily intakes of vitamin D (2000–4000IU with target levels >75nmol/l) and calcium (1200–1500mg).[12]

Other strategies include incorporating regular physical activity, especially strength training, while ensuring adequate intake of protein. However, these strategies can attenuate but not fully prevent bone and muscle loss after BS.[13]

What is less clear is who should be screened for low BMD prior to BS. Given the potential detrimental impacts on bone, it would be advisable for patients to have a fracture risk assessment (e.g. using FRAX®) before BS. Those identified to be at high fracture risk should undergo dual energy X-ray absorptiometry, with consideration of bone-specific (osteoporosis) therapies and close BMD monitoring after surgery.

It should be noted that there are no current data on the efficacy of standard bone-specific agents following BS, although a couple of studies are in progress (NCT04087096, NCT04742010). Parenteral agents (zoledronate, denosumab) are preferred treatment options after BS, as oral bisphosphonates are associated with increased risk of acid reflux and anastomotic ulceration. However, low vitamin D levels and hypocalcaemia are not uncommon and pose a major challenge for the safe administration of zoledronate or denosumab.

Those at a very high fracture risk or with a history of fragility fractures should ideally be managed in a specialised endocrine bone clinic that has expertise in this area.

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BONE HEALTH IN DIABETES: THE HIDDEN RISK OF FRAGILITY FRACTURES

WRITTEN BY TATIANE VILACA AND RICHARD EASTELL

The skeleton is not traditionally considered a common site for diabetes complications, yet people with diabetes – both type 1 (T1D) and type 2 (T2D) – face a significantly higher risk of fragility fractures. The increase in fracture risk should be addressed along with the other complications of diabetes.

INCREASED FRACTURE RISK IN DIABETES

The risk of fractures is notably higher in both forms of diabetes, although the extent differs between T1D and T2D. For instance, individuals with T1D have a fivefold increase in the risk of hip fractures compared to people without diabetes. In T2D, the risk is around 30% higher. Similarly, the risk of non-vertebral fractures is doubled in T1D and 20% higher in T2D.[1]

In T2D, the risk is even more pronounced for those who have had diabetes for a more extended period or who are using insulin.[1] However, insulin itself is not the culprit behind the increased fracture risk, as it is anabolic to bone, promoting bone formation. Instead, the heightened risk reflects the more severe nature of diabetes in these individuals.

BONE MINERAL DENSITY AND THE DIABETES PUZZLE

Bone mineral density (BMD) is a critical measure of bone strength and is commonly used to predict fracture risk. Interestingly, studies show that people with T1D often have slightly lower BMD than expected, but this reduction doesn't fully explain the increased risk of fractures.[2] This suggests that other factors are at play in increasing the risk of fractures in T1D.

The situation in T2D is even more intriguing. On average, individuals with T2D have a higher BMD than people without diabetes. Yet, despite this apparent advantage in bone density, the fracture risk is still elevated. It seems that BMD does not fully capture the effects of diabetes on bone health.[2] However, bone density still predicts fractures in this population, as a relationship between fracture risk and BMD is observed. People with T2D have the same risk of fractures as people without diabetes, with a T-score (a measurement of BMD) 0.5 points lower.[3] For example, a woman with diabetes and a T-score of −2.0 has the same risk of fractures as a woman without diabetes with a T-score of −2.5. This indicates that diabetes affects bone in ways beyond just density.

THE COMPLEX FEATURES ASSOCIATED WITH FRACTURE RISK IN DIABETES

The elevated fracture risk in diabetes is multifactorial, involving both skeletal and extra-skeletal factors.

Bone quality

Changes in bone microarchitecture (how bone tissue is organised on a microscopic level) have been observed in T1D and T2D.[4,5] Hyperglycaemia promotes the accumulation of advanced glycation end products (AGEs), proteins or lipids that become glycated due to high blood sugar. Haemoglobin A1c, which is used to diagnose and monitor diabetes, is an example of an AGE. The process also affects bone collagen, and evidence suggests this could affect the protein's properties, resulting in stiffer, more brittle bones that are prone to fractures.[6]

Fall risk

People with diabetes also face a higher risk of falls, which contributes to the fracture risk. Factors like poor balance, neuropathy (nerve damage) and vision problems are common in diabetes and increase the likelihood of falls. Episodes of hypoglycaemia, which can cause dizziness and confusion, also contribute to falls.[6]

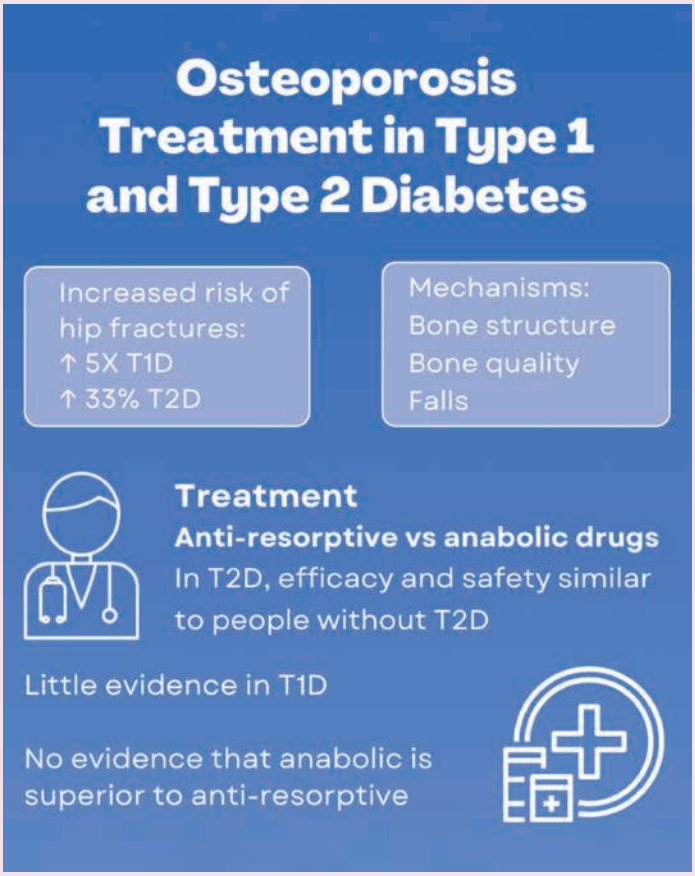

Figure. The increased risk of fragility fractures in both T1D and T2D highlights the need for greater attention to bone health. Reproduced under **CC BY 4.0 licence** from **Vilaca T & Eastell R 2023**.[10] ©2023 The Authors

Medications

Some medications used to treat diabetes can have negative effects on bone health. For example, thiazolidinediones (glitazones) are known to increase fracture risk. Some studies suggested that SGLT2 inhibitors lead to an increased risk of fractures, but this was not observed in all clinical trials.[6]

THE ROLE OF BONE TURNOVER

Bone turnover, the continuous process of bone resorption (breaking down) and formation, is essential for maintaining bone strength. In diabetes, most studies suggest that bone turnover decreases, as indicated by lower levels of bone turnover markers compared with people without diabetes.[7]

MANAGING BONE HEALTH IN DIABETES

Given the unique challenges diabetes poses to bone health, a proactive approach to managing fracture risk is essential.

