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THE ENDOCRINOLOGIST

THE MAGAZINE OF THE SOCIETY FOR ENDOCRINOLOGY

Options in obesity
EMBRACING OPPORTUNITIES

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A word from THE EDITOR...

Welcome to this supersize issue, which is rather fitting, considering it's all about obesity – one of the largest clinical problems facing us in the modern era. The good news is that there have been huge leaps in our understanding and treatments over the last few years.

The glucagon-like peptide-1 receptor agonist drugs, such as Ozempic/Mounjaro, have been a huge success story. However, these are relatively new to the market, so it is important that we understand any unexpected side effects. This topic is discussed by Jessica Wright and Nicoletta Charolidi from the MHRA, who highlight the **Yellow Card scheme and Biobank** to investigate genetic-based adverse responses to the drugs. It's a must-read for all healthcare professionals.

Also, as **Giles Yeo said when I interviewed him**, 'We mustn't blow the opportunity. We need to minimise risk and find other approaches to target the brain to reduce food intake.' So we can't stop now, we need to continue researching, including studies of **unexpected models such as the 'hungry Labrador'**, which are discussed by Enoch Alex and Eleanor Raffan.

The age of bariatric surgery has not passed. It is still a very useful tool in **the fight against obesity, for example in cardiovascular disease**, as highlighted by Safwaan Adam and Akheel A Syed. The management of patients after surgery also remains important, and we feature two articles on this. One discussing the **current thinking around same-day discharge**, the other on **supporting women with pregnancy after weight-loss surgery**.

I hope you enjoy this issue, which addresses the science and clinical aspects of obesity and, most importantly, shows you the exciting areas that endocrinology covers. There will no doubt be plenty more to absorb on this in the talks and posters at **SfE BES 2026, for which registration is open!**

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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 articles for the SPRING 2026 issue: **13 January 2026**.

Front cover image: ©Shutterstock

HOT TOPICS

Hot Topics is written by Victoria Chatzimavridou Grigoriadou, John Hough, Zin Htut, Edouard Mills, Gareth Nye, Bhavna Sharma, Vincent Simpson and Angela Taylor

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

Time-dependent effects of cadmium on pituitary gonadotrophs

Cadmium, a toxic heavy metal found in industrial emissions and cigarette smoke, has long been linked to reproductive toxicity. Cadmium is an endocrine-disrupting chemical that mimics essential metals such as calcium and zinc, interfering with hormone signalling.

Santiago-Andres *et al.* have now revealed that this pollutant directly disrupts the pituitary gland. They exposed adult male mice to cadmium, and monitored the effects on gonadotrophs and testicular function. They discovered that cadmium accumulates in the pituitary, where it alters calcium signalling, affecting hormone secretion. Gonadotroph responsiveness to gonadotrophin-releasing hormone decreases initially but, with prolonged exposure, calcium oscillation patterns shift, and gonadotrophin secretion rises, suggesting persistent intracellular signalling disruption. Downstream cadmium exposure also resulted in testicular atrophy, increased apoptosis, and reduced sperm count. A decline in testosterone concentration was observed while the gonadotroph population increased, highlighting an imbalance in endocrine regulation.

The study suggests that cadmium drives reproductive toxicity through both direct testicular damage and altered gonadotroph calcium signalling, resulting in hormone imbalance and testicular dysfunction which should be highlighted as a public health concern.

Read the full article in *Journal of Endocrinology*
https://doi.org/10.1530/JOE-25-0161

JOURNAL OF MOLECULAR ENDOCRINOLOGY

Implications of uterine artery endothelial cells for pre-eclampsia

Pre-eclampsia remains a mystery in terms of early diagnosis, with a number of potential markers being unreliable. New research on uterine arteries may provide opportunities for diagnosing this disease. These arteries have a key role in facilitating a successful pregnancy and so understanding their role in pregnancy immunology is a novel avenue to explore.

Dahn *et al.* analysed uterine artery endothelial cells from late-pregnant sheep (P-UAEC) for changes in chemokine and cytokine secretory and immunomodulatory properties at a single cell level. Using a combination of cell culture, spectral flow cytometry and cellular indexing of transcriptomes and epitopes by sequencing, the authors recorded distinct endothelial populations within the uterine arteries and a heterogeneous response to cytokine treatment.

This study furthers the idea of an immune basis for pre-eclampsia and suggests that, potentially, some people are more prone to severe presentations based on their own cellular populations and response to immune signalling, which may now mean new molecular targets for diagnosis are on the horizon.

Read the full article in *Journal of Molecular Endocrinology*
https://doi.org/10.1530/JME-24-0086

ENDOCRINE-RELATED CANCER

Breast–thyroid cancer link: revisiting a reciprocal risk

An association between breast and thyroid cancers has been repeatedly observed in epidemiological studies, though its nature and underlying causes remain unclear. In a recent systematic review and meta-analysis, Viola and colleagues synthesised data from 38 studies including nearly 3 million women to examine the reciprocal risk between these two common malignancies.

They reported a statistically significant bidirectional association. Women with thyroid cancer had a 40% higher risk of developing breast cancer (standardised incidence ratio (SIR) 1.4), while those with prior breast cancer had a 50% increased risk of subsequent thyroid cancer (SIR 1.5). The risk of secondary thyroid cancer appeared greater in women diagnosed with breast cancer before the age of 50 and in those who had received chemotherapy, whereas radiotherapy was not associated with a significant increase in risk.

While substantial heterogeneity and incomplete subgroup data preclude firm conclusions, this synthesis provides important quantitative evidence regarding a long-discussed association. The findings highlight the need for further research into shared hormonal and genetic pathways and advocate for an individualised approach to surveillance in potentially higher-risk patients.

Read the full article in *Endocrine-Related Cancer*
https://doi.org/10.1530/ERC-24-0338

ENDOCRINE CONNECTIONS

Transitioning adolescents with rare forms of diabetes to adult care

Paediatric and adult diabetes often share a common clientele, when patients are moved from a familiar environment of paediatric diabetic medicine to adult diabetes. This can be challenging for all three interested parties. Specifically, rarer forms of diabetes are logically considered to pose additional challenges.

This narrative review by Reschke and colleagues focuses on transition-specific barriers in rare diabetes syndromes such as Wolfram syndrome, Alström syndrome, Bardet–Biedl syndrome and maturity-onset diabetes of the young. It explores current initiatives and proposes recommendations for care models and health system reform.

This should make an enlightening, introspective article for an audience of various demographics working in diabetes at both paediatric and adult levels.

Read the full article in *Endocrine Connections*
https://doi.org/10.1530/EC-25-0451

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CLINICAL ENDOCRINOLOGY

Incidence of autoimmune disease before and after PCOS diagnosis

Polycystic ovary syndrome (PCOS) is the commonest endocrine disorder in women of reproductive age. It is characterised by hyperandrogenism (clinical/biochemical), chronic anovulation and/or polycystic ovaries/elevated anti-Müllerian hormone. Previous studies have reported a higher prevalence of autoimmune diseases in women with PCOS, but large prospective studies employing population-based cohorts are lacking.

Here, Glintborg *et al.* undertook a national register-based study to investigate the incidence of autoimmune disease before and after diagnosis of PCOS in a Danish population, compared with controls. In their study of 30,340 women with PCOS and 151,520 controls, they show that, after a diagnosis of PCOS, the incidence of any autoimmune disease was 1.5 times higher and that of type 1 diabetes was 3.5 times higher compared with controls. Furthermore, they highlight that, in women with PCOS, the higher incidence of autoimmune disease was associated with higher body mass index, co-morbidity, lower socioeconomic status and non-Danish ethnicity.

Based on these findings, the authors recommend continued awareness for autoimmune diseases in women with PCOS, not only at diagnosis, but also during follow up.

Read the full article in *Clinical Endocrinology* https://doi.org/10.1111/cen.70019

ENDOCRINOLOGY, DIABETES & METABOLISM CASE REPORTS

Muscle loss and immunosuppression in glucose dysregulation

Ectopic fat in the liver and pancreas is a well-recognised contributor to insulin resistance, but other factors can often significantly contribute to diabetes risk. For instance, skeletal muscle is responsible for about 80% of glucose uptake, although it remains under-appreciated in the pathogenesis of diabetes.

Motohashi *et al.* report two brothers with Becker muscular dystrophy, both with significant skeletal muscle degeneration but different glycaemic outcomes. The younger sibling developed diabetes following heart transplantation and immunosuppressive therapy (tacrolimus and everolimus). His brother maintained impaired glucose tolerance without progressing to diabetes. Despite similar degrees of muscle loss and fat accumulation (body mass index 25.9 and 26.4kg/m², body fat mass 46.2% and 50.7%), only the post-transplant case showed β-cell dysfunction. He had low HOMA-β (homeostasis model assessment of β-cell function) at 36.5%, and high HOMA-IR (homeostasis model assessment of insulin resistance) at 2.48, probably triggered by immunosuppressive agents. Treatment with metformin and dulaglutide achieved glycaemic control.

This highlights the synergistic effect of skeletal muscle loss and β-cell stress in tipping the metabolic balance towards diabetes, even in the absence of classical risk factors such as obesity. For clinicians managing muscular dystrophy or other muscle-wasting conditions, particularly in post-transplant settings, vigilance for diabetes is warranted even when traditional metabolic markers seem modest.

Read the full article in *Endocrinology, Diabetes & Metabolism Case Reports* https://doi.org/10.1530/EDM-25-0038

ENDOCRINE ONCOLOGY

Androgen receptor amino-terminal domain in prostate cancer

The androgen receptor regulates androgen signalling through three domains: a ligand-binding domain (LBD), a DNA-binding domain (DBD) and the flexible amino-terminal domain (NTD), which makes up more than half of the protein. Hunter *et al.* have reviewed the NTD as an emerging therapeutic target in prostate cancer, particularly in advanced and drug-resistant disease.

Unlike the structured LBD and DBD, the NTD is intrinsically disordered, allowing dynamic folding, multiple protein–protein interactions and allosteric regulation. Structural studies using molecular modelling, nuclear magnetic resonance and cryo-electron microscopy have revealed helical regions within the NTD (TAU1 and TAU5), and its role in forming complexes with cofactors such as SRC-3, p300 and TFIIF. The NTD also contributes to liquid–liquid phase separation, forming condensates that may drive resistance to anti-androgen therapies. Novel drugs targeting the NTD include covalent inhibitors (EPI series, ET516, UT-143), reversible inhibitors (SC428, compound 16) and degraders or PROTACs (UT-34, Z15, BWA-522). These agents block androgen receptor signalling even in splice variants lacking the LBD.

Continued research aims to translate these findings into next-generation treatments for castration-resistant prostate cancer.

Read the full article in *Endocrine Oncology* https://doi.org/10.1530/EO-24-0061

ENDOCRINE HIGHLIGHTS

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

Development and validation of a tool to predict type 2 diabetes mellitus

The increased prevalence of type 2 diabetes mellitus (T2DM) is a major public health issue, affecting 400 million individuals worldwide. Currently, management of T2DM comprises anti-diabetic drugs and lifestyle modifications, such as diet and exercise. Being able to predict the risk of this disease would help to delay onset of T2DM.

Satoh and colleagues developed and validated a predictive model of the onset of T2DM using health check-up data from the general population. They analysed data from 463,248 adults who had regular health checks, developing a prediction model from 308,832 of these and validating the model with the remainder. The model assigns scores based on a person's health and lifestyle characteristics to estimate their diabetes risk. Over a follow-up period of around five years, roughly 17% of people in both groups developed T2DM. When tested, the model showed a moderate ability to predict who would develop the disease.

The model assigns scores based on age, sex, body mass index, blood pressure, lipid profiles, liver enzymes, kidney function and lifestyle habits to estimate risk of diabetes. Because it uses information that is already collected in regular health exams, this tool could help identify people at higher risk and support earlier prevention efforts.

