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Plenary Lectures

Clinical Endocrinology Journal Foundation Visiting Professor Lecture

PL1

Abstract Unavailable

DOI: 10.1530/endoabs.117.PL1

Society for Endocrinology Starling Early Career Medal for Research Excellence

PL2

Using kisspeptin to interrogate hypothalamic dysfunction in reproductive disorders

Ali Abbara
Imperial College London, London, United Kingdom. Imperial College Healthcare NHS Trust, London, United Kingdom

Many common reproductive disorders are due to hypothalamic dysfunction but we have not previously had a mechanism to directly assess this. Kisspeptin can be used as novel diagnostic tool to evaluate hypothalamic dysfunction in reproductive disorders and aid in reaching an accurate diagnosis. Many current reproductive disorders have overlapping features and rely on exclusion of other causes. This is challenging in practice leading to delayed and inaccurate diagnosis. I will highlight how differentiating common reproductive disorders can be challenging, for example polycystic ovary syndrome (PCOS) can frequently be confused with functional hypothalamic amenorrhoea at low body weights, and with obesity-related hypogonadism at higher body weights. Kisspeptin can also help differentiate congenital from functional forms of hypogonadotrophic hypogonadism. Using kisspeptin to evaluate hypothalamic dysfunction in reproductive disorders could enable rapid accurate diagnosis and prompter institution of appropriate management.

DOI: 10.1530/endoabs.117.PL2

Society for Endocrinology Presidential Lecture

PL3

Abstract Unavailable

DOI: 10.1530/endoabs.117.PL3

Society for Endocrinology Dale Lifetime Achievement Medal

PL4

Abstract Unavailable

DOI: 10.1530/endoabs.117.PL4

British Thyroid Association Pitt-Rivers Lecture

PL5

From mutation to medicine: a story of MCT8 deficiency

W. Edward Visser
Erasmus MC, Rotterdam, Netherlands

Thyroid hormone signaling depends on active transport of thyroid hormones across the plasma membrane. The discovery of MCT8 in 2003 fundamentally changed our understanding of thyroid hormone biology by revealing that cellular thyroid hormone availability is transporter-dependent. One year later, mutations in the X-linked SLC16A2 gene were identified as the cause of MCT8 deficiency, a rare but devastating neurodevelopmental disorder. The phenotypic consequences of MCT8 deficiency arise from a complex mixture of hypothyroid and thyrotoxic tissues. Impaired thyroid hormone transport into the brain results in profound intellectual and motor disability. MCT8 deficiency has a characteristic biochemical signature of high (F)T3, low (F)T4, and normal TSH concentrations. Unrestricted exposure of peripheral tissues to T3 causes chronic thyrotoxicosis, which leads to tachycardia, muscle wasting, hypermetabolism and progressive reduction in body weight, constituting significant morbidity and mortality in this vulnerable population. Through a global, multidisciplinary collaboration integrating deep clinical phenotyping, functional assays, computational analyses, and population-based cohorts, we established a direct relationship between the functional severity of SLC16A2 variants and clinical outcomes. Loss-of-function stratification predicts survival and key neurodevelopmental, anthropometric, thyrotoxic features and thyroid hormone concentrations. Combining functional data with different machine learning models, we established disease-specific optimized variant pathogenicity and severity classifier. Preclinical work identified the thyroid hormone analogue TRIAC as a strategy to bypass MCT8. Clinical trial and real-world data demonstrated meaningful improvements in key outcomes, culminating in regulatory approval in the European Union. Ongoing studies address the impact on survival, quality of life, and neurodevelopment.