Importance of glycaemic control

First and foremost, maintaining appropriate glycaemic control is a crucial aspect of managing bone health in diabetes. Good glycaemic control reduces the risk of hypoglycaemic episodes, and the development of diabetic complications, which in turn decreases the likelihood of falls. Additionally, better blood sugar control helps limit the formation of AGEs, thereby preserving bone quality. Over time, these efforts can reduce fracture risk and improve overall bone health.

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Lifestyle interventions for bone health

Despite the presence of diabetes, basic bone health strategies remain vital:

- **Calcium and vitamin D:** Ensuring adequate intake of calcium and vitamin D is fundamental for maintaining strong bones.
- **Exercise:** Weight-bearing exercises, such as walking or resistance training, help build and maintain bone density.
- **Avoiding smoking and excessive alcohol:** Smoking and heavy alcohol consumption are harmful to bone health and should be avoided.

OSTEOPOROSIS TREATMENT IN DIABETES

Understanding that individuals with diabetes tend to suffer fractures at a higher T-score than those without the disease is key. As a result, osteoporosis treatment should be considered at a higher threshold: specifically, when the T-score reaches −2.0, which is less severe than the typical cutoff of −2.5 for people without diabetes.[8]

Current evidence suggests that osteoporosis treatments, such as bisphosphonates and anabolic therapies, are effective for people with T2D.[9] Less evidence is available in T1D, but osteoporosis medications also seem efficacious and safe for these individuals. There is no clear indication that one medication or class of drugs is superior to another in this population.[10]

CONCLUSION: PROACTIVE BONE HEALTH IN DIABETES

Although the skeleton is not typically the first area of concern in diabetes management, the increased risk of fragility fractures in both T1D and T2D highlights the need for greater attention to bone health.

Effective glycaemic control, lifestyle interventions, early screening and appropriate treatment thresholds are essential tools in reducing the risk of fractures and preserving bone strength in people with diabetes. By addressing these issues head-on, we can help ensure that patients with diabetes won't face fragility fractures as an extra complication of this disease.

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THE IMPACT OF EXERCISE ON BONE HEALTH

WRITTEN BY IAN VARLEY AND MARK HUTSON

Adverse bone health negatively impacts quality of life and healthcare systems worldwide. Millions of people, particularly the elderly and postmenopausal women, suffer from osteoporotic fractures each year, costing healthcare systems $17.9 billion in the USA and £4 billion in the UK.[1]

However, poor bone health is not exclusive to older populations. Bone mineral density (BMD) contributes to bone strength and low BMD has also been observed in younger individuals, especially endurance athletes, with studies reporting its prevalence in adolescent female runners[2] and cyclists.[3] Sub-optimal accrual of bone mineral during early life increases the risk of bone injuries and osteoporosis during adulthood, highlighting the need for preventive measures.

WEIGHT-BEARING EXERCISE AND ENERGY DEFICIT

Positive effects of habitual weight-bearing exercise on bone health are well established. Longitudinal intervention research has demonstrated the benefits of weight-bearing exercise on BMD and bone structure.[4] The anabolic effects of exercise on bone are evidenced in racquet sports, where the dominant arm has been shown to have 7–11% greater cortical bone content compared with the non-dominant 'control' arm.[5] This may seem paradoxical, given the prevalence of low BMD in athletes from certain sports. However, low BMD is most common in athletes who participate in non-weight-bearing sports,[6] where the loading stresses applied to bone tissue are insufficient to stimulate bone adaptation.

Additionally, athletes may be in a prolonged state of energy deficit, a condition known to negatively affect bone health,[7] and this should be avoided for those looking to optimise bone health. It is important to note that prolonged states of energy deficiency (and associated key nutrient deficiencies) are more likely in sports which demand high energy expenditures and often promote restrictive energy intakes, such as distance

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running and cycling, possibly creating the 'perfect storm' for suboptimal bone health.

WHAT IS THE BEST EXERCISE FOR BONE?

The optimal mode of exercise for enhancing bone health remains unclear. Methodological differences in populations (bone responds differently in the young versus the old), exercise types and duration, and the magnitude of bone stress make it difficult to compare studies and establish a hierarchy of exercises that benefit bone health.

Nevertheless, it has been shown that sports involving high load magnitudes, a high rate of load application (i.e. load rate) and irregular movement patterns consistently produce greater osteogenic effects than those involving lower magnitudes and impacts and more repetitive movement patterns (e.g. team sports such as football versus running or cycling).[6]

Adult males who regularly participate in football increased cortical BMD, cross-sectional area, circumference and tibial thickness compared with age-matched participants engaged in regular resistance training.[6] The anabolic bone response to football is probably due to high load magnitudes, rates, frequencies and multidirectional movements required during football training and match play. Additionally, nuanced differences in how an activity is performed can affect the extent of bone adaptation. For example, footballers who performed a greater number of decelerations during training and match play showed a greater increase in tibial strength compared with those who performed fewer decelerations.[8]

'It has been shown that sports involving high load magnitudes, a high rate of load application and irregular movement patterns consistently produce greater osteogenic effects than those involving lower magnitudes and impacts and more repetitive movement patterns.'

Interestingly, the bone anabolic response seems to plateau after a relatively low number of loading repetitions,[9] although the exact number will depend on a complex interplay between several factors, including load magnitude, rate, frequency and direction. Once plateaued, the mechanosensitivity of bone becomes fully restored after several hours of rest,[10] such that the time between exercise bouts also seems to be a determinant of the bone response to exercise. A recent *in vitro* study has shown that greater bone formation occurs in osteoblast cells subjected to intermittent loading bouts compared with continuous cyclic loading.[11] Furthermore, a larger bone adaptive response has been found when 14 seconds of rest are taken between each application of load, compared with shorter rest periods.[9]

Taken together, these data suggest that short bouts of high magnitude and high impact loads, with appropriate rest between each load and each exercise bout, may be most beneficial for optimising positive bone adaptation.

AN AREA FOR EXPERIMENTAL IMPROVEMENT

A limitation of current research assessing the optimal exercise for bone adaptation is the lack of quantification of exercise load. While studies have shown that various forms of exercise (jumping, hopping, football, etc.) can increase bone size and structure, few studies have accurately quantified the loading stress that has been applied to cause the response. Instead, researchers often rely on imprecise metrics, such as the number of jumps, time spent partaking in an activity, or retrospective recall, to quantify load. Although using these metrics can offer information about the characteristics of exercise (e.g. the amount of impact exercise, the multi-directional nature of the activity, and sometimes even the ground reaction forces), they do not provide objective data on factors such as magnitude, rate, frequency, direction and distribution of loading stress experienced at different sites on the bones of interest, all of which are influential in bone adaptation. If bone loading data could be more accurately quantified through technologies like force sensors, the prescription of osteogenic exercise could be improved.

'More precise measurement of exercise load is needed to fully optimise osteogenic exercise prescriptions.'

IN SUMMARY

Weight-bearing exercise is known to improve bone health, but the optimal type of exercise for this purpose remains unclear due to methodological variations. Sports with high impact and irregular movements, like football, produce better osteogenic effects compared with low impact, repetitive activities. Deficiencies in energy or key nutrients may interfere with the benefits of exercise on bone health. Additionally, factors such as rest periods and specific movement patterns, like decelerations, can influence the degree of bone adaptation. However, more precise measurement of exercise load is needed to fully optimise osteogenic exercise prescriptions.