Read the full article in *Scientific Reports* https://doi.org/10.1038/s41598-025-21831-8

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SHINING A LIGHT ON THE TARGETS OF DUAL GLP1R/GIPR AGONIST DRUGS

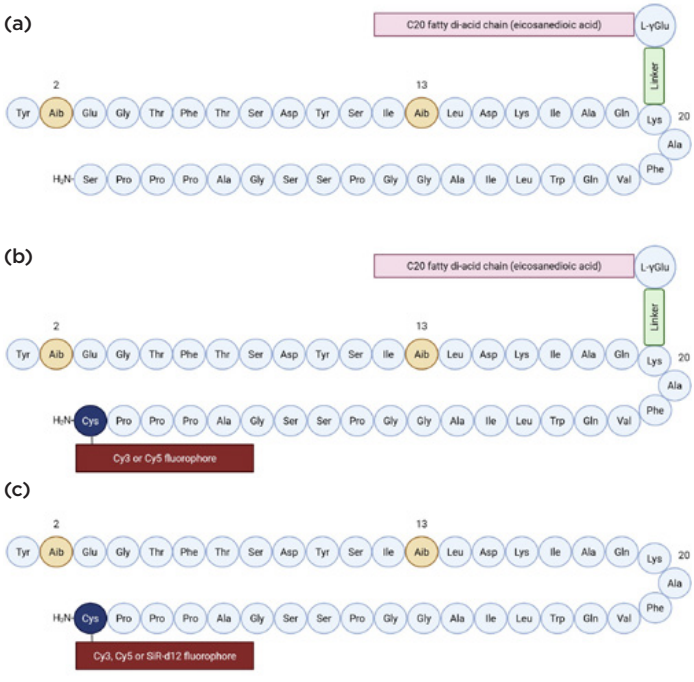
WRITTEN BY ANNE DE BRAY AND DAVID J HODSON

Obesity and type 2 diabetes are prevalent, chronic, metabolic conditions which have a significant impact upon the individual as well as on healthcare systems and economies. In addition to the daily burden of these conditions, obesity and type 2 diabetes increase the risk of developing serious long-term complications, such as heart attacks, kidney failure and lower limb amputations. The progressive nature of these conditions has driven the need to develop new, more efficacious medications, which allow patients to live healthier lives for longer.

Agonists of the glucagon-like peptide-1 receptor (GLP1R), such as semaglutide (Ozempic/Wegovy), have revolutionised the world of obesity and diabetes treatment. This is not only because they cause significant weight loss and improvement in glucose control, but also because dose escalation is permitted without the risk of hypoglycaemia.

More recently, tirzepatide, a dual agonist of the GLP1R and the glucose-dependent insulinotropic polypeptide receptor (GIPR), has shown even better results in people with obesity[1] and type 2 diabetes.[2] This dual agonism is curious, since GIPR agonism alone is associated with weight gain in rodents, and loss-of-function human variants in the GIPR are associated with lower body mass index.[3]

Figure 1. The chemical structures of (a) tirzepatide, (b) acylated daLUXendins544+/660+ and (c) non-acylated daLUXendin544/660/651-d12. The daLUXendin molecule is a mutant of tirzepatide, with a substitution of serine for cysteine at position 39 to allow for fluorophore conjugation, which can only be achieved with a C-terminal reactive amino acid such as cysteine. Images created using BioRender.com



QUESTIONS REGARDING DUAL GLP1R/GIPR AGONISM

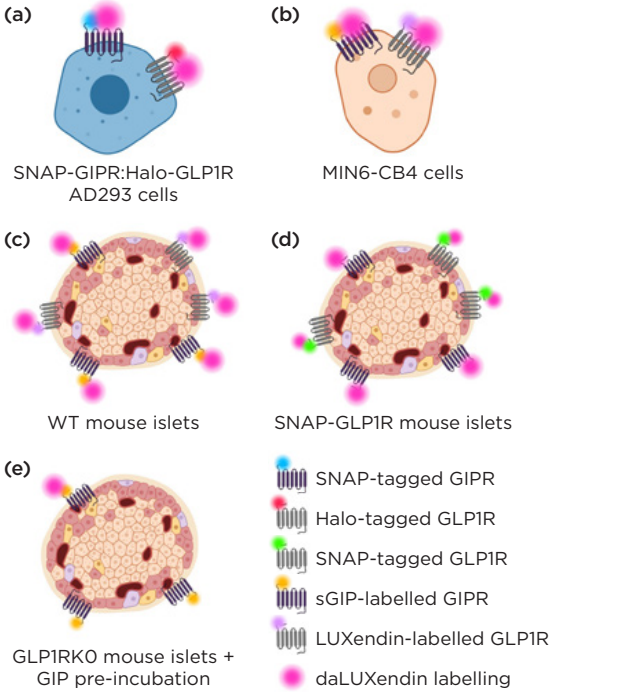
Whilst the pharmacology of tirzepatide has been explored, there remains uncertainty regarding tirzepatide's targets within the body, and whether differences in brain access play a role in its superior efficacy compared with GLP1R agonists.

There are many techniques to identify the presence of a receptor or its gene expression, such as reporter animals and antibodies. However, discordance has been reported between GLP1R gene expression and final protein expression.[4] Furthermore, the GLP1R and GIPR are low-abundance receptors, and generating antibodies with sufficient sensitivity and specificity is challenging.[5] Additionally, these techniques are unable to provide information on the brain and peripheral sites accessed by dual agonists, which is the key next step towards understanding their efficacy as well as informing future drug development.

daLUXendins TO EXPLORE DUAL GLP1R/GIPR AGONISM

To allow us to address these questions, we generated novel, fluorescent, dual GLP1R/GIPR probes, termed dual agonist LUXendins (daLUXendins), by coupling a fluorophore directly onto a modified tirzepatide molecule. We had previous success in using this coupling technique to generate a range of highly fluorescent and specific GLP1R probes, LUXendins.[6] The coupling technique is versatile and permits the addition of fluorophores with a range of properties and colours to suit various experiments.

Figure 2. daLUXendins show the ability to label GIPR and GLP1R when overexpressed and endogenously expressed. daLUXendin labelling (pink) co-localised with labels for GIPR/SNAP-GIPR and GLP1R/Halo-GLP1R in (a) AD293 cells, (b) MIN6-CB4 cells and (c) wild-type (WT) mouse islets. (d) daLUXendin also labelled endogenously expressed GIPR and co-localised with SNAP-GLP1R in islets from the transgenic SNAP-GLP1R mice. (e) daLUXendin labelling was reduced by around 50% in islets from GLP1R knockout mice and further reduced by pre-incubation with excess GIP agonist. Images created using BioRender.com



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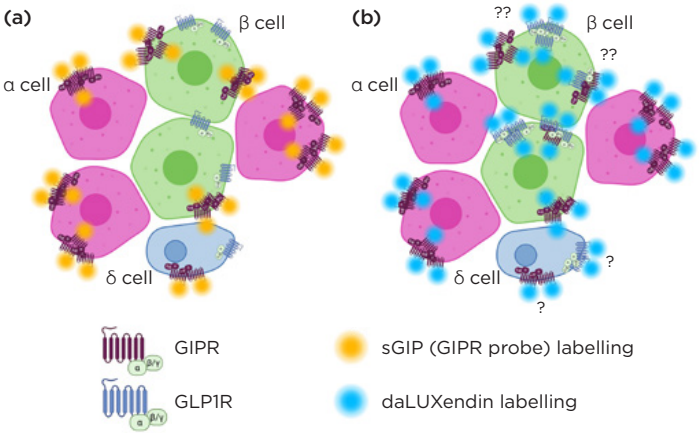

Figure 3. dSTORM imaging found that (a) the GIPR agonist probe sGIP engaged receptors into clusters, or nanodomains, which typically engage many more than the three receptors depicted in this simplified schematic. (b) daLUXendin engaged a greater number of nanodomains. However, daLUXendin engaged the same number of receptors per nanodomain and nanodomains were the same size as sGIP-induced nanodomains. The presence of GLP1R on α and δ cells remains unclear, and whether the increase in nanodomain formation with daLUXendin is due to increased homotypic interactions (GIPR–GIPR and GLP1R–GLP1R) or heterotypic interactions (GIPR–GLP1R) is uncertain. Created using BioRender.com

Acylated (+) and non-acylated red (daLUXendin544+/daLUXendin544) and far-red (daLUXendin660+/daLUXendin660) probes were synthesised for conventional imaging, as well as a probe adapted for super-resolution imaging (daLUX651-d12) (Figure 1).

TESTING OUR HYPOTHESES

We hypothesised that the superior efficacy of dual GLP1R/GIPR agonism over single GLP1R agonism could be due to:

- a different profile of receptor(s) engaged on synergistic cell and neurone types
- increased access into the brain, to more potently target appetite regulation centres
- differences in higher-order signalling events, such as preferential interactions between GLP1R and GIPR at the cell surface.

To interrogate each of these lines of investigation, we first assessed the daLUXendin probes pharmacologically and then validated their specificity in a range of relevant settings, including cell lines which over-expressed self-label enzyme-tagged GLP1R/GIPR, and mouse islets (Figure 2).

Both daLUXendin probes are potent GLP1R/GIPR agonists at mouse and human receptors. Tirzepatide is an imbalanced agonist, favouring GIPR over GLP1R in humans, but the opposite in mice.[7] The chemical modifications made to daLUXendin increased functional selectivity at the mouse GIPR, allowing daLUXendin660 to confer more human-like properties on dual agonism in mice.

Differing from single GLP1R agonists, which primarily target β cells, daLUXendin labels α, β and δ cells in mouse islets and islets derived from human induced pluripotent stem cells. Further testing in mouse islets revealed that daLUXendin probes generate the formation of GLP1R/GIPR nanodomains, which are important for GLP1R signal amplification.[8] The number of nanodomains is increased compared to that seen with single GIPR agonist probes, but without change to the number of receptors engaged per nanodomain or the size of the nanodomain (Figure 3).

After peripheral administration, the depth of daLUXendin access to the brain was similar to that previously reported for single agonists and limited to the circumventricular organs, specialised areas of the brain with a reduced and plastic blood-brain barrier. Following intraventricular administration, daLUXendin probes were able to label tanycytes, specialised ependymal cells which line certain circumventricular organs, the third ventricle and hypothalamus, and which mediate the transport of peptides across these areas.

Together, these results suggest that the superior efficacy of dual GLP1R/GIPR agonists stems from differences in the types of engagement and manner by which they engage islet cells, neurones and receptors, rather than the extent of brain penetration. In the islet, dual agonists engage α, β and δ cells, and therefore probably activate multiple paracrine mechanisms to enhance insulin secretion.[9] Tanycytes probably convey dual agonists from the bloodstream to the cerebrospinal fluid to important feeding centres within the brain. Engagement of GLP1R/GIPR nanodomains is likely to contribute to signalling robustness within target organs.

THE NEXT STEPS

Going forward, functional interrogation of the islet cells, neurones and supporting cells targeted by dual GLP1R/GIPR agonists would help confirm their contribution to glucose lowering and food intake.

Additionally, agonists are under development that target the glucagon receptor (GCGR) in the form of triple GLP1R/GIPR/GCGR agonists, showing superior efficacy to dual GLP1R/GIPR agonists. The daLUXendin probes could be modified to incorporate GCGR action and address current uncertainties, such as how superior weight loss is achieved when GCGRs are considered to be largely absent in the brain.