DOI: 10.1530/endoabs.117.PL5

Society for Endocrinology Outstanding Contribution Medal

PL6

Stress, steroids and serendipity

Karen Chapman
The University of Edinburgh, Edinburgh, United Kingdom

During most of my research career I have been fascinated by how steroid hormones act and how their action is regulated. In my talk I will take a light-touch look at the role that serendipity has played in the directions my research has taken me. I will focus mainly on the vital role that glucocorticoids play in the transition to independent life that occurs at birth. I will describe how glucocorticoids might programme perinatal cardiac maturation with life-long consequences for cardiovascular health. I will also illustrate the important part that team-work and collaboration have played in my research and in my professional development.

DOI: 10.1530/endoabs.117.PL6

Society for Endocrinology Medal for Research Excellence (Clinical)

PL7

Pituitary Troubles and the Mitos for the Labyrinth

Niki Karavitaki[1,2]
[1]Department of Metabolism and Systems Science, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom; [2]Department of Endocrinology, Queen Elizabeth Hospital Birmingham, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

The lecture will cover collaborative work we have done over the years investigating the management and outcomes of patients with various pituitary pathologies. Data particularly on pituitary tumours and their impact on management algorithms will be discussed, and future perspectives on the, as ever, fascinating field of pituitary disease will be highlighted.

DOI: 10.1530/endoabs.117.PL7

Society for Endocrinology Medal for Research Excellence (Science)

PL8

Abstract Unavailable

DOI: 10.1530/endoabs.117.PL8

Clinical Endocrinology Journal Foundation Lecture

PL9

Abstract Unavailable

DOI: 10.1530/endoabs.117.PL9

Pitch Session

Should Weight-Loss Medications Be Routinely Offered for Managing Obesity in the NHS?

D1.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.D1.1

D1.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.D1.2

D1.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.D1.3

Awards and Prizes

Outstanding Teacher of the Year Award

TA1

My journey in medicine and endocrinology

Ketan Dhatariya
Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom. University of East Anglia Medical School, Norwich, United Kingdom

This talk will take you though my journey from medical student to professor of medicine - all the while talking about the science I've been involved with. In particular, it will focus on where I've been able to enhance the education of others - through my work with the SCE in diabetes and endocrinology, as president of the diabetes and endocrine section of the RSM through to my time as chair of ABCD

DOI: 10.1530/endoabs.117.TA1

Outstanding Clinical Practitioner Awards

OCP1

First do no harm

Antonia Brooke
Royal Devon University Healthcare, Exeter, United Kingdom

What is outstanding care in Endocrinology? Are we personally, departmentally and nationally delivering this and how can we network to prevent wide variance in experience for patients? Where can we really add value? What outcome measures do we have to help us, using a top down systemic evidence base and bottom up individualised care to achieve change? Reducing the variation in delivery of care within our hospitals (beyond our specialty), can we minimise threats to safety (and litigation)? A combination of evidence and standards alongside a 'person-centred' approach can provide holistic, timely care, with improved patient partnership at the centre (when willing and able). Adopting a less traditional 'paternalistic' model of care is potentially a cost efficient and effective solution. There are a number of potential opportunities and strengths of improved partnership with patients and support charities, exploring what is important to patients, through systemic engagement, noting particular challenges from the expectations of patients; for example when negotiating results and opinions from alternative providers, not necessarily following evidenced based practice. These challenges and opportunities will be discussed, including how we consider training and population needs, whilst rationalising care. It will use personal experience through leading the Society for Endocrinology Peer Review, Chairing the Specialist Advisory Committee for specialty trainees and as a trustee of the Pituitary Foundation, as well as being a parent relying on NHS services. It will challenge where we sit on the 'bell shaped curve' when delivering care, including case examples and areas of excellence in clinical practice. A bottom up, patient centred model of care. First do no harm.