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Society for Endocrinology

SfE BES HARROGATE 2025

SfE BES IS BACK!

After taking a break in 2024, the Society for Endocrinology BES conference will return to Harrogate from 10 to 12 March 2025.

Join the largest gathering of endocrine professionals in the UK, as we learn from each other, share our passion for endocrinology and collectively work towards advancing research and patient care in our field.

SAVE ON YOUR REGISTRATION

Early bird deadline Wednesday 18 December 2024 (11:59pm GMT)

An interview with…
DONNA ROWE
SETTING UP A FRACTURE LIAISON SERVICE

Donna Rowe is a clinical nurse specialist at Imperial College Healthcare NHS Trust in London. She was bought into post in 2019 to establish the Imperial Trust Fracture Liaison Service (FLS). This remote-working 'helicopter' nurse-led service has achieved the best overall statistics on consecutive national Royal College of Physician FLS Database audits over the past two years. We spoke to her about establishing this service, her day-to-day work and her amazing career trajectory.

Please tell us about the Fracture Liaison Service
The service covers all Imperial College Healthcare NHS Trust sites, to identify all patients above 50 years of age presenting with a potential fragility fracture at any of the entry points to secondary care. We also monitor the orthopaedic wards daily for patients who may have transferred from another Trust, for example. We identify patients for assessment against FLS criteria (mechanism of injury, age, type of fracture, etc.) to determine whether they are appropriate for our service and a bone health review.

Is it challenging to work with both outpatients and inpatients?
It could, without doubt, be perceived as challenging, given the actual numbers involved! The majority of patient identification utilises electronic systems to streamline our service, improve its efficiency and maximise our reach. One example is our daily review of fracture admissions/fracture clinic lists/radiology and all incoming referrals. Our radiology improvement project, which began in 2022, ensures we include incidentally reported vertebral fractures; this is crucial for an effective FLS proactively delivering a continuing reduction in re-fractures – the 'fragility fracture trajectory' – including major osteoporotic fractures.

Incidentally reported vertebral fractures are significant, and require assessment/treatment to positively impact future fracture rates, including hip fracture. To date, our vertebral fracture detection rates are consistently positive – we currently achieve 204% of the anticipated figure for our Trust.

What exactly is the cycle that the patient goes through?
We initially review the fracture mechanism of injury. The FLS excludes various fracture sites, including patella/cranium/cervical spine/metatarsals/metacarpals. We ensure the patient is within our North West London catchment and review accessible GP notes/documented medications/clinical history (specifically whether the patient is known to another specialism or Trust, for example). We look at radiology, particularly in the case of vertebral fractures, to assess the fracture against the Genant grading scale. That is pretty much our starting point for an early FLS review post-fracture.

If accepted, patients are then contacted and the review process begins, if they consent. A letter to the patient will include an appointment and, most importantly, information in relation to our service, and osteoporosis.

It's really vital for our patients to understand why we have been in touch and what we may propose following a consultation (blood tests, DEXA (dual energy X-ray absorptiometry), etc.). This transparency is important as patients will be receiving a letter from a service that they have probably not heard of. I facilitate our patients' understanding of osteoporosis as a frequently occurring problem that is not always well identified. Our literature supports our patients' understanding of FLS involvement and the process of a bone health review with our service.

During our planned telephone consultation, we collate both modifiable and unmodifiable risk factors to bone health, including falls risks, and seek consent to initiate further elements of the FLS review. This includes arranging DEXA, requesting thoracolumbar imaging (when indicated – i.e. if a loss of height >2 inches in 12 months is reported, or if the patient describes a kyphotic posture etc.), bloods, community specialist input re falls/mobility, etc. To ensure consistency, we utilise a template which has continually evolved to ensure we capture modifiable and unmodifiable risk factors.

Following all investigations, we use the results and the risk assessment responses to determine both treatment and onward management in the community. At this point, we can also refer to community services, or signpost other services to the patient (such as smoking cessation or alcohol services). We aim to deliver a further positive impact on patients' bone health in the longer term and engage the patient in improving their bone health.

FLS patients are retained in our service for 12 months post-fracture. This is really important in maximising patient concordance with the treatment recommendations. Literature shows average concordance at 12 months following treatment initiation is about 14%. Throughout the identification, assessment and treatment initiation phases, we maintain personalised contact with our patients. They have a named nurse, and we use regular touch points, around every 3 months or so, and at the 12-month point, to make sure the treatment plan is in place. We liaise with primary care providers if patients are experiencing issues with their medication during that time.

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We also follow up patients who've had either inpatient or outpatient parenteral treatment (zoledronic acid). At 12 months, patients' GPs are contacted by letter, and recommended to consider oral bisphosphonate or referral to the Metabolic Bone Clinic for a consultant review regarding further infusion or other treatment options, if oral medication is contraindicated.

'It's really vital for our patients to understand why we have been in touch and what we may propose following a consultation.'

You're achieving a lot in that time: how big is the team for this service?
We are a tiny team of two clinical nurse specialists, with access to a consultant endocrinologist, Professor Alex Comninos, as clinical lead. The multidisciplinary team (MDT) meeting is every 2–3 weeks. We present any patients outside our clinical remit, who may require a clinic appointment to see a consultant, for instance if other treatment options may be required (such as teriparatide, romozosumab). We collectively present around eight patients. The vast majority of our remaining FLS patients are not discussed, and will remain within the nurse-led service and not require clinic review.


©Rawpixel

Do you have any memorable patient experiences?
Oh gosh, so many. One that stands out for me is a chap late last year. I identified the fracture but he wouldn't have been a classic FLS patient. because of the fracture site (radial head). However, he was in his early 50s and without any particular medical history. I'm really glad I identified the patient and that he consented to my review. He had an underlying myeloma and was fast-tracked to haematology, via the MDT. That really was a memorable moment for me.

What would your top tips be for a Trust wanting to set up this service?
As you may know, there is a recently publicised Government commitment for an FLS in all Trusts in England by 2030. (At the moment there is an FLS in about 50%.) With my previous experience at the Royal Osteoporosis Society as a Service Delivery Lead, my general top tips would be to ensure you have the right key stakeholders, the up-to-date data detailing fracture incidence, your Trust's national Hip Fracture Database figures for the preceding 5 years, say, and a well-written, cohesive business case (presented by a credible, relevant clinical lead) to effectively promote the need for the service.