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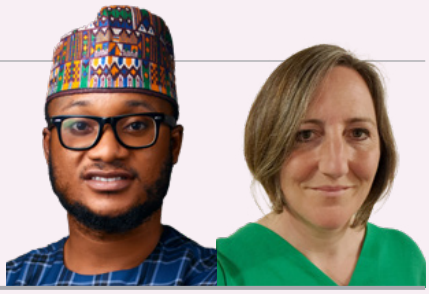
MAN'S BEST FRIEND
AN UNLIKELY ALLY IN THE FIGHT AGAINST OBESITY

WRITTEN BY ENOCH ALEX AND ELEANOR RAFFAN



Obesity is a global health challenge for both humans and our canine companions. In the UK, over 60% of adult humans and a similar proportion of pet dogs are overweight or obese.[1] Living alongside us in our homes, dogs share an 'obesogenic' environment, characterised by ready access to energy-dense food and increasingly sedentary lifestyles.[1]

For decades, researchers have relied on rodent models to unpick the complex biology of energy balance. Whilst invaluable, these models have their limitations, particularly as key metabolic pathways in rodents can have important differences compared with human physiology.[1–3] Given these limitations, dogs may become a powerful ally in this field of research.

THE CANINE ADVANTAGE IN GENETIC DISCOVERY

Studying the genetics of common obesity in humans is notoriously complex, with thousands of genetic variants, each contributing incrementally to an individual's susceptibility to weight gain.[1] This makes moving from a statistical association to biological insight a significant task.[4]

Dogs, however, offer a unique genetic architecture. Centuries of selective breeding have created distinct breeds, each representing a closed genetic population with long stretches of linkage disequilibrium.[1,5] This unique population structure makes it more straightforward to map genes for complex traits such as obesity.[5,6] In essence, the genetic signals are stronger and easier to find.

A CASE STUDY: THE HUNGRY LABRADOR

A compelling example of this canine advantage can be seen with Labrador retriever, a breed famously predisposed to obesity. Raffan *et al.* identified a 14-bp deletion in the pro-opiomelanocortin (*POMC*) gene,[3] which is carried by approximately a quarter of all Labradors. This gene is a cornerstone of the leptin–melanocortin pathway, which is the master regulator of food intake and energy balance in the brain.[3,7]

The Labrador *POMC* mutation doesn't disrupt the entire gene. Instead, it specifically prevents the production of two neuroactive peptides derived from cleavage of the gene product: β-melanocyte-stimulating hormone (β-MSH) and β-endorphin, while leaving production of a third peptide, α-MSH, intact.[3] This is an important detail, because rodent models, the workhorse of metabolic research, naturally lack the cleavage site to produce β-MSH.[2,3] They rely solely on α-MSH for melanocortin signalling. Humans, like dogs, produce both, but patients with variants affecting only β-MSH were hard to find and not available for systematic study. The Labrador, therefore, provides a naturally occurring model to investigate the specific roles of these peptides, an opportunity not readily available elsewhere.[2,3]

So, what happens when these peptides are missing? In a follow-on study, our group showed that affected dogs are not just hungrier, displaying greater motivational salience for food in a 'sausage in a box test', but they also have a significantly lower resting metabolic rate, burning approximately 25% fewer calories at rest than dogs without the mutation (Figure).[2] This 'double whammy' of increased hunger and reduced energy expenditure powerfully explains their predisposition to weight gain.[2] This finding implicates β-MSH and/or β-endorphin as critical in regulating energy expenditure, a role that was previously obscured by the limitations of rodent models. In a pleasing corroboration of our findings, a large biobank-scale project recently identified a *POMC* mutation in Northern Europeans that increases obesity by disrupting β-MSH production in people.[8]

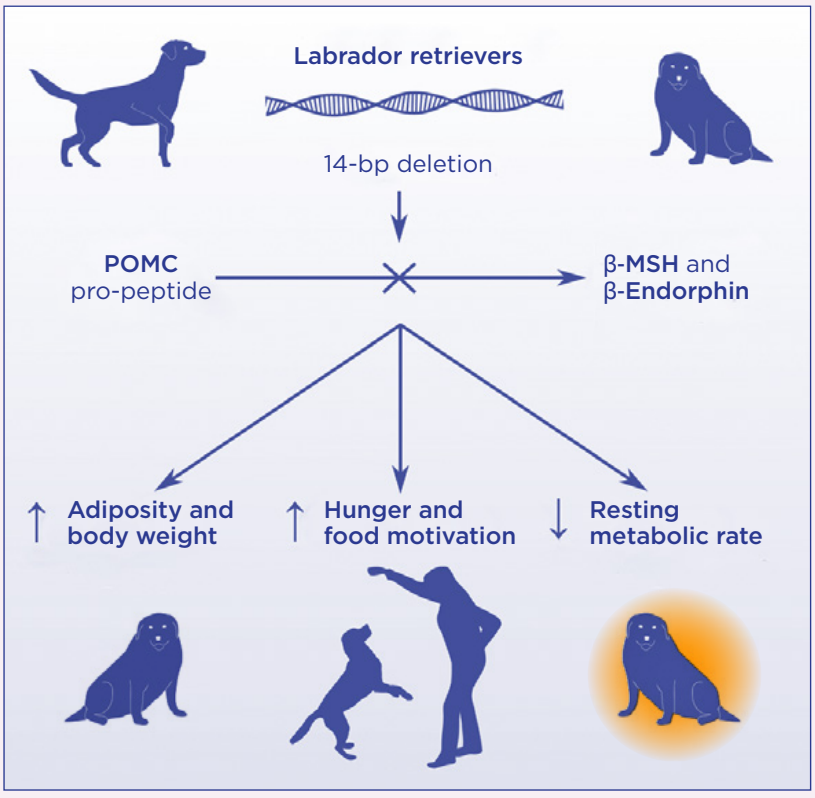
FROM CANINE GWAS TO HUMAN BIOLOGY

The story doesn't end with single-gene discoveries. The tractability of the dog genome now allows for successful genome-wide association studies (GWAS). In a recent study, our group conducted the first successful canine GWAS for a canine measure of adiposity, body condition score, identifying several new obesity-associated loci.[9]

The top hit was within a gene called *DENND1B* (DENN domain-containing 1B). Each copy of the risk allele was associated with approximately 8% greater body fat.[9] Taking an innovative cross-species approach, this gene was further investigated in human obesity datasets and it was found that variants in the human *DENND1B* gene are also associated with both common and rare forms of obesity.[9]

Molecular studies revealed that *DENND1B* plays a previously unsuspected role in regulating the trafficking of the melanocortin 4 receptor, a critical controller of energy homeostasis.[9] The work validated a powerful new paradigm: using the canine model not just to confirm known pathways, but to discover entirely new obesity genes and mechanisms that are directly relevant to human health.

A 14-bp deletion in the *POMC* gene in Labrador retrievers prevents the production of β-MSH and β-endorphin. This genetic variant is associated with increased adiposity, higher food motivation and decreased resting metabolic rate. POMC, pro-opiomelanocortin; MSH, melanocyte-stimulating hormone.



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MAN'S BEST FRIEND IN RESEARCH

Our pet dogs are more than just companions; they can be valuable, spontaneously occurring models of complex human disease. By studying their unique genetics in the context of our shared environment, we can accelerate the pace of discovery. The insights gained from the hungry Labrador retrievers have already refined our understanding of the melanocortin pathway.[2,3] As we continue to study dogs, there is potential to uncover new therapeutic avenues that could one day benefit both ends of the leash.

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OBESITY AND CARDIOVASCULAR DISEASE: CORE RELATIONSHIPS AND MANAGEMENT OPTIONS

WRITTEN BY SAFWAAN ADAM AND AKHEEL A SYED

Obesity is commonly defined as a body mass index (BMI) ≥30kg/m^2. Lower cut-offs are used in high-risk groups, such as South Asian, Chinese, Arab and Black populations. It is a long-term metabolic disease that exerts a substantial but modifiable influence on cardiovascular disease (CVD).[1]

Obesity confers increased CVD risk in a multimodal fashion by its association with established CVD risk factors including hypertension, dyslipidaemia and insulin resistance.[1] It is also now increasingly clear that obesity itself independently contributes to coronary artery disease (CAD) and heart failure.[1,2]

PATHOPHYSIOLOGICAL PATHWAYS LINKING OBESITY TO CAD

Obesity is associated with pathological alterations in systemic and vascular inflammation, adipokines, insulin resistance, lipids and endothelial function (Figure). Individuals with obesity typically demonstrate a chronic pro-inflammatory profile, with elevations in tumour necrosis factor-α, high-sensitivity C-reactive protein and interleukins including IL-1α, IL-1β and IL-6.[1,3] These cytokines contribute to endothelial dysfunction, oxidative injury and macrophage lipid accumulation within arterial walls.[1]

Obesity-related adipokine changes with increases in leptin (pro-inflammatory) and reductions in adiponectin (anti-inflammatory) have also been demonstrated to increase the risk of CAD.[1] Furthermore, by worsening insulin resistance, with a consequent excess of advanced glycation end products and reactive oxygen species, excess delivery of fatty acids to the myocardium (cardiac lipotoxicity) and endothelial dysfunction, obesity markedly increases the risk of atherosclerosis and CAD.[1]

OBESITY AND HEART FAILURE

Epidemiological data consistently show a higher incidence of heart failure among people with obesity, even when accounting for traditional risk factors. Progressive elevations in BMI correspond to higher risk of heart failure in a graded manner.

Clinically, this risk expresses itself most clearly in heart failure with preserved ejection fraction (HFpEF). Patients typically demonstrate a combination of increased left-ventricular (LV) wall thickness, impaired diastolic filling, reduced natriuretic peptide release and elevated pulmonary pressures during exertion.

These abnormalities translate into reduced exercise tolerance and symptom burden disproportional to structural findings. Additionally, obesity-prevalent respiratory conditions, such as obesity hypoventilation syndrome and obstructive sleep apnoea, compound the pathology by amplifying sympathetic drive, promoting intermittent hypoxia and increasing haemodynamic load.[1,4]

THE OBESITY PARADOX: METHODOLOGICAL ARTEFACT

Although obesity clearly contributes to the pathogenesis of heart failure, some studies have suggested that higher BMI may be associated with improved survival, once heart failure is established: the so-called 'obesity paradox'.[5]

Closer examination, however, indicates that these findings are prone to methodological bias. Frailty and unintentional weight loss disproportionately affect individuals with lower BMI, while treatment patterns often differ across weight categories. A study incorporating more detailed anthropometric measures of visceral obesity (waist-to-height ratio), rather than solely BMI, demonstrated that any apparent survival advantage is attenuated in people with central obesity.[6] Therefore, the 'obesity paradox' probably does not represent a true biological phenomenon, but rather reflects methodological limitations such as collider bias.[7]

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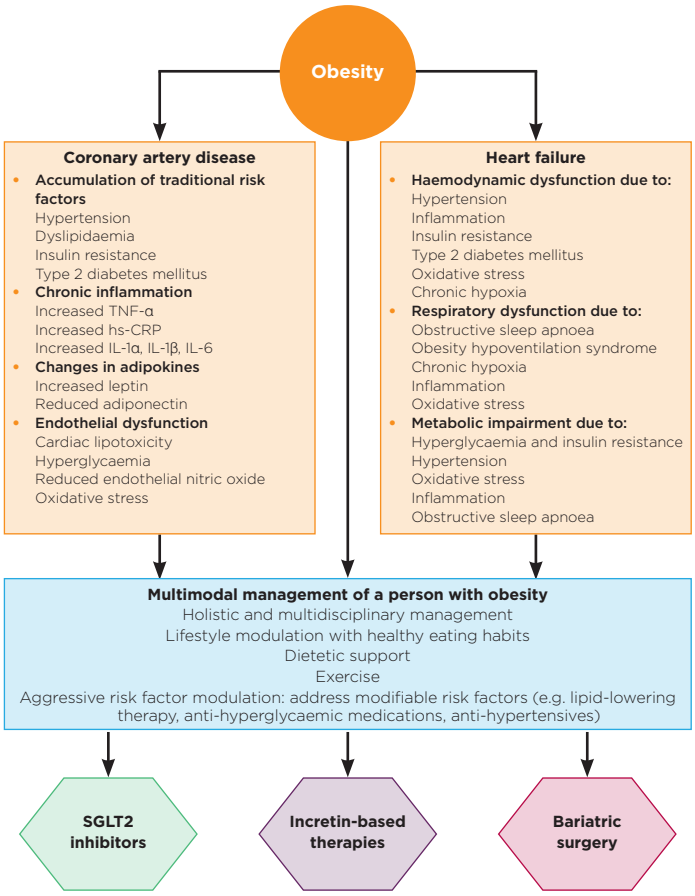

A summary of the key pathogenic mechanisms by which obesity increases the risk of both coronary artery disease and heart failure. Also demonstrated are the key therapeutic considerations for managing a patient with obesity, to prevent adverse cardiovascular conditions in those without established cardiovascular disease and to improve outcomes in those with pre-existing cardiovascular disease. hs-CRP, high-sensitivity C-reactive protein; TNF-α, tumour necrosis factor-α.