DOI: 10.1530/endoabs.117.OCP1

OCP2

Improving the treatment of patients with reproductive hormonal disorders

Channa Jayasena
Imperial College, London, United Kingdom

This talk will discuss a programme of clinical and translational work that has aimed to improve care for people with complex reproductive and hormonal disorders within the NHS. The focus has been on areas of high patient need but limited evidence. Key work has evaluated the safety, efficacy and cost-effectiveness of treatment for symptomatic men aged over 40 years with low testosterone. This has included research and expert consensus to refine biochemical testing and assay interpretation, allowing clinicians to use more accurate and clinically meaningful thresholds when diagnosing hypogonadism. The increasing trend for testosterone seeking behaviour in men imposes a new challenge for NHS clinicians; novel community-based research to delineate the characteristics of androgen withdrawal may help us support men who are motivated to stop self-medicating. Other recent work has revealed improvements in spermatogenic markers in men with obesity following dietary weight loss. Furthermore, development of novel seminal markers has revealed a male determinant of previously unexplained recurrent pregnancy loss. Developing NHS services, is a major theme of this work. The Society for Endocrinology Specialist Endocrinology Network for Andrology was established to bring individual centres of excellence together to harmonise service development, manage drug shortages, and undertake collaborative research. This work has also contributed directly to national and international guidelines, helping shape evidence-based standards for reproductive endocrine care. Education and workforce development underpin this programme. Training clinicians in the UK and worldwide to confidently manage complex reproductive endocrine conditions, and has build sustainable expertise within the NHS. Overall, a case is made for integrating clinically driven research, training, service design, and guideline development to advance the treatment of reproductive hormone disorders across the NHS.

DOI: 10.1530/endoabs.117.OCP2

Nikki Kieffer Medal

NKM1

Abstract Unavailable

DOI: 10.1530/endoabs.117.NKM1

Emerging Researcher and Plenary Orals

ER1.1

Role of Obesity Gene PLXNA4 in Neurodevelopment and Anxiety

Madeleine Cowie
University of Edinburgh, Edinburgh, United Kingdom

Obesity is a growing public health concern, with genetic factors significantly influencing risk. Genetic variants in the hypothalamic melanocortin pathway, which regulates satiety through pro-opiomelanocortin (POMC) neurons, are frequently implicated in obesity. Plexin A4 (PLXNA4), a receptor expressed on POMC neurons, regulates cytoskeletal remodeling and maintains structural circuit integrity. Loss-of-function mutations in PLXNA4 impair axonal growth and have been linked to severe obesity, potentially through disrupted development of hypothalamic satiety circuits. Additionally, PLXNA4 variants are associated with neuropsychiatric traits, including anxiety. However, PLXNA4's specific role in the development of these conditions remains largely unexplored. Zebrafish are tractable models for investigating hypothalamic maturation, as their caudal hypothalamus (cH), containing POMC, serotonergic, and dopaminergic neurons, is involved in both satiety regulation and anxiety-like behaviours. Consequently, the cH may serve as a nexus for PLXNA4's dual functionality in these processes. This study compared neurodevelopmental changes in the cH of *plxna4* mutants and wild-type controls using immunofluorescence to assess neuronal populations at 5, 8, and 14 days post-fertilization (dpf). Anxiety-like behaviour was evaluated using a thigmotaxis assay, measuring the tendency of zebrafish to remain near the walls of their well in response to paramecia, reflecting a more anxious state. *plxna4* mutants exhibited disrupted neuronal development, particularly in POMC and serotonergic populations. At 14 dpf, mutants showed a 482.8μm reduction in mean total POMC neurite length ($P = 0.033$), and a 1,584.8μm^2 decrease in serotonin-positive area ($P < 0.0001$). Dopaminergic neurons displayed a milder reduction, with a 742.8 μm^2 difference ($P = 0.38$) by 14 dpf. Behaviourally, *plxna4* mutants demonstrated increased thigmotaxis, consistent with elevated anxiety-like responses. These findings indicate that PLXNA4 loss impairs hypothalamic neurogenesis, offering insight into the shared genetic basis of obesity and anxiety. This work establishes a foundation for future research into PLXNA4's pleiotropic roles in neurodevelopment and metabolic-psychiatric comorbidity.