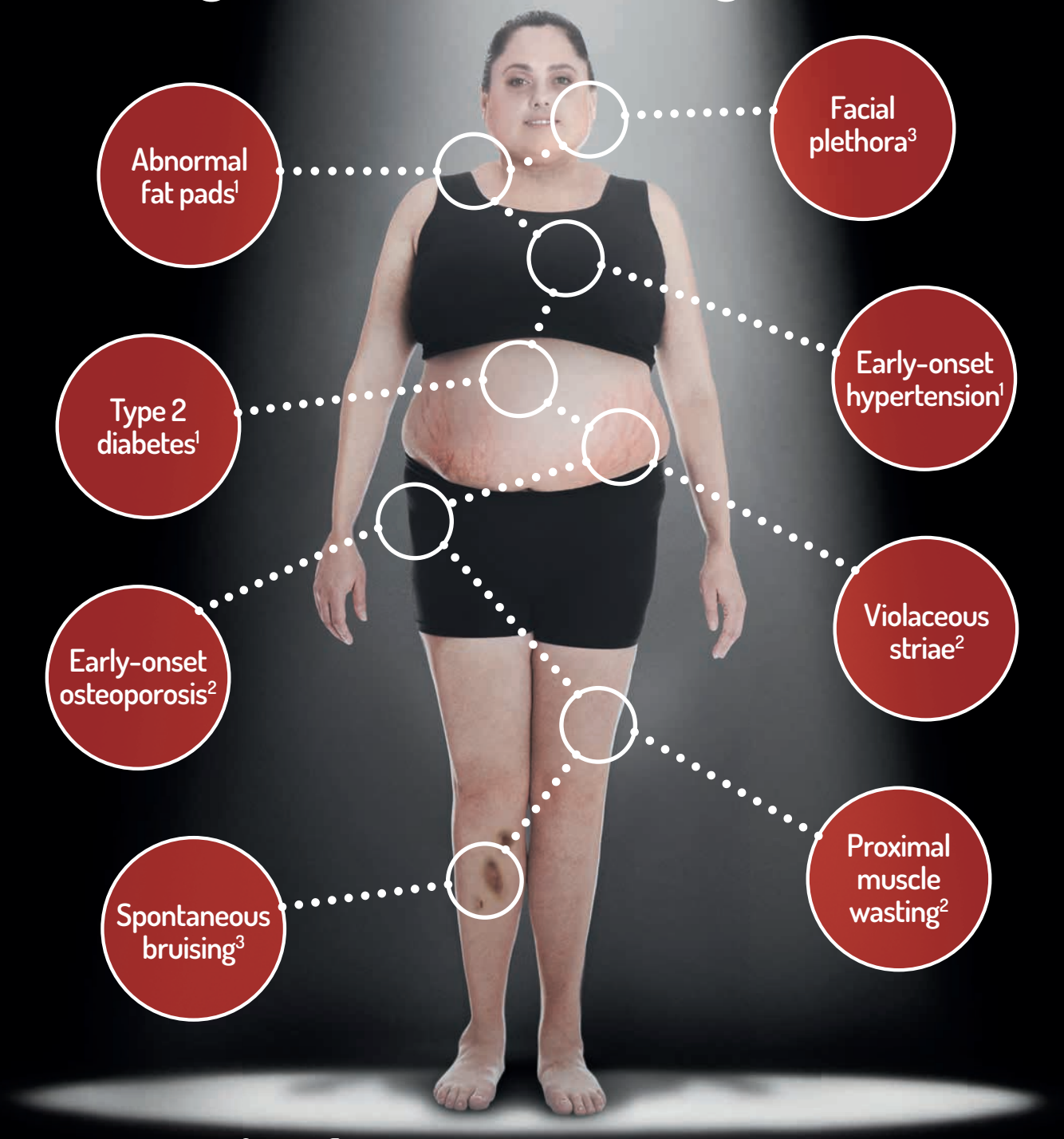
Often, FLS services are underfunded and there are misconceptions about the skill required of its nursing team. Fortunately, my colleague and I come from FLS backgrounds elsewhere. I previously set up a community FLS and community infusion service across Nottinghamshire. We both provide an excellent breadth of highly transferable skills and experience. FLS clinical staff recruitment and subsequent staff retention are frequently problematic, and may be a stumbling block for those looking to establish and deliver an effective, sustainable FLS.

Please tell us about your career journey, as others may want to follow in your footsteps
I've had quite an interesting career over the last 12 years or so. Initially working in medicine, and then moving to emergency care, I was subsequently offered a promotional post in the Trust's Risk Management Team. Following another promotion opportunity, I worked with the cross-boundary Palliative Service. During that time, following structural changes and after attaining an MSc in advanced nursing, I began to take an active interest in service development/design, and was presented with an opportunity to move into a community-based senior role to develop/deliver an intravenous service to administer zoledronic acid in patients' GP practices or their own homes in Nottinghamshire, which would incorporate elements of fracture liaison. During that time, I undertook a Level 7 Postgraduate Certificate in osteoporosis and falls management.

Ever since, I have remained within an FLS/osteoporosis role and have nearly 10 years' experience. In the early days of my FLS experience it was very challenging: seeking to deliver a service whilst engaging with all opportunities (both ad hoc and academic) to develop knowledge and skill in a new specialty. I have never lost my passion for the FLS and it continues to be an extremely satisfying role, providing me with clinical development opportunities, extensive patient engagement and wider MDT engagement, which is rarely available.

I always enjoy sharing information about the FLS and what can be achieved. My patients and our service are very dear to me. So thank you for this opportunity.

Although the condition might be rare...



...the features are common

Perhaps it's Cushing's syndrome, perhaps it's something else? If you connect any of these dots within a patient, consider referring them to a specialist endocrinologist.

For a clinician's guide to recognising Cushing's syndrome's signs and features, email **cushings@connectthedots.health** and help shine a light on this rare condition.

HRA Pharma Rare Diseases is now part of ESTEVE

Connect the dots

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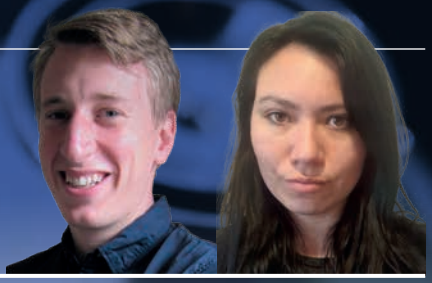
UK/NPR/0031 Date of preparation: August 2024

HOW TO... PRACTISE MORE SUSTAINABLY

WRITTEN BY VINCENT SIMPSON AND ESME GIRDWOOD



The world is warming faster than ever, caused mainly by the ongoing burning of fossil fuels. Crude oil consumption has increased by 33% since 2000 (4000 metric tons of crude oil consumed worldwide in 2023). Without urgent action to reduce carbon emissions, we are on track to exceed the 1.5°C limit set in the Paris climate agreement, with temperatures estimated to rise by 3°C by the end of the century.[1]

Healthcare is one of the major contributors to the climate crisis and, in England, the NHS accounts for 4% of the country's total carbon footprint. Some 33% of the NHS's carbon footprint is associated with pharmaceuticals.

Despite this, no national guidelines currently provide advice on sustainable prescribing. If we are to have a meaningful impact on the current trajectory, we need to start reflecting on our prescribing habits, to make healthcare more sustainable.

DIABETES PRESCRIBING

Diabetes is a key area where action can be taken. An estimated 5.6 million people live with diabetes in the UK, many of whom require daily insulin injections. Insulin is commonly delivered via either disposable or reusable cartridge pens. Currently, disposable insulin pens are prescribed about 50% of the time, and contribute 60 tonnes of plastic waste and 1000 tonnes of CO_2eq annually in England (equivalent to driving approximately 2.5 million miles by car).

WHY SWITCH TO REUSABLE INSULIN PENS?

Switching to reusable cartridge insulin pens offers the potential for significant environmental as well as cost savings. Using reusable insulin pens would reduce plastic waste by 89% and the carbon footprint by 40%. If all patients in England swapped a disposable pen for a reusable cartridge insulin pen, this would save 59 tonnes of plastic waste and 400 tonnes of CO2eq (equivalent to about 1 million miles by car) annually.