THERAPEUTIC STRATEGIES: A CARDIOMETABOLIC APPROACH

Managing obesity in the context of CVD requires a broad, co-ordinated approach. Although dietary and behavioural interventions are essential foundations for weight management, durable success is difficult to achieve without additional therapeutic support, particularly in those with significant or long-standing obesity.[8]

Medical management options

In recent years, pharmacotherapy has become an increasingly important component of cardiometabolic care. Sodium–glucose cotransporter-2 (SGLT2) inhibitors, for example, provide consistent reductions in heart failure hospitalisations and cardiovascular mortality – benefits that appear across BMI categories and are not solely attributable to weight loss.[1] These therapies modulate renal sodium handling, improve circulatory efficiency and confer metabolic advantages that contribute to their cardiovascular effects.[1]

Glucagon-like peptide-1 receptor agonists (GLP1-RAs) have demonstrated substantial weight-loss efficacy alongside favourable cardiovascular risk factor modulation.[1] Emerging data in obesity-related HFpEF suggest improvements in symptoms, exercise capacity, inflammatory markers and mortality.[1,9] Dual incretin agonists also show promise and may provide even greater CVD risk reduction,[10,11] although long-term data are awaited.

Bariatric surgery for cardiometabolic disease

For individuals with severe obesity, bariatric surgery remains the most effective long-term strategy for achieving significant weight reduction. Beyond weight loss, improvements have been observed in LV mass, diastolic performance, endothelial function, inflammation, lipid transport and multiple cardiometabolic risk factors, with demonstrable reductions in CVD mortality.[1,12]

However, individuals with CAD or heart failure require thorough cardiovascular evaluation and careful perioperative planning. Procedures with lower physiological demand, such as sleeve gastrectomy, may be preferable in those with advanced cardiac disease.[1]

CONCLUSION

Obesity is a complex, multisystem disease that plays a critical role in the development and progression of CAD and heart failure. Recognising obesity as a primary driver of CVD reinforces the need for early, proactive intervention. Treatment of obesity (both medical and surgical) can potentially alter the pathological trajectory from excess adiposity to cardiovascular failure.

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An interview with…
GILES YEO
GENES, OBESITY AND COMMUNICATION

Giles Yeo MBE is Professor of Molecular Neuroendocrinology and programme leader at the MRC Metabolic Diseases Unit in Cambridge. He is the Honorary President of the British Dietetic Association, President of the British Society for Neuroendocrinology and a high-profile and prolific science communicator. He was awarded the Society for Endocrinology Medal in 2022. Editor of *The Endocrinologist*, Kate Lines, caught up with Giles to discuss his career and work in the genetics of body weight and obesity.

What led you to the field of obesity?
My PhD, at Cambridge, was on the molecular genetics of Japanese pufferfish, which wasn't going to pay the rent. I had a post-doc position waiting for me back in California, where I'm from, but I'd met a girl (now my wife), so I decided to stay in the UK.

I went knocking on doors looking for a position, and the second door I knocked on belonged to Steve O'Rahilly. This was in 1998, six months after publication of the first paper to provide genetic evidence that leptin was a regulator of energy balance in humans. Steve and Sadaf Farooqi (then a PhD student) had begun to collect a cohort of severely obese children and they needed a geneticist. They hired me on the spot.

On my first day, Steve said 'Here's the melanocortin 4 receptor gene. Go screen it.' We found the first cause of obesity linked to that gene. It was my first paper of my post-doc and a big success. I've been in the field ever since.

'Genetics can now be done well at scale, but we need to be able to match behaviour and observable characteristics with this insight.'

What are you working on right now?
Now we know that the genetics of body weight are the genetics of how our brain controls feeding behaviour.. So, I've become an accidental neuroscientist, looking at how the brain regulates food intake, as well as a glorified cartographer, making maps of the feeding circuits within the human brain.

At the beginning of 2025, we produced a spatial cellular map of the human hypothalamus from the donated brain of a normal-weight individual, and we're currently putting together the same thing for the hindbrain. These will be the benchmark against which we can map differences in donated brains from individuals across the body weight spectrum. We have brains donated from people who were extremely obese and people who were severely underweight, so we're going to map the feeding circuits in these.

Using these maps and other tools, including neurones derived from induced pluripotent stem cells, we want to continue to functionally characterise human genes that are potentially linked to obesity. We're also looking at how the new generation of incretin-based weight-loss therapies are working, or could work, mechanistically.

What is the biggest current challenge in your field?
Genetics can now be done well at scale, but we need to be able to match behaviour and observable characteristics with this insight, and the difficulty is in phenotyping. For instance, measuring what people eat accurately, at scale. This will help us understand things like variation in response to weight-loss therapies or why obesity comes with ill health in some and not others. I'm hoping there will be engineering solutions to these challenges.

And the most exciting development?
Never have we had more successful tools to treat a lot of people with obesity. The new weight-loss therapies have been a complete game changer and, since they hit, my world has gone bananas. No-one in the field would've predicted the broad effectiveness and safety of these drugs, and it has generated so much interest in what we do.

But we mustn't blow the opportunity. We need to minimise risks and find other approaches to target the brain to reduce food intake.

'Be more of a pain to replace than to keep. Find a niche, fill it and be useful to people. Make yourself invaluable.'

What do you enjoy most about your work?
Of course, I love the science, but the aspect that thrills me the most is speaking about the field. From public outreach to teaching students and speaking at conferences.

What is your advice for people starting in research?
When I dropped my son off at uni a few years ago, I gave him a piece of advice that I've lived by through my career, 'Be more of a pain to replace than to keep. Find a niche, fill it and be useful to people. Make yourself invaluable.'

INSIGHTS INTO METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE

WRITTEN BY CHIOMA IZZI-ENGBEAYA

Metabolic dysfunction-associated steatotic liver disease or MASLD (previously known as non-alcoholic fatty liver disease or NAFLD) occurs when there is excessive accumulation of fat in the liver, in the presence of cardiometabolic risk factors and without a history of high alcohol intake.

Recent estimates suggest MASLD affects 32–38% of adults worldwide.[1] Worryingly, the high prevalence of MASLD in adults is mirrored in children (5–11% in the general paediatric population, 30–50% in children with obesity).[2] Insulin resistance, elevated free fatty acid delivery to the liver (from dietary sources and peripheral lipolysis), and increased intrahepatic *de novo* lipogenesis play key roles in the pathogenesis of MASLD, with significant contributions from genetic and environmental factors.

UNDERSTANDING MASLD

MASLD ranges from liver steatosis (MASL), to liver steatosis with inflammation and hepatocyte ballooning (metabolic dysfunction-associated steatohepatitis, MASH), through to fibrosis (F1–F3) and cirrhosis (F4). All stages of MASLD are associated with increased morbidity and mortality. However, the strongest associations exist between fibrosis stage and all-cause mortality, with clinically significant fibrosis (i.e. ≥F2) associated with more than double the risk of dying compared with MASLD without fibrosis.[3]

'As the awareness of MASLD increases … endocrinologists need to be involved in developing care pathways and delivering care to patients with MASLD.'

Varying fibrosis progression rates (18–41%) and regression rates (13–37%) have been reported, with higher rates of progression occurring as the severity of fibrosis increases.[4] On average, progression from one stage to the next occurs over 10 years.[4] If progression of MASLD is not halted or reversed, the potential future consequences for society in terms of poor patient outcomes and high healthcare utilisation are significant. For instance, MASH cirrhosis has become one of the leading causes of liver failure requiring transplantation.[5]

The main causes of mortality in patients with MASLD are cardiovascular events and extra-hepatic cancer, with liver failure and/or hepatocellular cancer accounting for the minority of deaths.[6] Therefore, addressing cardiovascular, metabolic and/or hepatic risk factors (i.e. weight reduction in people with overweight/obesity, smoking cessation, optimisation of blood pressure and hyperlipidaemia, dietary modification, alcohol intake reduction) have been the mainstay of the management of MASLD. However, there is now an emerging pipeline of disease-modifying agents.

ITS RELEVANCE TO ENDOCRINOLOGISTS

Amongst people with type 2 diabetes or obesity, ~70% have MASLD and ~35% have MASH. Both type 2 diabetes and obesity are associated with increased likelihood of progression to advanced fibrosis.[7,8] Patients with other endocrine conditions (polycystic ovary syndrome, male hypogonadism, Turner syndrome, growth hormone deficiency) and postmenopausal women may have elevated risks of developing MASLD and/or MASH fibrosis.[9] Therefore, endocrinologists are likely to manage many patients who have MASLD as a co-morbidity.

Due to the central role of insulin resistance in the pathophysiology of MASLD, as well as the novel endocrine treatments for MASLD that are being developed, endocrinologists are well-placed to take leading roles in the management of this condition.

Resmetirom (a liver-directed thyroid hormone receptor-β agonist) is the first agent to be licensed specifically for the management of MASH fibrosis. It leads to MASH resolution and fibrosis regression, and lowers low-density lipoprotein cholesterol.[10] In addition to causing weight loss, semaglutide (a glucagon-like peptide-1 (GLP-1) receptor agonist), tirzepatide (a GLP-1–glucagon receptor co-agonist), retratrutide (a GLP-1–glucagon–glucose-dependent insulinotropic polypeptide receptor tri-agonist) have been demonstrated to have beneficial effects on steatosis, MASH and/or fibrosis. Multiple randomised control trials are underway to investigate the activity of other gut hormone mono- and co-agonists in MASLD. Non-gut hormone treatments (e.g. fibroblast growth factor-21 analogues) are also being assessed, with phase 3 studies in progress.

PATIENT CARE AND IMPROVING OUTCOMES

Due to the high prevalence of MASLD in the population, most patients will be managed in primary care. International guidelines suggest risk stratification to identify patients with MASLD who require specialist review. Patients with more advanced disease are currently managed in secondary care, predominantly by hepatologists. However, practice is evolving, with some patients being managed in specialist joint hepatology–endocrinology clinics, including input from dietitians and other healthcare professionals. This approach provides more holistic care, which may lead to better outcomes for patients.

As the awareness of MASLD increases, and evidence for the efficacy of different management options emerges (with subsequent licensing of medications for MASLD), endocrinologists need to be involved in developing care pathways and delivering care to patients with MASLD. Alongside the ever-increasing plethora of medications for the management of obesity and type 2 diabetes, the diverse emerging pipeline of drugs for MASLD, and the opportunity for management of multi-morbidity with single agents, there is a need for high-quality prospective studies and expertise in endocrinology to guide selection of agents tailored to patients with different co-morbidity profiles.

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PHARMACOGENOMICS A CHANCE TO MAKE MEDICINES SAFER FOR EVERYONE

WRITTEN BY JESSICA WRIGHT AND NICOLETTA CHAROLIDI

From appetite suppression to social-media hype, 'glucagon-like peptide-1 (GLP-1) medicines' have transformed the conversation around obesity treatment. But their rise has added fresh urgency to the enduring question, 'Why do some patients experience severe side effects while others don't?'

Adverse drug reactions (ADRs) currently account for one in six hospital admissions, with an estimated cost to the NHS of over £2 billion annually.[1] ADRs represent a significant burden on patients, clinicians and the healthcare system as a whole. Hence, there is both an economic and a public health imperative to better manage ADRs.