DOI: 10.1530/endoabs.117.ER1.1

ER1.2

Kisspeptin-54 accurately identifies the cause of delayed puberty

Maria Phylactou[1,2], Kanyada Koysombat[1,2], Megan Young[1,2], Sandhi Nyunt[1,2], Jovanna Tsoutsouki[1,2], Arthur C. Yeung[1], Pei C. Eng[3], Sophie A. Clarke[4], Edouard G. Mills[1,2], Rachel Varughese[5,6], Ruben H. Willemsen[6], Jayanti Rangasami[7], Evelien Gevers[6,8], Alexander N. Comninos[1,2], Sasha R. Howard[8,6], Ali Abbara[1,2] & Waljit S. Dhillo[1,2]
[1]Imperial College London, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, London, United Kingdom; [3]National University of Singapore, Singapore, Singapore; [4]University College London Hospital, London, United Kingdom; [5]Queen Mary University Of London, London, United Kingdom; [6]Barts Health NHS Trust, London, United Kingdom; [7]Chelsea & Westminster NHS Foundation Trust, London, United Kingdom; [8]Queen Mary University of London, London, United Kingdom

Background
Pubertal delay causes significant psychosocial distress for affected young people and their families, which is markedly exacerbated by diagnostic uncertainty. Delayed puberty is commonly due to self-limited delayed puberty (SLDP) but can be due to congenital hypogonadotrophic hypogonadism (CHH). Differentiating these two conditions is challenging and often takes years. The hypothalamus plays a key role in initiating puberty. Kisspeptin offers the possibility to directly interrogate hypothalamic function in humans and could offer a novel approach for identifying the cause of pubertal delay.
Methods
Twenty-two young people with delayed puberty (16 boys and 6 girls) were categorised into three groups according to pre-determined criteria (Group 1: likely SLDP, Group 2: likely CHH, Group 3: indeterminate pending follow-up). Participants received an intravenous bolus of kisspeptin-54 and GnRH on two separate occasions. Reproductive hormone levels were assessed every 15min for 6h (kisspeptin visit), and for 2h (GnRH visit). LH rise was compared between the three groups by Kruskal-Wallis test with post-hoc Dunn's, and between SLDP and CHH by Mann-Whitney U test.
Results
Mean age ($\pm$SD) at time of assessment was 16.2 $\pm$2.2 years. Seven boys had likely SLDP, 10 young people (4 boys and 6 girls) had likely CHH, whilst the remaining five were indeterminate (Group 3). Maximal rise in LH after kisspeptin-54 was higher in SLDP than CHH (SLDP: 3.39 $\pm$1.16, CHH: 1.10 $\pm$0.84, Indeterminate 3.46 $\pm$2.40 IU/l; *P*-value = 0.0004). By contrast, LH responses after GnRH did not differ (*P*-value = 0.14). The LH-rise as early as 90 minutes following administration of kisspeptin-54 fully differentiated participants with SLDP from those with CHH (area under ROC curve 1.0; *P*-value = 0.0006), but not after GnRH (auROC 0.65; *P*-value = 0.33).
Summary
Kisspeptin-54 offers promise as a diagnostic test for delayed puberty to enable earlier identification of the underlying cause, which could expedite more timely and appropriate management.

DOI: 10.1530/endoabs.117.ER1.2

ER1.3

Improved Skeletal Dynamics in Adults Treated with Palopegteriparatide for Chronic Hypoparathyroidism: 214-Week Results from the Phase 2 PaTH Forward Trial