As well as contributing to a more sustainable healthcare system, reusable cartridge insulin pens also offer practical benefits to patients. These include the cartridges taking up less fridge space and the pens sometimes coming with features such as memory functions, which help patients keep track of their doses.

A further significant benefit is that cartridges are often cheaper (1–5%) than disposable pens,[2] meaning that we can be more sustainable while saving the NHS money.

HOW DO I SWITCH?

Switching to a reusable insulin pen is simple – as easy as switching from a disposable ballpoint pen to a refillable fountain pen. Healthcare providers can either give patients a reusable pen or ask their GP to prescribe one.

The key is to ensure that patients also receive the corresponding insulin cartridges.

We have developed **local guidelines to help make the switch easy**.

WHAT IF REUSABLE PENS AREN'T AN OPTION?

While most patients can switch to reusable pens without an issue, there may be exceptions, such as problems with dexterity or forgetfulness. It's important to take advantage of the available recycling schemes for those unable or unwilling to make the switch.

Novo Nordisk PenCycle and **Sanofi RePen** are product-specific recycling schemes. Unfortunately, not all manufacturers have similar programmes: Lilly, for example, does not currently offer a recycling scheme for its insulin products (such as Humalog and Humulin I).

Remember, whatever you do, patients should be advised to dispose of their insulin responsibly. For insulin which is not recycled, cartridges and unused insulin should be disposed of in sharps bins for incineration. It should not be put in landfill or domestic recycling bins, as it can leach into water systems and soil.

HOW DO I SUPPORT SUSTAINABLE DIABETES CARE?

As healthcare professionals, we play a key role in shaping a more sustainable future. Here's how you can make a difference:

1. Update local guidance to make reusable insulin pens the default option, reducing both plastic waste and carbon emissions.

2. Engage your colleagues in discussions about how to improve the environmental impact of diabetes care.

3. Seek further training, such as carbon footprint training provided by **sustainable healthcare organisations**, to better understand the environmental impacts of your care.

Only through small, sustainable changes can we start to change the way we practise medicine to be more environmentally friendly and reduce the wider impact of the care we provide.

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A farewell message from OUR CHIEF EXECUTIVE

As I prepare to step down from my role as Chief Executive of the Society for Endocrinology at the end of this year, I find myself reflecting on the journey we've shared over the past nine-and-a-half years.

It has been an honour and a privilege to lead this remarkable organisation and to work with such dedicated colleagues and passionate members, especially those who freely give their precious time to serve on our committees, to help advance such an important specialty.

> "On behalf of the Trustees and members, I wish to thank Ian for his unwavering commitment to the SfE Group and his strong leadership in navigating challenges over recent years. As a colleague, we all hold Ian in the highest regard and have enjoyed our time working with him. We wish him the very best for his next phase."
> *Ruth Andrew, General Secretary*

During my tenure, we have navigated numerous challenges, including the unprecedented impact of the pandemic. We have weathered these storms, and our collective efforts have ensured that the Society is doing more than ever to support the field of endocrinology in meaningful ways. I am immensely proud of what we have achieved together. From advancing research and education to fostering a supportive community for our members, our accomplishments are a testament to the hard work and commitment of everyone involved. I am particularly grateful for the tireless support of the Society's Officers and Council members whose dedication has been instrumental in driving positive change.

As I move on to the next chapter of my career, I am pleased to be handing over my responsibilities to Kate Sargent as the incoming Chief Executive. As many of you will know, Kate is a long-standing member of staff who has deep knowledge of, and incredible passion for, the Society and its work. The Society is therefore in excellent hands, and I am certain that Kate will bring fresh perspectives and continue to move the organisation forward, to provide effective and impactful support for the endocrinology community.

Thank you for the trust and support you have shown me over almost a decade; I look forward to seeing the Society for Endocrinology continue to flourish.

With heartfelt gratitude,

IAN RUSSELL

An introduction from OUR NEW CHIEF EXECUTIVE

I am honoured and excited to introduce myself as the next Chief Executive of the Society for Endocrinology and Managing Director of Bioscientifica.

Having dedicated 18 years to this incredible organisation, I am deeply committed to our mission, purpose and values. I am grateful for the confidence and trust placed in me, and look forward to leading our organisation from 2025. I am privileged to succeed Ian Russell, whose leadership over nearly ten years has been instrumental in our resilience, especially during the challenges of the pandemic and its aftermath.

As we move forward, my vision is for the SfE Group to operate as a cohesive, unified organisation, with rich synergies across our activities, delivering our two principal strategies: driving commercial activities to generate revenue, and utilising this revenue effectively to deliver our charitable objectives.

With over 20 years of experience in national-level charity governance and management, gained through both professional roles and volunteer positions, my career has been dedicated to charitable organisations. I will lead the SfE Group with passion and dedication, championing innovative strategies, nurturing our collaborative office team, driving transformation, and strengthening our communities. I am also committed to ensuring Bioscientifica's profitability while staying true to our shared purpose and values. I believe in our organisation and will fight hard for its future, ensuring we excel at continuing to provide valued services to you, our members.

I would like to take this opportunity to acknowledge the hard work and dedication of our office team and our Society members. Your contributions are the backbone of our Society and, together, we will continue to make significant strides for the field of endocrinology and future generations of endocrinologists.

Finally, I extend my sincere thanks to Ruth Andrew and all our Trustees for the comprehensive and robust recruitment process they conducted, which required significant effort and time commitment on their part.

> "We are delighted to welcome Kate Sargent as our new Chief Executive. Kate's extensive experience, passion for and dedication to our Society make her the perfect leader for this next chapter. We very much look forward to developing our future together."
> *Ruth Andrew, General Secretary*

For those I have already crossed paths with during my tenure at the Society, thank you for your continued support and engagement. For those I do not yet know, I look forward to working closely with you all as we embark on this exciting journey together, and to seeing many of you at the SfE BES conference in Harrogate next spring.

KATE SARGENT

Showcasing diversity
NEW SOCIETY AWARDS AND PRIZES

Our Society is dedicated to recognising excellence, celebrating achievements and inspiring future advancements in our discipline. We aim to ensure that all members have the opportunity to be acknowledged, to share their successes, and to celebrate them within our community.

In 2023, as part of the Society's commitment to better represent and support more of our members, we established a working group to review the full portfolio of our awards and prizes. Led by Professor Julia Buckingham, the group was tasked with reimagining the awards to celebrate a broader range of member achievements. The group also reviewed the processes for application, nomination, review and selection, to ensure that these are welcoming, inclusive, transparent and fair.

INTRODUCING A NEW PROGRAMME OF AWARDS AND PRIZES

Following careful review by the working group, we have now relaunched our programme of awards and prizes to better showcase the incredible diversity of talent across endocrinology. Alongside these changes, the Nominations Committee will also be transformed into a new Awards and Prizes Committee, which will include up to 16 members from across the Society. Individuals from all member types and career stages are welcome to judge the applications and nominations for this new portfolio.

We are currently welcoming applications for the following awards:

- **Dale Medal** for Lifetime Achievement
- **Mid-Career Medal** for Research Excellence
- **Early Career Medal** for Research Excellence
- **Outstanding Contribution Medal**
- **Nikki Kieffer Medal**
- **Excellence in Clinical Service Delivery**
- **Outstanding Clinical Practitioner**
- **Outstanding Teacher of the Year**

Submit your applications by **12 January 2025**.