Personalised medicine offers a new opportunity to reduce, or even prevent, ADRs before they occur. The Government's recent '10 Year Health Plan for England' highlights the potential of pre-emptive testing before prescription to increase both the effectiveness and the safety of medicines.[2]

GLP-1 receptor agonists and dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists (or 'GLP-1 medicines') are a relatively new class of drugs with a number of recognised side effects, particularly during the first months of use.[3] These medicines are often viewed as a breakthrough in supporting weight management and treating obesity.[4] However, careful safety monitoring is essential, and pharmacogenomic research may assist with ensuring these medicines continue to be both safe and effective.

THE MHRA'S ROLE AND GUIDANCE

The Medicines and Healthcare products Regulatory Agency (MHRA) plays a central role in ensuring that medicines used in the UK remain safe and effective throughout their lifecycle. For all medicines, including GLP-1 medicines, this means continuously reviewing safety data as new information emerges, and communicating findings through regular safety communications and guidance available on the MHRA website.[5]

THE YELLOW CARD SCHEME

The MHRA continuously gathers and evaluates suspected ADRs via the Yellow Card scheme, which plays a vital role in tracking the safety of medicines in real world use.[6] New medicines are closely monitored to ensure that any emerging safety concerns are identified promptly.

Recently authorised GLP-1 medicines are included in the Black Triangle scheme, meaning that healthcare professionals are asked to report all suspected ADRs for these products through the Yellow Card scheme.[7] Healthcare professionals can also subscribe to the MHRA's Drug Safety Update for the latest advice and regulatory news.[8]

THE YELLOW CARD BIOBANK PILOT STUDY

The Yellow Card Biobank is a collaboration between the MHRA and Genomics England designed to improve our understanding of how a patient's genetic makeup might increase their risk of side effects.[9] By taking part, patients contribute to research that could explain why some individuals experience ADRs while others do not.

The Biobank expands the utility of the Yellow Card scheme by inviting patients, or healthcare professionals reporting on their behalf, to support the study. Participants can access study information and sign up online or by post, answer a short questionnaire and provide a saliva sample using a kit delivered to their home. The samples are whole-genome sequenced, and the resulting data will be hosted in the Genomics England Research Environment for analysis by MHRA, Genomics England and the research community.[10]

GLP-1 MEDICINES AND ACUTE PANCREATITIS

Pancreatitis, specifically in its acute form, is a clinical diagnosis associated with GLP-1 medicines, and the focus of both regulatory reviews and Biobank recruitment. It is a recognised but uncommon side effect of GLP-1 receptor agonists, and is included in the product information for these medicines. While cases have been observed in both clinical trials and post-marketing settings, the biological mechanisms and potential genetic factors remain unclear.

The Yellow Card Biobank is now investigating whether an individual's genes may influence their risk of developing acute pancreatitis while taking GLP-1 medicines. This work could help explain why only a small number of people are affected, and also support more tailored, evidence-based, regulatory decisions in the future.

RECRUITMENT

Until January 2026, the Biobank is recruiting patients aged 18 years and over from across the UK, who have been hospitalised with acute pancreatitis after taking a GLP-1 medicine for any indication, including weight loss. Cases of pancreatitis caused by gallstones or bile duct stones, which can occasionally occur following rapid weight loss, are excluded from the study.

HOW HEALTHCARE PROFESSIONALS CAN HELP

We are asking healthcare professionals to submit Yellow Card reports on behalf of patients taking GLP-1 medicines who develop acute pancreatitis. Please provide as much detail as possible when completing the form, selecting 'Yes' when asked whether you agree to be contacted about the Yellow Card Biobank.

If the patient is eligible, the Biobank team will contact you for help in reaching out to the patient. Further participation will always be the patient's choice. The Yellow Card Biobank also welcomes direct contact from healthcare professionals with patients who may be eligible.

For more information about the study, or to make a request to access the data, email the study team on yellowcardbiobank@mhra.gov.uk.

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CONSIDERATIONS IN SAME-DAY DISCHARGE IN BARIATRIC SURGERY

WRITTEN BY SARA JAMEL, PATRICIA ORTEGA AND SANJAY PURKAYASTHA

Obesity is a major global health concern, due to its association with multiple chronic diseases and increased mortality risk. Conventional treatment approaches, including lifestyle modification and pharmacotherapy, have limited long-term effectiveness in achieving sustained weight loss. Metabolic and bariatric surgery (MBS) has emerged as the most effective intervention for severe obesity, and the postoperative length of stay following these procedures has progressively shortened over the past decade.[1]

Same-day discharge (SDD) following MBS has gained increasing attention, particularly for the two most common procedures: Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). The majority of published studies originate from the USA and predominantly involve SG. High success rates for SDD in both SG and RYGB have been demonstrated through recent meta-analyses and systematic review, with acceptable morbidity and reoperation rates.[1] Importantly, readmission rates remain low: typically under 4%. Among readmissions following SDD SG, nausea and vomiting are the most frequent causes, emphasising the importance of optimal perioperative anaesthesia and robust postoperative management protocols.[2,3]

PATIENT SELECTION

Appropriate patient selection is crucial for ensuring the safety and success of an SDD approach. Most studies had similar inclusion criteria, typically involving thresholds for age, body mass index (BMI) and ASA (American Society of Anesthesiologists) classification. A large cohort study of SDD SG identified female sex, gastroesophageal reflux disease, renal insufficiency and intraoperative drain placement as independent predictors of 30-day readmission.[2] In addition, data from the Bariatric Outcomes Longitudinal Database assessing SDD for RYGB demonstrated that male sex, age >50 years, BMI 50–70kg/m^2 and the presence of more than five co-morbidities were independent risk factors for mortality for this cohort.[4]

'With careful patient screening, standardised perioperative care and well-defined discharge protocols, SDD can deliver outcomes comparable to inpatient care, while reducing costs and improving patient experience.'

DISCHARGE CRITERIA

Discharge criteria and protocols were described in few studies, with an emphasis on established discharge guidelines, assessing parameters such as consciousness, oxygenation, circulation, respiration and mobility, along with oral intake, urine output, pain and nausea control.[5] A common criterion was perioperative intravenous hydration to facilitate recovery and minimise readmission risk,[6] with other studies incorporating blood testing, including a haemoglobin check.[3,7]

ROUX-EN-Y GASTRIC BYPASS VERSUS SLEEVE GASTRECTOMY

Understandably, surgeons have been more cautious about applying SDD to RYGB, as it is technically more complex than SG, involving two gastrointestinal anastomoses and consequently longer operative times and a higher potential for perioperative complications. Despite these concerns, studies report near 100% SDD success rates for RYGB, with readmission rates under 4%, comparable to those observed with standard inpatient care.[1] Furthermore, comparative studies between SDD and inpatient RYGB revealed no significant differences in readmission rates.[8] Notably, nausea and vomiting were not significant causes for readmission following SDD RYGB, contrasting with findings for SG.

COST CONSIDERATIONS

Cost considerations play an important role in improving access to MBS. However, data directly comparing the economic impact of SDD versus inpatient pathways remain limited. A single-centre prospective economic analysis by Ignat *et al.*[9] compared total costs (spanning preoperative evaluation to one-month postoperative follow up) between SDD and conventional inpatient bariatric surgery (SG and RYGB). The study demonstrated a 14.4% overall cost reduction in the SDD group, highlighting the potential financial benefits of this approach, without compromising patient safety or outcomes. Data on patient experience are not yet published but will provide an insight into patient views and expectations of their care pathways.

IN SUMMARY

SDD after MBS (particularly SG and, increasingly, RYGB) has proven to be a safe, efficient and cost-effective approach in appropriately selected patients. With careful patient screening, standardised perioperative care and well-defined discharge protocols, SDD can deliver outcomes comparable to inpatient care, while reducing costs and improving patient experience. As pressures build on healthcare systems, SDD represents a critical step in modern bariatric practice, combining safety, efficiency and patient-centred care.

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HOW DO I... MANAGE PREGNANCY AFTER WEIGHT-LOSS SURGERY?

WRITTEN BY RAJ VALAIYAPATHI AND TRICIA TAN

Weight-loss surgery offers the most effective long-term treatment for people living with obesity and its related complications, such as type 2 diabetes.[1] Of the metabolic bariatric surgery types, Roux-en-Y gastric bypass (RYGB) achieves the most significant and sustained weight loss.[2]

Around 80% of these procedures are performed on women, many of whom are of reproductive age.[3] For many, one of the most profound outcomes of surgery is the restoration of fertility. This has, in turn, given rise to a new and rapidly growing cohort in our antenatal clinics: women presenting with pregnancy after weight-loss surgery (PaWS).

This new patient population presents a distinct clinical paradox. On the one hand, PaWS is associated with welcome improvements in traditional obesity-related complications, such as hypertension and gestational diabetes (GDM). On the other, it introduces a new, challenging set of risks, including a higher prevalence of babies born small-for-gestational age (SGA), preterm delivery, and even neonatal death.[4]

For clinicians, this is not just a variation of a high-risk pregnancy; it is an entirely new frontier. It requires a fundamental shift in our grasp of the underlying mechanisms and has important implications for management.

MECHANISMS

Understanding why these new risks emerge is key. The exact surgical changes that instigate weight loss create a unique physiological environment for pregnancy.

Balancing nutrition

Bariatric procedures are designed to cause malabsorption of key nutrients. Although patients are on micronutrient supplementation, the nausea and vomiting common in early pregnancy can upset this delicate balance. This can quickly lead to significant deficiencies in iron, vitamin B12 and vitamin D, all of which are critical for both maternal health and fetal development.

A battle for resources

The timing of pregnancy is critical. The first 12 months post-surgery are a period of rapid weight loss – a catabolic state. By contrast, pregnancy – particularly early gestation – is an anabolic state.[5] In a woman who conceives within the first 12 months of surgery, these two opposing metabolic drives compete, often resulting in reduced gestational weight gain and restricted fetal growth. The data are striking: the overall risk of a baby born SGA in PaWS is 23%, but this risk leaps to 31% if conception occurs within the first year.[6]

Post-bariatric hypoglycaemia

For many women, especially after RYGB, eating high-glycaemic index foods triggers a cascade. The altered gut anatomy contributes to changes in both gut hormones and glucose dynamics. There is accelerated glucose absorption with subsequent rapid, substantial, insulin secretion. This, in turn, can cause a 'crash', or severe post-prandial hypoglycaemia. This extreme glycaemic variability makes the standard oral glucose tolerance test (OGTT) for GDM not just non-diagnostic, but actively dangerous.

MANAGEMENT

Given these unique mechanisms, PaWS management must be proactive, multidisciplinary and evidence-based.

Collaboration with obstetric colleagues

These pregnancies should be managed as 'high-risk' pregnancies, and therefore it is critical that there is clear and frequent communication with supervising obstetric colleagues.

Vigilant nutritional surveillance

Offer nutritional monitoring with blood tests *in each trimester* as per British Obesity and Metabolic Specialist Society guidance.[7]

- **Blood tests:** ferritin, folate, vitamin B12, calcium (bone profile) and vitamins D and A. Those with long-limbed bypass or biliopancreatic diversion/duodenal switch also need monitoring of vitamins E and K.
- **Supplementation:** ensure women are on adequate multivitamins, vitamin D, calcium, folic acid, vitamin B12 and iron as needed.

Rethinking screening for GDM

Despite a higher risk of GDM in this cohort, the OGTT can trigger severe hypoglycaemia. The consensus recommendation is to screen at 24–28 weeks by self-monitoring of blood glucose or continuous glucose monitoring.

Managing the 'crash'

For women experiencing post-bariatric hypoglycaemia, specialist dietetic advice is essential. This includes small, frequent meals, omitting fluid intake 30 minutes prior to and after eating, increasing protein intake, and strict avoidance of high-glycaemic index foods.