Jeremy Turner[1], Mishaela Rubin[2], Aliya Khan[3], Peter Schwarz[4], Andrea Palermo[5], Elena Tsourdi[6], Filomena Cetani[7], Lynn Kohlmeier[8], Rajesh Jain[9], Bart Clarke[10], Carol Zhao[11], Michael Ominsky[11], Bryant Lai[11], Jenny Ukena[11], Christopher Sibley[11] & Lars Rejnmark[12]
[1]Norfolk and Norwich University Hospital, Norwich, United Kingdom; [2]Columbia University, New York, USA; [3]McMaster University, Hamilton, Canada; [4]Rigshospitalet, Copenhagen, Denmark; [5]Unit of Metabolic Bone and Thyroid Disorders, Fondazione Policlinico Campus Bio-medico, Rome, Italy; [6]Department of Medicine III and 6Center for Healthy Aging, Technische Universität Dresden, Dresden, Germany; [7]Department of Clinical and Experimental Medicine, Endocrine Unit, University of Pisa, Pisa, Italy; [8]Endocrinology and Spokane Osteoporosis, Spokane, USA; [9]University of Chicago, Chicago, USA; [10]Mayo Clinic, Rochester, USA; [11]Ascendis Pharma Inc, Palo Alto, USA; [12]Aarhus University Hospital, Aarhus N, Denmark

Background
Hypoparathyroidism is associated with low rates of bone remodeling and increased bone mineral density (BMD) due to insufficient levels of parathyroid hormone (PTH). Palopegteriparatide (TransCon PTH), a prodrug of PTH (1-34) administered once daily, is designed to provide active PTH within the physiological range for 24 hours/day in adults with chronic hypoparathyroidism. Palopegteriparatide has received regulatory approval in the US, EU, UK and several other countries. This analysis investigated skeletal endpoints through week 214 of the PaTH Forward trial.
Methods
PaTH Forward was a phase 2, randomized, double-blind placebo-controlled 4-week trial followed by an open-label extension though week 266. Serum bone turnover markers procollagen type 1 N-terminal propeptide (P1NP) and C-terminal telopeptide of type 1 collagen (CTx) and BMD measured by DXA at the lumbar spine, total hip, femoral neck, and 1/3 distal radius were assessed.
Results
Of the 95% ($n = 56$) of participants who continued to receive palopegteriparatide treatment through week 214, 93% were independent from conventional therapy ($\leq$600 mg/day elemental calcium and no active vitamin D) and 98% had albumin-adjusted serum calcium levels in the normal range (8.3-10.6 mg/dl). Mean CTx and P1NP were in the low end of normal at baseline, and increased with palopegteriparatide treatment, peaking at weeks 12 and 26, respectively. Thereafter, mean CTx and P1NP declined and remained stable and above baseline levels through week 214. The elevated baseline mean BMD Z-scores trended towards age- and sex-matched norms at the lumbar spine, femoral neck, and total hip and largely stabilized after 26 weeks of treatment, remaining above zero through week 214. No new safety signals were identified.
Conclusions
In adults with chronic hypoparathyroidism, continued treatment with palopegteriparatide through week 214 of PaTH Forward showed sustained skeletal remodeling with trends toward a new skeletal steady state closer to age-appropriate norms.

DOI: 10.1530/endoabs.117.ER1.3

ER1.4

Visualising microvascular changes in digestive organs during the onset of type 2 diabetes with super-resolution ultrasound

Cecilia Dunsterville, Clotilde Vie, Krish Desai, Yuanji Zhou, Jacob Broughton-Venner, Jipeng Yan, Meng-Xing Tang & Kevin G Murphy
Imperial College London, London, United Kingdom