To find out all the details for these awards, including eligibility and criteria, visit **www.endocrinology.org/grants-and-awards**.

From 2025 onwards, we will be introducing further awards, including Team Science, Outstanding Specialist Technologist Working in Endocrinology, and the International Endocrinology Development Award.

WOULD YOU LIKE TO HELP MARK AND SELECT OUR AWARDEES?

Applications for these awards and prizes will be marked by the newly formed Awards and Prizes Committee. We are still looking for additional committee members, at any career stage. The committee will carry out marking from the end of January each year, and participate in a selection meeting in the spring. **Apply to be on the committee**

Society for Endocrinology

Events and Training 2025

The Society for Endocrinology provides a broad range of events, designed to facilitate networking in our community, and to support your professional development.

ASPIRING RESEARCH LEADERS

9 March 2025
Crown Plaza, Harrogate

This pre-SfE BES conference event offers a unique opportunity for late-stage PhDs, postdocs and early-career researchers to connect with peers and gain insights from established researchers. You'll learn about balancing teaching and research responsibilities, discover the right funding options for your career stage, and get personalised feedback on your CV and grant applications.

SfE BES 2025

10–12 March 2025
Harrogate Convention Centre, Harrogate

SfE BES is back in Harrogate! Join the largest gathering of endocrine professionals in the UK as we learn from each other, share our passion for endocrinology and collectively work towards advancing research and patient care in our field.

WOMEN'S HEALTH SUMMIT

20 June 2025
The Eastside Rooms, Birmingham

A Building on the success of last year's event with brand new topics and a line up of world-renowned speakers, this event will explore the latest advances in women's health. We've introduced a host of practical sessions to address real-world clinical challenges, aiding problem-solving and communication in the clinic. Whether you're a consultant, GP, nurse or trainee, this summit will provide invaluable insights into best clinical practice in women's healthcare.

CLINICAL UPDATE

Date: TBC
Venue: TBC

Clinical Update is an indispensable event for trainees and new consultants preparing to sit the RCP's Specialty Certificate Examination in endocrinology and diabetes.

ENDOCRINE NURSE UPDATE

Date: TBC
Venue: TBC

This event is designed to support endocrine specialist nurses. The programme features two days of lectures, workshops and a range of networking opportunities.

Find out more at **www.endocrinology.org/events**

Shaping the future of menopause care
REAL-WORLD EVIDENCE ON TREATMENT OUTCOMES

The Society for Endocrinology has recognised a critical gap in menopause management and outcome data.

At a pivotal moment when increasing access to hormone replacement therapy (HRT) is enabling more women (particularly those with complex comorbidities) to seek treatment outside traditional clinical trials, we have launched our data registry: 'patient-reported outcomes for menopause management intervention study' (PROMMIS). This initiative will capture real-world data on menopause management, filling gaps in our understanding of treatment outcomes to positively shape the future of evidence-based care in women's health.

Health inequalities relating to various aspects of menopause care are increasingly being highlighted and scrutinised.[1–3] Many questions remain unanswered. While some modern HRT formulations may be safer than older regimens, there is a lack of clinical outcome data, particularly for high-risk women with complex health issues. The outcomes of HRT regimens that fall outside regulator-approved dosing schedules are unknown. From another angle, many women who are deemed unsuitable for HRT feel excluded from online and media discussions about menopause, and express frustration over the lack of effective alternatives for managing menopause symptoms. Moreover, there is a significant lack of data to guide menopause clinical management for those with adverse cardiometabolic health, gynaecological-endocrine problems, and oestrogen-related cancers.

Large-scale randomised trials using modern HRT formulations and unconventional regimens, especially in high-risk women, are unlikely to receive ethical approval or funding. Therefore, formally collecting real-world evidence through the Society's new PROMMIS registry will provide one of the best opportunities to capture experiences and treatment outcomes related to menopause in modern cohorts of women.[4]

This registry is unashamedly patient-centric. The data collection process is innovative, utilising an online platform that can be accessed via a QR code, making it suitable for smartphone users (**www.peoplewith.com**). Relevant clinical data from primary care records will be obtained through automation, with options for additional input from secondary care providers.

Our new PROMMIS registry is ambitious and bold. It is a long term initiative supported by a steering group of leaders from endocrinology and allied specialties across the devolved nations, alongside collaborations with charities and patient groups. The Society will host the registry with funding support from unrestricted educational grants.

I am proud to be a member of an organisation with such a brilliant strategic vision. I look forward to seeing evidence emerging from this pivotal registry, which promises to shape future research and clinical practice in women's health for decades. I hope you share my excitement.

ANNICE MUKHERJEE
Steering Group Chair, Sp. – PROMMIS

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3. Harlow SD *et al.* 2022 *Women's Midlife Health* https://doi.org/10.1186/s40695-022-00073-y.
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Find out more about the **PROMMIS registry**.

Call for papers: Exploring Osteoporosis and Sarcopenia

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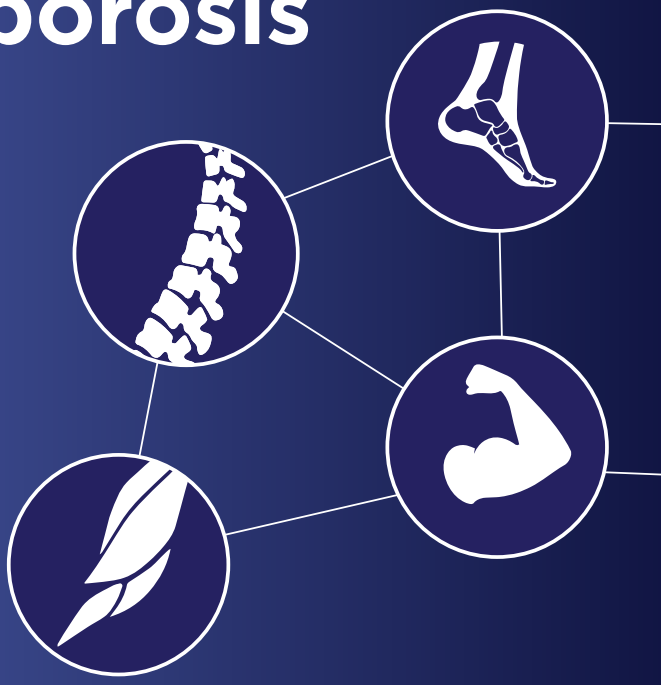

Guest Editor
Dr Naibedya Chattopadhyay,
Central Drug Research Institute, India

Topics of interest include:

- ☑ Bone-muscle crosstalk
- ☑ Metabolic factors
- ☑ Therapeutic targets
- ☑ Translational aspects

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Md Rameez Moin, Shubhrajyoti Das and Sabyasachi Sanyal

An interview with…
GEORGE MASTORAKOS
A SPIRIT OF CURIOSITY FOR ENDOCRINE RESEARCH

George Mastorakos is based at the Medical School of the National and Kapodistrian University of Athens, Greece, where he is Professor of Endocrinology and Director of the Postgraduate MSc on Research in Female Reproduction. He is Senior Reproduction Editor for the Society's open access journal *Endocrine Connections*. Here, he tells us about his passion for endocrinology and its many interconnecting disciplines, and some of the current hot topics in the field.