Fetal growth monitoring

Given the high risk of SGA, clinicians should offer increased fetal growth monitoring, especially in GDM or if maternal gestational weight gain is inadequate.

Postpartum care

The need for supplementation does not end at delivery. Women must be supported with adequate micronutrients during breastfeeding, and reminded to continue lifelong multivitamins.

UNANSWERED QUESTIONS

While we have a strategy for managing the pregnancy itself, we are only just beginning to understand the longer-term effects in this cohort. The most pressing questions are no longer just about the mother, but also about the child. What are the effects of this unique *in utero* environment – one characterised by potential micronutrient deficiency and, crucially, extreme glycaemic variability – on a child's future cardiometabolic and neurocognitive development?

Studies across the world are following up women with PaWS longitudinally, to explore what these alterations in their physiology mean for both maternal health and the long-term development of the child. This research is vital. We must be able to counsel women not only about the risks to their pregnancy but also about the potential lasting health outcomes for their children. As bariatric surgery becomes more common, the PaWS population is growing. It is our responsibility to fill these gaps in our knowledge, to ensure the best possible start in life for the next generation.

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OBESITY AND DIABETES CARE INSIGHTS FROM AN ADVANCED CLINICAL PRACTITIONER

WRITTEN BY ALLAN DAVASGAIUM

Delivering joined-up care for people living with obesity and diabetes remains one of the most important and challenging aspects of metabolic medicine. Many patients transition between diabetes, weight-management, psychological and cardiovascular services, yet their needs often do not align with existing pathways.

As an Advanced Clinical Practitioner (ACP) within a busy endocrine and metabolic clinic, these service gaps are evident on a daily basis. Drawing on training through the World Obesity Federation's SCOPE Certification programme and postgraduate study in diabetes and endocrinology, my practice is grounded in evidence-based obesity management and guided by current international standards.[1,2]

MY BACKGROUND

My professional journey spans over 25 years, combining a foundation in applied biomedical science with extensive clinical experience across acute medicine, surgery, emergency care and critical care. This has provided deep insight into complex metabolic and systemic conditions, reinforcing the importance of multidisciplinary collaboration. These experiences underpin my specialisation in endocrinology, diabetes and metabolism, where clinical practice and research closely overlap. Integrating scientific understanding with frontline clinical expertise continues to shape my holistic, person-centred approach to metabolic care.

CLINICAL EXPERIENCE AND INCRETIN-BASED THERAPIES

My experience as lead nurse on multiple clinical trials involving glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptor analogues has provided insight into patient experiences across all phases of therapy. These include initiation, titration, long-term use, follow up and the effects of discontinuation. These observations align with major trial findings on incretin-based therapies, including semaglutide and tirzepatide.[3,4,5] While these agents have transformed therapeutic options, access and implementation across NHS services remain complex.[6]

'Demand for incretin-based therapies continues to rise, accompanied by longer waiting lists and a need for close follow up during dose escalation.'

ELIGIBILITY AND ACCESS

A persistent challenge is the narrowness of current commissioning criteria. GLP-1 receptor agonists are usually approved for people with type 2 diabetes or for those referred to specialist weight-management services, often requiring additional co-morbidities such as hypertension, dyslipidaemia or sleep apnoea.[2,6] In practice, referrals also come from cardiology, renal, respiratory and orthopaedic teams, where excess weight contributes to disease progression or delays essential procedures. For some, weight reduction is a prerequisite for surgery or transplantation, making timely pharmacological support clinically important.

For individuals with severe obesity, whose functional limitations significantly affect daily life, a multidisciplinary review within specialist services allows discussion of whether GLP-1 therapy may be appropriate under exceptional circumstances. Such multidisciplinary team decisions, supported by consultant oversight and clear documentation, help ensure equitable, evidence-based care.

OPERATIONAL AND PATIENT FACTORS

Demand for incretin-based therapies continues to rise, accompanied by longer waiting lists and a need for close follow up during dose escalation.[7] Variation in local interpretation of guidance can create inequities, while intermittent supply issues disrupt continuity of care.

Structured education and realistic expectations are vital. Glycaemic improvement often precedes measurable weight loss, which typically evolves over months.[3,8] Discontinuation is most often related to gastrointestinal effects or difficulties accessing medication rather than lack of efficacy.[9] Consistent follow up, dietetic and psychological input, and reinforcement of non-scale outcomes (energy, glycaemic stability, cardiometabolic risk reduction) support long-term engagement.[1,2]

THE EVOLVING ROLE OF THE ACP

Obesity pathways have historically centred on dietetic, psychological and surgical interventions, and the role of advanced nursing practice in pharmacological management is still emerging. With clear governance structures and close consultant collaboration, ACPs provide continuity, safety monitoring and holistic care that enhance patient experience and outcomes.[10]

'Ultimately, effective metabolic care extends beyond weight reduction: it encompasses improved health, function, confidence and overall quality of life.'

Within our GLP-1/GIP clinic, each patient undergoes a comprehensive baseline assessment, including anthropometry, metabolic and safety markers, and structured education on injection technique, side-effect management and lifestyle strategies.[6,11] Prescribing and titration of GLP-1 and GIP/GLP-1 receptor agonists are undertaken within my Trust-approved ACP prescribing scope, aligned with departmental governance and national guidance. Pharmacotherapy is positioned as an adjunct to sustained behaviour change, with gradual titration guided by clinical response and tolerability.[9]

Continuing professional development remains central to my role. The SCOPE Certification programme[1] provides an internationally recognised framework, while postgraduate training and ongoing clinical updates ensure alignment with evolving evidence and standards.

INFORMED AND SAFE PRESCRIBING

Patient understanding and safety-netting are fundamental. Before initiation, medications are reviewed, adjustments agreed upon and, where relevant, plans for insulin titration established. Enhanced retinal monitoring is arranged for patients with retinopathy due to the potential for early worsening with rapid glycaemic improvement.[9] 'SADMAN' sick-day rules (embedded within national acute-illness guidance) are reinforced, and GLP-1 therapy is aligned safely with SGLT2 (sodium–glucose co-transporter-2) inhibitor use when appropriate.[11]

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LOOKING AHEAD

Demand for integrated pathways addressing diabetes and obesity continues to grow. Establishing consistent national criteria, clearer referral routes for people without diabetes and greater recognition of ACP-led contributions would support equitable and sustainable care.[6] Patient feedback and peer-support initiatives are equally important in ensuring that service design remains responsive to real-world needs.

Ultimately, effective metabolic care extends beyond weight reduction: it encompasses improved health, function, confidence and overall quality of life. Continued collaboration across clinical, commissioning, research and patient networks will be essential to sustain progress in this evolving field.

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Disclaimer: the views expressed are those of the author and do not necessarily represent those of the NHS or any affiliated institutions.

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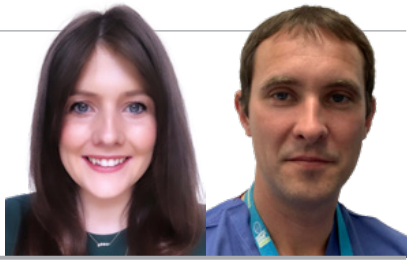
RECOGNISING ANDROGEN EXCESS LONG-OVERDUE PROGRESS IN WOMEN'S HEALTH

WRITTEN BY LAUREN CUSSEN AND MICHAEL O'REILLY



The first Society for Endocrinology Clinical Practice Guideline for the Evaluation of Androgen Excess in Women[1] provides a structured, evidence-based approach to identifying hyperandrogenism, as well as understanding its origins and its metabolic consequences.

Androgen excess is often dismissed as merely cosmetic, yet it affects millions of women. The inaugural guidelines from the Society for Endocrinology on female androgen excess offer an essential framework for assessment. These guidelines encourage clinicians to look beyond reproductive symptoms to identify underlying health issues and address the significant, lifelong metabolic risks associated with hyperandrogenism.

> "We are proud to pull together this Clinical Practice Guideline on the investigation of androgen excess in women, drawing on expertise from endocrinology, gynaecology and clinical biochemistry. This breadth of experience reflects the complexity of androgen excess in women and the multidisciplinary approach required to dissect challenging cases."
> Michael O'Reilly, Lead Author

AN UNDER-RECOGNISED EPIDEMIC

Androgen excess is a common, yet under-appreciated, condition in women's health, defined by clinical or biochemical evidence of increased androgen production.[2] It affects up to one in ten women of reproductive age and, less frequently, those who are postmenopausal. Hyperandrogenism most often presents with hirsutism, acne or female-pattern hair loss and, in more severe or prolonged cases, can progress to overt virilisation, including clitoromegaly, deepening of the voice and erythrocytosis.[3]

Despite its prevalence and lifelong impact, androgen excess may often be dismissed as a cosmetic or fertility-related concern. This reductive perspective contributes to prolonged diagnostic delays and fragmented care, with many women never investigated beyond reproductive symptoms. In a minority of cases, overlooking key red-flag features – such as rapid progression, severe biochemical disturbance or postmenopausal onset – can mean missing serious underlying pathologies, including malignancy.

PCOS IS NOT THE FULL PICTURE

Polycystic ovary syndrome (PCOS) is rightly identified as the predominant cause of androgen excess, affecting up to 13% of women globally and imposing a substantial healthcare and economic burden, estimated at upwards of $15 billion annually.[4] However, its high prevalence can lead to a diagnostic shortcut. Not every woman with hyperandrogenism has PCOS, and it is essential to identify those patients with non-PCOS pathology.

Other aetiologies, including non-classic congenital adrenal hyperplasia, hormone-secreting adrenal or ovarian tumours, Cushing's syndrome

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and severe insulin resistance syndromes, can mimic the clinical and biochemical phenotype of PCOS. An automatic assumption of PCOS, without a structured workup, risks overlooking these rarer but critical diagnoses, delaying appropriate management and, in some cases, life-saving intervention.

BEYOND APPEARANCE: THE METABOLIC ICEBERG

The dermatological and reproductive features of hyperandrogenism often prompt clinical presentation. However, beyond their immediate impact, they indicate a broader risk of systemic metabolic burden. Androgen excess has profound, and frequently direct, effects on metabolic health, as follows.

Insulin resistance

Profound insulin resistance, present in up to 70% of women with PCOS, is a key driver of the associated dysglycaemia and markedly increases the lifetime risk of type 2 diabetes.[5]

Adiposity

Approximately two-thirds of women with hyperandrogenism live with overweight or obesity.[6] This is a bidirectional relationship, where excess adiposity amplifies metabolic strain, while androgens themselves promote visceral fat accumulation.

Cardiovascular disease

Growing evidence demonstrates a direct link between androgen excess, hypertension and a higher incidence of adverse cardiovascular events, independent of obesity.[7]

Liver disease

Metabolic fatty liver disease (MASLD) is not only more prevalent in women with androgen excess, but its severity often correlates directly with androgen levels, suggesting a causal role.[8]

Psychological health

The prevalence of anxiety and depression is higher than in the general population, reflecting both the psychosocial impact of the clinical features and potential neuroendocrine effects of the hormonal imbalance.[9]

These findings firmly position androgen excess as a systemic metabolic disorder, intricately linked to the core drivers of cardiometabolic disease. Yet it continues to be under-recognised in mainstream metabolic care.

NEW GUIDELINE: A TURNING POINT

In this context, the new Society for Endocrinology Clinical Practice Guideline for the Evaluation of Androgen Excess in Women represents a critical intervention.[1] Developed by a multidisciplinary expert panel, it provides a much-needed, evidence-based and pragmatic framework for clinical practice.

Key contributions include:

- A **structured diagnostic pathway** for women presenting with common features such as acne, alopecia, hirsutism or menstrual irregularities
- Clear guidance on **biochemical investigations and imaging**, clarifying which tests are appropriate and when
- Suggested **referral criteria** for specialist and multidisciplinary care
- Emphasis on the **lifespan relevance** of androgen excess, from adolescence through to the postmenopausal phase of life.