Hyperglycaemia drives microvascular damage in type 2 diabetes (T2D) and while this link is well established, its timing and causality are not fully understood. Using non-invasive contrast-enhanced ultrasound (CEUS) imaging and post-processing super-resolution ultrasound (SRUS) to generate high-resolution structural and dynamic maps of the microvasculature in digestive and associated organs, we aimed to study the microvascular changes in T2D. Male Tally Ho (TH) mice develop diabetes spontaneously around 10 weeks old, allowing us to monitor their microvascular health throughout the onset of T2D. Subsequently, we treated diabetic TH mice with glucagon-like-peptide2 analogue Teduglutide (0.3 mg/kg) with the aim of correcting the observed decrease in blood velocity (BV). Our results showed a significant negative correlation between fasted glycaemic levels and BV in the microvasculature of the duodenal wall ($R^2=0.1896$, $P = 0.0001$), pancreas ($R^2=0.1527$, $P = 0.0002$) and kidney ($R^2=0.0626$, $P = 0.0181$), but not liver ($R^2=0.0251$, $P = 0.1718$). There was a significant reduction in microvascular BV in the duodenal wall and the pancreas between heathy mice and diabetic mice ($P = 0.0011$ and $P = 0.0019$, respectively). Chronic 14-day twice-daily injections of Teduglutide resulted in a trend towards increased BV in the duodenum and liver compared to the mice given a vehicle control. These results suggest that microvascular changes occur before frank diabetes and that hyperglycaemia may be driving both islet damage and impaired nutrient sensing through microvascular damage. BV reduction in digestive organs may have important endocrine consequences beyond T2D, especially in appetite and energy homeostatic pathways. Preliminary results seem to suggest that chronic Teduglutide administration may correct this change in BV in the duodenum and liver, but further work is required. More broadly, these results illustrate the use of CEUS and SRUS as novel tools to non-invasively and longitudinally visualise microvascular beds, providing insight into mechanisms of disease and potential drug targets.

DOI: 10.1530/endoabs.117.ER1.4

Symposia

Symposium 1 – Phone a friend adrenal and NET cases

S1.1

Phone a friend adrenal and NET cases

Sam O'Toole[1], Ruth Casey[2], Safwaan Adam[3], James Pittaway[4], Peter Truran[5] & Agnieszka Falinska[6]
[1]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; [2]Cambridge University Hospitals, Cambridge, United Kingdom; [3]The Christie NHS Foundation Trust, Manchester, United Kingdom; [4]Barts and the London School of Medicine and Dentistry, QMUL, London, United Kingdom; [5]Newcastle Hospitals NHS Foundation Trust, Newcastle, United Kingdom; [6]Royal Surrey County Hospital, Guildford, United Kingdom

Endocrinologists have a vital role to play in the investigation and management of people with adrenal and neuroendocrine tumours within the setting of the expert multidisciplinary team. The "Phone a friend adrenal and NET cases" symposium aims to recreate the spirit of an endocrine MDT by bringing together 6 expert speakers to discuss interesting and complex adrenal and NET cases that they have encountered in their clinical practice. The speakers will highlight key learning points and clinical pearls as they take the audience through cases in turn. The aim is for the session to be fun and dynamic, with lots of interaction between the speakers. Dr Sam O'Toole from Sheffield will be talking about secretory paraganglioma, Dr Ruth Casey from Cambridge will discuss her approach to insulinoma, Dr Safwaan Adam from The Christie will talk about paraneoplastic Cushing's, Dr James Pittaway from Barts will talk about secretory adrenocortical carcinoma, Mr Peter Truran, endocrine surgeon in Newcastle, will discuss his approach to managing growing indeterminate adrenal lesions and Dr Agnieszka Falinska from Royal Surrey will discuss her approach to managing adrenal lumps in pregnancy.

DOI: 10.1530/endoabs.117.S1.1

Symposium 2 – Novel mechanisms in metabolic disease

S2.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.S2.1

S2.2

Endothelial insulin resistance induced by adrenomedullin mediates obesity-associated diabetes

Haaglim Cho & Stefan Offermanns
Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

Insulin resistance is a hallmark of obesity-associated type 2 diabetes. Insulin's actions go beyond metabolic cells and also involve blood vessels, where it increases capillary flow velocity and delivery of insulin and nutrients. We show that adrenomedullin, whose plasma levels are increased in obese humans and mice, inhibited insulin signaling in human endothelial cells through PTP1B-mediated dephosphorylation of the insulin receptor. In obese mice lacking the endothelial adrenomedullin receptor, insulin-induced endothelial NO-synthase activation and skeletal muscle perfusion were increased. Treatment of lean mice with adrenomedullin mimicked the effect of obesity and induced systemic insulin resistance through the endothelial adrenomedullin receptor. Endothelial loss or blockade of the adreno-medullin receptor improved obesity-induced insulin resistance. This identifies a mechanism underlying obesity-induced systemic insulin resistance and suggest approaches to treat obesity-associated type 2 diabetes.