What inspired you to choose endocrinology?
I was drawn to endocrinology as a distinct part of human physiology. Even before it was named, researchers in endocrinology were interested in mechanisms explaining the intricate interconnections among subcellular, intercellular, organ and whole-body environments. They were among the first to study the cause–effect counter-regulatory response in a physiologic phenomenon (feedback), including the factor of time in the description of this response. Subsequently, many other fields in medicine followed this approach.

While, some decades ago, the nervous system was considered a key system in the regulation of the body, nowadays the hormonal system is recognised as the body's principal regulator and reaction integrator.

Being attracted to endocrinology demands a certain curious spirit for research. I became interested in research at the bench in my second year at medical school and, since then, I've tried to combine translational or basic research with my clinical duties. I am, as a result, the author or co-author of more than 340 published papers.

Following last issue's focus on stress and trauma, please tell us about your research interests in this area
During my years training in research at the National Institutes of Health (NIH), I was fortunate to be introduced to the study of stress and trauma by George P Chrousos, a world-renowned, prominent scientist in this field.

Since Hans Selye (1907–1982) introduced the term 'stress' and gave the first description of the stress reaction, research has revealed that reactions originating from stress and trauma are major adaptive responses by most human physiology systems. Whether acutely excessive or chronic, these responses lead, in turn, to the development of pathologic entities, which (before becoming irrevocable) are functional and, therefore, correctable.

Along these lines, I was interested in revealing the development of stress reactions in normal and pathologic aspects of situations related to endocrinology, particularly female physiology, such as:

- the involvement of the immune/inflammatory reaction in the stress response
- the role of stressors in female fertility during *in vitro* fertilisation
- the deleterious effects of stressors (internal and external) for both the mother and the fetus (i.e. intrauterine growth restriction) during pregnancy, when stress reactions can epigenetically reprogramme the fetus to develop deleterious diseases in adult life (i.e. the development of insulin resistance)
- the combination of stressors with metabolic derangements during pregnancy that can occur at the origin of the development of autoimmune disorders, polycystic ovary syndrome, type 2 diabetes mellitus, arterial hypertension, sensitivity to psychiatric diseases, etc.
- the role of stressors (internal or external) in precipitating the timing of labour
- the role of stress in hypothalamic amenorrhoea.

What recent studies have you been involved with?
We used treadmill exercise (a model of a stressor) to compare flow-mediated dilation changes in women with and without PCOS, and found that the adaptation capacity of arterial endothelium is limited in PCOS.

We are also studying the role of chronic stress during pregnancy and its outcome on the neonate, having already reported that it negatively affects neonatal birth weight.

Information we have gathered (for a paper recently accepted by *Endocrine Connections*) strongly indicates that the use of synthetic corticoids during pregnancies with suspected premature labour (to prepare fetal respiratory system adaptation) might accelerate the unwanted premature labour via stimulation of placental corticotrophin-releasing hormone secretion.

Which are the current hot topics in your specialism?
Endocrinology is involved in many physiological aspects and diseases across a wide range of medical specialties. Hot topics arising from these overlaps include:

- endocrine aspects of female fertility, particularly explaining the abrupt loss of fecundability after the age of 40
- treating women hormonally in pre- and postmenopause
- investigating the endocrine aspects (positive and negative) of exercise
- endocrinology of psychiatric diseases, particularly in their milder aspects, which represent an important percentage of the population
- preventing the development of negative endocrine phenomena in individuals who receive bad nutrition and who are predisposed to obesity, as well as treating them successfully
- mobilising healthcare professionals to understand that *in utero* life predisposes us to diseases in adult life, by eventually developing the endocrinology of pregnancy as a subspecialty (not just a field of research).

What is involved in being a Senior Editor for *Endocrine Connections*?
Endocrine Connections, from its conception, was designed to go beyond the traditionally defined borders of endocrinology, covering basic to clinical (via translational) research needs in overlapping fields. As an Editor specialising in reproductive endocrinology, I have been focusing on further enhancing the quality of publications coming from fields adjacent to endocrinology, attracting scientists and clinicians in interconnecting disciplines to review for the journal. I think *Endocrine Connections* could become an important meeting point for scientists working across endocrine physiology and pathophysiology.

STEPPING OUT OF THE COMFORT ZONE: THE VALUE OF LIFELONG LEARNING

WRITTEN BY COSMINA SCHITEANU

While browsing the Society for Endocrinology website, I stumbled upon an intriguing advertisement for a 'Masters-level module in endocrine nursing,' which was promoted as a work-based learning opportunity. Having not long completed my non-medical prescribing module – an experience I found quite challenging – I thought to myself that I wasn't ready to jump back into learning.

However, I realised that the format of the endocrine nursing module would allow me to build on the foundation I established during my non-medical prescribing studies, while applying what I learned in a real-world context. Despite my initial reservations about diving back into academia, I recognised that the challenges I faced in the prescribing module ultimately contributed to my growth. The complexities of endocrine disorders require a robust understanding, and I was eager to enhance my skills further.

I began to envision how this module could complement my existing qualifications and improve my practice. It would not only empower me to provide better care for my patients, but also open up new opportunities for professional development. So, I decided to reach out to the programme co-ordinators and the Society for Endocrinology to gather more information and discuss potential pathways for enrolment.

'The more I learned, the more excited I became about the possibilities this module offered.'

I completed my application in May 2023 and, in September 2023, I received the thrilling news that I had been funded to start the module. To say I was over the moon would be an understatement – it felt like another significant milestone in my career! However, with that excitement came a wave of worries and fears about how I would balance the demands of the module with my work responsibilities.

The more I learned, the more excited I became about the possibilities this module offered. It was a chance to refine my expertise in a specialised area and connect with fellow nursing professionals who were passionate about endocrinology. I felt invigorated by the prospect of learning in a collaborative environment, where I could share experiences and strategies with peers facing similar challenges.

Fortunately, I had the support of a fantastic tutor who guided me through the initial stages of the course. Their expertise and encouragement were invaluable, especially as I navigated the complexities of the curriculum. I quickly learned that I wasn't alone in this journey; many endocrine nurse specialists who had completed the module before me were eager to share their insights and experiences.

Their willingness to help was incredibly reassuring. They provided practical tips on managing time effectively, balancing clinical duties with study commitments, and staying organised. I found their stories inspiring, which motivated me to push through any doubts I had about my abilities. As the module progressed, I began to develop a structured approach to my studies. I created a weekly plan that allocated specific times for coursework, practical experience and self-care. This not only helped me stay on track but also reduced my anxiety about falling behind. But there were definitely moments when I felt overwhelmed throughout the module.

I also engaged actively in discussions with my peers, which fostered a sense of community. Sharing challenges and triumphs made the learning experience much richer and reinforced my commitment to the module. The collaborative atmosphere encouraged me to embrace the knowledge that was shared and to ask questions, enhancing my understanding of endocrine nursing.

'The collaborative atmosphere encouraged me to embrace the knowledge that was shared and to ask questions, enhancing my understanding of endocrine nursing.'