By standardising the assessment process, this guideline is designed to shorten diagnostic delays, improve the patient experience and ensure that serious endocrine pathologies are not missed.

METABOLIC IMPLICATIONS: CLOSING THE LOOP

The relationship between hyperandrogenism and adiposity is bidirectional and self-perpetuating. Excess adipose tissue increases peripheral androgen production and alters hormone metabolism, while androgens, in turn, exacerbate insulin resistance and promote the accumulation of metabolically harmful visceral fat. This vicious cycle is a powerful driver of metabolic dysfunction.

Early recognition and intervention aimed at breaking this cycle have the potential to mitigate not only reproductive complications, but also the long-term sequelae of type 2 diabetes, cardiovascular disease, and MASLD. Viewing hyperandrogenism through a metabolic lens, rather than a purely reproductive one, is essential for improving long-term health outcomes.

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Challenges in endogenous Cushing's syndrome management

Endogenous Cushing's syndrome is a rare, serious, and complex endocrine disorder characterised by chronic exposure to elevated cortisol levels. Cushing's is associated with increased mortality and significant multisystem comorbidities, including cardiovascular and metabolic impairment, infections, neuropsychiatric disorders and reduced quality of life; which are reduced following successful management.[1]

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Prof Mark Gurnell, Consultant Endocrinologist,
Addenbrooke's Hospital, Cambridge

Preparing patients for surgery

Date: Thursday 22nd January 2026 | **Time:** 18:30-19:30 GMT

Prof Niki Karavitaki, Consultant Endocrinologist,
Queen Elizabeth Hospital, Birmingham

Beyond cortisol - Managing comorbidities in Cushing's syndrome

Date: Monday 23rd February 2026 | **Time:** 18:00-19:00 GMT

Prof Stephanie Baldeweg, Consultant Endocrinologist, UCLH, London

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IE-NPS-0257 November 2025

Your Society in 2025

Here we share just a few of our top achievements from 2025 in supporting careers, inspiring the future, and advancing research and patient care.

Society for Endocrinology

ADVANCED CLINICAL PRACTICE...

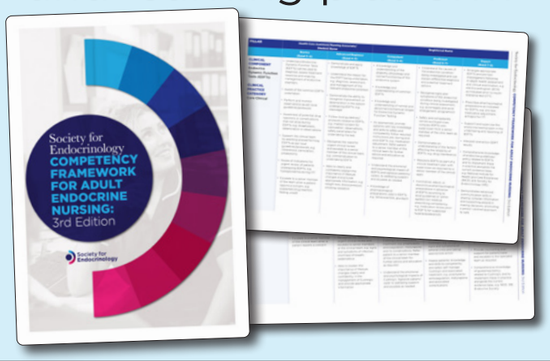
Opened 33 sites across
3 real-world data registries

NSAT **PROMMIS** **CORE**

recruiting **over 340 patients***

**As of November 2025*

Launched the 3rd edition of the **Competency Framework for Adult Endocrine Nursing** hosted on an online mentoring and learning platform



SUPPORTED OUR DIVERSE COMMUNITY...

Welcomed
577
new Society members

Awarded
80 grants
across travel, research, teaching and outreach

Launched a new **Career Development Framework for Scientists**

Collaborated with **37 companies**, including **4 industry partnerships**

PROMOTED HIGH-QUALITY ENDOCRINE RESEARCH...

Maintained or
increased Impact Factors

Reduced time from **acceptance to publication**

from ~30 days

to ~15 days

across Society journals*

**Published by Bioscientifica*

News update
SOCIETY AND PARTNER JOURNALS

It's been a busy few months for the Society's journals, from the announcement of our latest Journal Impact Factors (see **issue 157, Autumn 2025**) to journal representation at international conferences such as ENDO 2025 in San Francisco, USA, in July and the ESA-SRB-ANZOS Annual Scientific Meeting in Perth, Australia, in October. Read on to discover the latest highlights from Society publications.

HIGH QUALITY OBESITY RESEARCH

As this issue of *The Endocrinologist* shows, recent therapeutic progress in body weight has led to an exciting new era in obesity research. Here we've picked out a few of the latest papers on obesity from *Journal of Endocrinology* and *Journal of Molecular Endocrinology*:

- **Osteoprotective effects of lifestyle interventions against obesity-induced bone loss in rats by Imerb *et al.***
- **Effects of tryptophan-selective lipidated GLP-1 peptides on the GLP-1 receptor by Lu *et al.***
- **Contrasting roles for GLP-1R and GIPR in diet-induced obesity by Gao *et al.***
- **Effect of metformin on the endometrial proteome of diet-induced obese mice by Malliou-Becher *et al.***

DEDICATED SECTION ON GROWTH

Endocrine Connections has launched a new section, 'Growth, Growth Hormone and Growth Factors', led by Professor Justin Davies. This section specialises in publishing research on all aspects of growth and growth disorders, including growth regulation and growth factor signalling, aiming to advance understanding and support new diagnostic and therapeutic strategies.

IMMUNE FOCUS IN REPRODUCTION

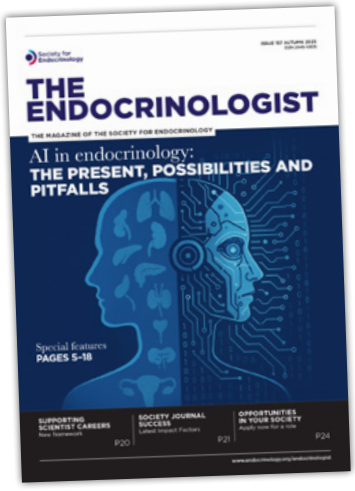
Reproduction and Fertility presents a flagship special collection, 'Immune Regulation and Inflammatory Mechanisms in Reproductive Health and Disease', edited by Dr Erin Greaves, Dr Christiane Pleuger and Dr Erick JR Silva. The collection will explore how immune and inflammatory processes shape male and female reproduction, with implications for infertility, pregnancy loss and therapeutic interventions. To propose an article for the collection, contact **raf@bioscientifica.com**.

WELCOMING A NEW EDITOR-IN-CHIEF

Endocrine-Related Cancer welcomes Professor Karel Pacak as Editor-in-Chief from January 2026. A globally renowned expert in neuroendocrine tumours, Professor Pacak brings a wealth of experience and is recognised as the 94th Most Influential NIH Scientist in Medicine. Dr Matthew Ringel will step down, leaving a legacy of strong leadership in cancer biology research.

Career-boosting opportunity
JOIN *THE ENDOCRINOLOGIST*

Shape the future of endocrinology and advance your scientific career – join our Editorial Board!



Are you an experienced scientist, passionate about shaping the conversation in endocrinology? This is your opportunity to influence how knowledge is shared across our field's global network. *The Endocrinologist* is seeking new Editorial Board members to start in January 2026.

The Endocrinologist is a well-loved and valuable resource that helps to foster a sense of community among members of the Society for Endocrinology. Its Editorial Board members work together to decide the focus of each issue and to commission articles from endocrinologists and other experts around the globe, helping to produce a vibrant and topical publication for colleagues in the field.

As part of the Board, you'll help contribute to defining these themes for each issue, have the exciting chance to commission articles from leading experts worldwide, and ensure the publication remains a dynamic, trusted resource for the endocrine community. This role is an excellent opportunity to broaden your professional network, develop editorial and leadership skills, share insights and contribute to the Society's mission of keeping members informed about the latest developments.

Join us in shaping a publication that fosters collaboration, as well as celebrating innovation in endocrinology and making a lasting impact on the scientific community. We want to hear from you!

ELIGIBILITY AND TIME COMMITMENT

To apply for this exciting role, it is essential that you are a current member of the Society for Endocrinology with a strong scientific background in endocrinology.

Previous editorial experience would be great but is not essential – enthusiasm and commitment matter most!

The Board meets virtually four times per year, with occasional email discussions between meetings. Members typically serve a two-year term, which would start in January 2026.

Find out more and apply by **31 December 2025**

Celebrating excellence
NEW AWARDEES

We are excited to congratulate this year's recipients of the Society's Leadership & Development Awards.

The **Leadership & Development Awards Programme** is designed to recognise and nurture emerging talent in endocrinology, to help develop the future leaders of our discipline. The **Selection Panel** has selected a broad range of early- to mid-career scientists, clinical academics, clinicians-in-practice and, excitingly, for the first time ever, a nurse awardee. All recipients began their three-year programme at the start of November.

This programme was devised as part of the Society's strategy to advance and support endocrinology. It provides a wide range of opportunities for early-career endocrinology professionals, to enable them to develop naturally into future leaders of our discipline, enhancing their careers and professional profiles.

We hope you will join us in congratulating our 2025 awardees. Watch out for updates on their progress over the coming three years. You can read more about them below.

Learn more about the **aims and benefits of the Leadership & Development Awards Programme** and send us your questions by **email**

AHMAD AL-MRABEH

Ahmad is an MRC Career Development Fellow at the University of Edinburgh. He is interested in translational medicine approaches for diabetes remission. His group is currently working on the mechanisms of reversible pancreas lipotoxicity in type 2 diabetes, with a particular focus on the role of hepatic *de novo* lipogenesis.

ALDONS CHUA

Aldons is a Clinical Nurse Specialist at St Bartholomew's Hospital, London, with expertise in adrenal disorders and multiple endocrine neoplasia. He is an independent nurse prescriber, with a Master's degree in clinical research. Additionally, he actively participates in regional, national and European endocrine networks. His research focuses on enhancing patient self-management strategies and advancing endocrine nursing practice.

KERRI DEVINE

Having qualified in medicine in Glasgow, Kerri trained in north east England, where she obtained her PhD with Brian Walker, exploring tissue-specific regulation of glucocorticoids. She delivers a regional reproductive endocrinology service, including induction of puberty and spermatogenesis, and has a clinical interest in the care of women with Turner syndrome.

KATE LAYCOCK

Kate, an endocrinology registrar in north east London, recently took on a NIHR Clinical Lecturer post. During her clinical training, Kate also undertook a PhD in endocrine hypertension, where she investigated the cell of origin of aldosterone-producing adenomas. She has worked on large clinical trials in primary aldosteronism.

BEN LOUGHREY

Ben is an academic clinical lecturer in Belfast who recently obtained his Certificate of Completion of Training. His research interest is pituitary neuroendocrine tumours/adenomas, particularly the application of digital pathology to assess biomarkers in these tumours and the role of *AIP* mutations in pituitary tumorigenesis.

REBECCA SAGAR

Rebecca is an NIHR Clinical Lecturer and specialist registrar in endocrinology at Leeds Teaching Hospitals. She undertook a PhD investigating the effects of insulin resistance on platelet function, and has an interest in glucocorticoid-related multi-morbidity. Alongside her research and clinical work, she is also current Chair of the Young Diabetologists and Endocrinologists' Forum.

LISA YANG

Lisa completed her specialist training in north west London as an NIHR Academic Clinical Fellow. She was awarded an MRC Clinical Research Training Fellowship to complete her PhD in reproductive neuroendocrinology at Imperial College London. Her research has led to award-winning presentations and numerous publications. Lisa leads specialist clinics in reproductive endocrinology and has active research interests in adrenal disorders and congenital adrenal hyperplasia.

What's in store for you?
REGISTER NOW FOR SfE BES 2026

SfE BES 2026 in Harrogate on 2–4 March 2026 is the UK's biggest celebration of endocrinology. It will bring together the brightest minds, the latest discoveries and the most inspiring conversations in our field.

OBESITY IN THE SPOTLIGHT

As well as celebrating the Society's 80th anniversary, we are excited to be including many obesity-related talks. You will have plenty of opportunities to learn about the latest developments in obesity research from experts in endocrinology.

Among these, you can look forward to:

- an Endocrine Network Session looking at Metabolism, Obesity and Diabetes
- a Meet the Expert session on Metabolism and Obesity with Dimitri Pournaras (Consultant Upper GI and Bariatric/Metabolic Surgeon), focusing on approaches to weight loss in obesity, with a panel discussion.