As I approached the final month of my course, we prepared to submit our formative assessments. I had received a good mark on my preliminary work, but my tutor encouraged me to aim even higher. I reached out to academic support and, with their guidance, I began to restructure my essay. After submitting my final work, I eagerly awaited my results. A few weeks later, I checked my mark and was thrilled to see that my efforts had paid off – I had improved my overall score to 72 out of 100. What a relief!

Reflecting on my journey, I realised that stepping out of my comfort zone could lead to new insights and growth. I am ready to embrace the challenge and take the next steps in my professional development.

COSMINA SCHITEANU
Endocrine Nurse Specialist

FURTHER READING

M Qanbari Qalehsari *et al.* 2017 *Electronic Physician* http://doi.org/10.19082/5541.

Find out more about the Masters-level module in endocrine nursing, offered by the Society for Endocrinology in collaboration with Oxford Brookes University.

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1. Signifor® Powder and Solvent for Suspension for Injection Summary of Product Characteristics
2. Gadelha R, *et al. Lancet Diabetes Endocrinol* 2014;2:875-884

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Increase to a maximum of 60 mg for patients whose growth hormone (GH) and/or insulin-like growth factor-1 (IGF-1) levels are not fully controlled after 3 months of treatment with Signifor at 40 mg. *Cushing's disease (adults including elderly and those with renal impairment):* The recommended initial dose is 10 mg by deep intramuscular injection every 4 weeks. Dose may be titrated every 2 to 4 months based on response and tolerability. The maximum dose of Signifor in Cushing's disease is 40 mg every 4 weeks. *Patients with hepatic impairment*: Dose adjustment is not required in patients with mildly impaired hepatic function (Child Pugh A). Not for use in severe hepatic impairment. *Acromegaly:* the recommended dose with moderate hepatic impairment (Child Pugh B) is 20 mg every 4 weeks, and the maximum is 40 mg every 4 weeks. *Cushing's disease:* the recommended initial dose for Cushing's disease patients with moderate hepatic impairment (Child Pugh B) is 10 mg every 4 weeks, and the maximum recommended dose for these patients is 20 mg every 4 weeks. *Method of administration:* Signifor is to be administered by deep intramuscular injection, alternated between left and right gluteal muscle, by a trained healthcare professional. Signifor suspension must only be prepared immediately before administration. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Severe hepatic impairment (Child Pugh C). **Special warnings and precautions for use:** Hyperglycaemia and, less frequently, hypoglycaemia, were observed in subjects participating in clinical studies with pasireotide. Glycaemic status (fasting plasma glucose/haemoglobin A_{1c} [FPG/HbA_{1c}]) should be assessed prior to starting treatment with pasireotide. FPG/HbA_{1c} monitoring during treatment should follow established guidelines. Self monitoring of blood glucose and/or FPG assessments should be done weekly for the first three months and periodically thereafter, as clinically appropriate, as well as over the first four to six weeks after any dose increase. Monitoring of FPG at 4 weeks and HbA_{1c} 3 months after the end of the treatment should be performed. In patients with poor glycaemic control (HbA_{1c} values > 8%), diabetes management and monitoring should be intensified prior to initiation and during pasireotide therapy. Monitoring of liver function is recommended prior to treatment with pasireotide intramuscular use and after the first two to three weeks, then monthly for three months on treatment. Thereafter liver function should be monitored as clinically indicated. Bradycardia has been reported with the use of pasireotide. Careful monitoring is recommended in patients with cardiac disease and/or risk factors for bradycardia. Dose adjustment of medicinal products such as beta blockers, calcium channel blockers, or medicinal products to control electrolyte balance, may be necessary. Pasireotide should be used with caution and risk benefit carefully assessed in patients who are at significant risk of developing prolongation of QT. A baseline ECG is recommended prior to initiating therapy with Signifor. Monitoring for an effect on the QTc interval is advisable 21 days after the beginning of the treatment and as clinically indicated thereafter. Hypokalaemia and/or hypomagnesaemia must be corrected prior to administration of Signifor and should be monitored periodically during therapy. The suppression of ACTH secretion can result in hypocortisolism in patients treated with Signifor. It is therefore necessary to monitor and instruct patients on the signs and symptoms associated with hypocortisolism. Ultrasonic examination of the gallbladder before and at 6 to 12 month intervals during Signifor therapy is recommended. The presence of gallstones in Signifor-treated patients is largely asymptomatic; symptomatic stones should be managed according to clinical practice. As the pharmacological activity of pasireotide mimics that of somatostatin, inhibition of pituitary hormones other than GH and/or IGF-1 in patients with acromegaly and ACTH/cortisol in patients with Cushing's disease cannot be ruled out. Monitoring of pituitary function (e.g. TSH/free T_4) before and periodically during Signifor therapy should therefore be considered, as clinically appropriate. If concomitant use of coumarin-derivative or heparin-derivative anticoagulants with Signifor intramuscular use cannot be avoided, patients should be monitored regularly for alterations in their coagulation parameters (PT and PTT) and the anticoagulant dose adjusted accordingly. Signifor should be used with caution in patients with severe renal impairment or end stage renal disease. **Interactions:** Concomitant administration of pasireotide and ciclosporin may require adjustment of the ciclosporin dose to maintain therapeutic levels. Pasireotide should be used with caution in patients receiving medicinal products that prolong the QT interval. Caution also with bradycardic, insulin and antidiabetic medicinal products. **Pregnancy and lactation:** Pasireotide is not recommended for use during pregnancy and in women of childbearing potential who are not using contraception. Breast-feeding should be discontinued during treatment with Signifor. **Effects on ability to drive and use machines:** Patients should be advised to be cautious if they experience fatigue, dizziness or headache during treatment with Signifor. **Side effects:** Effects seen are largely similar between the acromegaly and Cushing's disease indications, and consistent with the class, except for higher degree and frequency of hyperglycamia. *Very common* (≥ 1/10); Hyperglycaemia, diabetes mellitus, diarrhoea, nausea, abdominal pain, cholelithiasis and fatigue. *Common* (≥ 1/100 to < 1/10); Anaemia, adrenal insufficiency, type 2 diabetes mellitus, impaired glucose tolerance, decreased appetite, headache, dizziness, sinus bradycardia, QT prolongation, abdominal distension, vomiting, cholecystitis, cholestasis, alopecia, pruritus, injection site reaction, glycosylated haemoglobin increased, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, blood glucose increased, blood creatine phosphokinase increased and lipase increased. Other adverse events can include asymptomatic elevations in lipase and amylase and pancreatitis. **Please consult the full SmPC for further information**. **Marketing Authorisation Numbers:** EU/1/12/753/013-019. PLGB 15266/0035-0039. **Legal Classification**: POM. **Price:** One vial of Signifor 10 mg, 20 mg, 30 mg, 40 mg or 60 mg £2,300.00. **Name and Address of the Business Responsible for Sale**: Recordati Rare Diseases UK Ltd., Breakspear Park, Breakspear Way, Hemel Hempstead, HP2 4TZ. Further information is available on request. **Date Prescribing Information Revised**: January 2023.

Adverse events should be reported.
Reporting forms and information can be found at (UK) https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in Google Play or Apple App Store.
(Ireland) Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigiliance www.hpra.ie. Adverse events should also be reported to Recordati Rare Diseases at Tel: +44 (0) 1491 414 333 or RRDpharmacovigilance@recordati.com.