A WORLD OF OTHER OPPORTUNITIES

- Discover breakthroughs shaping the future of endocrinology
- Enhance your expertise with dynamic sessions, hands-on workshops and game-changing research
- Connect and collaborate with peers and leaders from across the UK and beyond
- Boost your career and return inspired, informed and energised.

Flick through the scientific programme to find out more and **book your place today!**

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Society grants 2025
SUPPORTING THE FUTURE OF ENDOCRINOLOGY

The Society for Endocrinology is proud to have awarded **80 grants** in 2025, supporting research, education, outreach and professional development across the endocrine community.

These grants have empowered scientists to investigate hormonal and metabolic disorders, mentor the next generation and engage the public in understanding endocrine health. We have provided funding for travel and collaboration, fostering networking, exposure to cutting-edge techniques and global knowledge exchange.

Collectively, these opportunities enhance scientific impact, career growth and the translation of discoveries into improved health outcomes.

These awards reflect our commitment to nurturing talent and accelerating progress in endocrinology. 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 be celebrated within our community.

THIS YEAR'S GRANTS:

68 TRAVEL GRANTS
enabling attendance at key conferences and collaborative visits

4 TEACHING GRANTS
nurturing innovative educational initiatives

6 RESEARCH GRANTS
supporting the drive for new discoveries in endocrinology awareness

2 OUTREACH GRANTS
promoting public engagement and awareness

PLUS! THE CLINICAL ENDOCRINOLOGY JOURNAL FOUNDATION RESEARCH GRANT
advancing critical research in endocrine science

Learn more about **how Society grants are awarded**

Is this role for you?
TARGETING FUNDS FOR CLINICAL ENDOCRINOLOGY

The Clinical Endocrinology Journal Foundation (CEJF) is looking for volunteers to help distribute its funding.

Formerly known as the Clinical Endocrinology Trust, the CEJF uses independent financial support from profits generated by the journal *Clinical Endocrinology* to promote teaching, audit and research within the field. Its committee helps steer the foundation to achieve these aims.

The Foundation is seeking new committee members, consultants as well as clinicians-in-training. The committee meets online two or three times per year.

For further details or to apply, **contact the CEJF Secretary, Marie Freel**

BRIDGING SPECIALTIES
STEROID-INDUCED HYPERGLYCAEMIA IN AUTOIMMUNE HEPATITIS

WRITTEN BY MADIHA MIRZA AND VISHAKHA BANSIYA

While working on the hepatology ward as an internal medicine trainee, I looked after several patients with autoimmune hepatitis who developed steroid-induced hyperglycaemia. It quickly became clear how varied the glycaemic responses to steroids can be, and how differently hepatology and endocrinology services approach monitoring and management.

CASE PRESENTATIONS

One case that stood out was a 54-year-old woman with newly diagnosed autoimmune hepatitis and chronic liver disease, though without cirrhosis. She had no previous history of diabetes, and her baseline glycated haemoglobin (HbA1c) was 37mmol/mol. Treatment began with intravenous methylprednisolone pulses, followed by high-dose oral prednisolone once daily.

Her glucose was checked four times daily from the start. While on intravenous methylprednisolone, she showed a steady rise in glucose across the day, with intermittent post-meal spikes. Once switched to oral prednisolone, her fasting levels remained normal, but she developed clear post-lunch and evening peaks – a pattern typical of morning prednisolone dosing.[1,2,3]

She was initially started on gliclazide, which gave partial improvement, but didn't fully control her glucose. The diabetes outreach team were then involved and switched her to Humulin® I once daily in the morning, which helped cover the afternoon and evening peaks. As her course continued, her glucose rose again, and she was stepped up to biphasic insulin (NovoMix® 30). Later, as her steroids were tapered, her insulin requirements dropped quickly and she had mild hypoglycaemia, which resolved with dose reduction and close follow up.

Another patient on the ward, also with autoimmune hepatitis, was started on oral prednisolone, but only fasting glucose checks were done initially. These appeared reassuringly normal, and her hyperglycaemia wasn't noticed until four-point testing was eventually introduced. Her post-lunch and evening readings were high, showing how easy it can be to miss steroid-induced hyperglycaemia if only fasting levels are monitored.[2,4]

DISCUSSION

These cases highlighted a pattern I saw several times: glucose monitoring after starting steroids isn't consistent on hepatology wards. Hepatologists are excellent at managing immunosuppression, but glucose checks can be easily overlooked in non-diabetic patients, especially when fasting levels appear normal. On the other hand, endocrinologists may not always appreciate how complex glucose control can be in patients with liver disease, poor appetite, or fluctuating steroid doses.

Guidelines from the Joint British Diabetes Societies for Inpatient Care (JBDS-IP)[1] and the Endocrine Society[4] recommend at least twice-daily glucose monitoring when starting high-dose glucocorticoids, moving to four-point testing if readings exceed 10–11mmol/l or if treatment is prolonged. Relying on fasting glucose alone can easily miss the afternoon and evening spikes typical of oral prednisolone.[2,4]

In patients with chronic liver disease, HbA1c can be misleadingly low due to anaemia and shortened red-cell lifespan, so capillary or continuous glucose monitoring gives a better reflection of true control.[4,5] Tight glycaemic control should also be avoided: hypoglycaemia is particularly dangerous when hepatic glycogen stores and gluconeogenesis are impaired. The JBDS-IP suggest aiming for 6–10mmol/l, prioritising safety over perfection.[1]

Different steroid regimens produce distinct glycaemic patterns. Intravenous methylprednisolone and dexamethasone often cause a sustained rise in glucose throughout the day and night, while morning prednisolone tends to cause post-lunch and evening spikes. Recognising these patterns helps tailor insulin: morning intermediate-acting insulin (e.g. Humulin® I) for prednisolone, and basal–bolus or biphasic regimens for the more sustained rises seen with intravenous or long-acting steroids.[1,2,3]

In hepatology, practical barriers can add to the challenge. Nursing staff and resident doctors may be less familiar with insulin initiation, and there is often uncertainty about appropriate targets in liver disease. Early involvement of the diabetes outreach or endocrinology team can make a real difference by helping to spot hyperglycaemia early, choosing suitable regimens and safely reducing doses when steroids are tapered.

Overall, these cases reinforced the value of collaboration between hepatology and endocrinology. At present, there are no hepatology-specific guidelines for steroid-induced hyperglycaemia. A shared local protocol, developed by both teams, could help standardise practice and prevent cases from being missed.

KEY LESSONS

- Steroid-induced hyperglycaemia can appear quickly, even in patients with normal HbA1c and no prior diabetes.
- HbA1c should not be relied upon to exclude dysglycaemia, particularly in liver disease, where it may underestimate glucose levels.
- Start with twice-daily glucose monitoring when initiating high-dose steroids, and move to four-point testing if readings exceed 10–11mmol/l or if treatment is prolonged.
- Different steroids produce different patterns: intravenous methylprednisolone and dexamethasone cause sustained rises, while morning prednisolone leads to afternoon and evening spikes; divided or evening doses can cause all-day hyperglycaemia.
- Select insulin regimes where the action profiles most closely match glycaemic patterns, but factor in the feasibility of implementation.
- Sulfonylureas can help in mild, short courses if oral intake is good, but should be avoided in advanced liver disease.
- Target glucose largely between 6–10mmol/l (up to 12mmol/l is acceptable) and personalise as needed.
- Early multidisciplinary collaboration between hepatology, endocrinology and nursing teams ensures safer, more consistent care.

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DAVID BOYER RAMSDEN 1941–2024

> "Life is what it is, and one must enjoy every moment, no matter what the situation. That does not mean one is always laughing, but even the saddest moments in one's life have their wells of contentment."
> David Ramsden, 2023

David Ramsden, Emeritus Professor at the University of Birmingham, passed away in 2024, just a year after the Department of Metabolism and Systems Science held a festschrift in his honour. David was one of the great unheralded catalysts of modern UK endocrinology, particularly thyroid hormone research. This article belatedly pays tribute to his achievements as a research scientist and his role in the evolution of endocrinology at Birmingham over the last 50 years.

David joined the then Department of Medicine at Birmingham in 1973. He worked first as a Lecturer, then as Senior Lecturer, and Reader, until 2006. He was Honorary Reader in medicine until 2016, when he became Honorary Professor.

David had already worked with Raymond 'Bill' Hoffenberg at Northwick Park Hospital, Harrow, before he followed Hoffenberg in joining the University of Birmingham in 1973. Their first collaborative thyroid paper was published a year later.[1] In 1984, David published his final collaborative paper with Bill[2] but, by then, the team had expanded to include two other future stars of UK endocrinology: Jayne Franklyn and Mike Sheppard. David played a major role in mentoring both Jayne and Mike, and from the mid-1980s to mid-1990s they co-published more than 30 thyroid hormone-related papers, being joined by some other prominent Birmingham researchers, such as Kevin Docherty and Joe Bradwell. Notable publications from this time included David's 1993 paper on the human thyroxine-binding globulin gene.[3]

From the mid-1990s onwards, David's research shifted away from specific thyroid hormone studies to include an interest in plasticisers and endocrine disruptors,[4] as well as biotransformation and sulfation pathways.[5] In 2017, long after his retirement, David participated in an international conference on sulfation pathways, held in Birmingham, and registered as a Student for this event – equivalent to the discount for the Society's Senior Members, which we had forgotten to implement!

These later studies led to David's great research passion in the final phase of his career, which was Parkinson's disease. Working with Rosemary Waring, Adrian Williams and Richard Parsons at Birmingham, David published over 30 papers on a wide range of mechanisms linked to Parkinson's disease, typified by a 1999 review.[6] This new avenue of research also introduced David to a fresh community of collaborators, notably Shu-Leong Ho from Hong Kong, who was initially a Clinical Research Fellow in neurology, recruited by Adrian Williams.

In 2011, David was appointed Royal Society Kan Tong Po Visiting Professor at the University of Hong Kong. Long before the advent of Zoom, he would often be heard to say, 'I have a Skype appointment with Hong Kong', in response to requests for meetings. David's very fruitful collaboration with Leong and his team resulted in more than 40 original research papers, book chapters and reviews on topics related to Parkinson's disease. They even filed an international patent. Their first jointly co-authored paper was on monoamine oxidase B.[7] Soon they were joined by Philip Ho.[8] David's high reputation abroad and his commitment to supporting and mentoring international students was also reflected by his research group's nickname, 'The United Nations'.

Until the very last days of his life, David remained incredibly active, unwavering in his research effort, features of a truly respected and committed scientist and mentor. Indeed, one of David's papers was published posthumously.[9] It had a special mention of David in the acknowledgements section:

'We would like to express our deepest gratitude to the late Professor David Boyer Ramsden for his invaluable guidance and mentorship that laid the foundation for our research. David was an extraordinary scientist and a true visionary, whose passion for knowledge and scientific excellence inspired us all. Though no longer with us, David's impact on our professional growth will forever be remembered and cherished.'

David was more than the sum of many collaborations and his research expertise. He was also a great mentor and champion of teaching, who continued his commitment to the University of Birmingham in retirement through his volunteer activities for student recruitment and admission. This was all the more impressive as David's mobility was increasingly limited in his final years, after he was diagnosed with progressive supranuclear palsy.

The many people at Birmingham and across the globe who worked with David would all agree that he was one of the last of a dying breed of academics who 'did not suffer fools gladly'. David looked at the world from different angles. We will miss his frank views on academia, but also his achievements in the field of endocrinology and his incredible generosity to his colleagues and students. We send our belated commiserations to his wife Pamela and children Aidan, Miles and Katrina.

JONATHAN WOLF MUELLER, PHILIP WING-LOK HO, SHU-LEONG HO and MARTIN HEWISON

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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.

ESTEVE
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Connect the dots

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