DOI: 10.1530/endoabs.117.S2.2

S2.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.S2.3

Symposium 3 – New approaches to neuroendocrine established disease

S3.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.S3.1

S3.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.S3.2

S3.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.S3.3

Symposium 4 – State of the Art in managing thyroid disease

S4.1

Novel treatments for managing autoimmunity in Graves' disease

Simon Pearce
Newcastle University, Newcastle upon Tyne, United Kingdom

Graves' disease is characterised by autoantibodies that stimulate the TSH receptor (TRAb) by engaging with its extracellular domain. Unlike most other autoimmune conditions, where prolonged tissue destruction or inflammation is required for the patient to present, hyperthyroidism may occur quickly after TRAb appear, meaning the autoimmune process may be evident at a much earlier stage. As neither antithyroid drugs, radioiodine or thyroidectomy are perfect options for long-term Graves' disease management, novel therapies are being developed. The humoral immune system can be targeted in several ways, including by B lymphocyte depleting therapeutic antibodies, immunoglobulin recycling blockers and cytokine inhibitors (both IL6 and BAFF). TSH receptor may also be directly targeted by blocking TSH receptor antibodies such as K1-70 and potentially by direct small molecule inhibitors, although these have yet to be trialled in humans. Lastly, TRAb-capture molecules which may bind to TRAb using a TSHR-ECD bait in the circulation and target them for rapid clearance are being developed. Some of these approaches will translate into clinically available modalities of treatment over the next few years.

DOI: 10.1530/endoabs.117.S4.1

S4.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.S4.2

S4.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.S4.3

Symposium 5 – Teaching and Outreach

S5.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.S5.1

S5.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.S5.2

S5.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.S5.3

Symposium 6 – The ovary: from physiology to pathophysiology

S6.1

Abstract Unavailable

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S6.2

Luteinizing Hormone-Responsive Metabolic Signaling Regulates Luteal Steroidogenesis

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The corpus luteum, a transient endocrine organ, is the major source of progesterone, the essential hormone of pregnancy. It also secretes estradiol and metabolites of both progesterone and estrogen. Furthermore, the corpus luteum produces angiogenic factors, prostaglandins and relaxin. Luteinizing hormone (LH) is of major importance in regulating corpus luteum structure and function. It stimulates ovulation and differentiation of follicular granulosa and theca cells into steroidogenic luteal cells. During the early luteal phase, endothelial cells within the corpus luteum proliferate to establish a rich capillary network critical for the delivery of gonadotropins and precursors for progesterone production. LH is responsible for maintenance of luteal function and progesterone biosynthesis. Here we summarize recent progress towards understanding cellular and organelle-specific changes induced by LH in steroidogenic luteal cells. LH activates a protein kinase A (PKA)-hormone-sensitive lipase (HSL) signaling pathway. A dynamic relationship has been established among AMP Kinase, PKA, HSL, and lipid droplets (LD) in luteal progesterone synthesis. Analysis of the LD proteome following activation of PKA revealed increased association of active HSD3B with LD. LH via PKA also acutely regulates mitochondrial (Mito) dynamics via phosphorylation of dynamin-related protein 1 (DRP1), decreasing the association of DRP1 with Mito and stimulating Mito fusion. Inhibition of DRP1 of association with Mito elevates LH-induced progesterone biosynthesis. LH also rapidly induces changes in key metabolic pathways including glycolysis, tricarboxylic acid cycle, pentose phosphate pathway, *de novo* lipogenesis, and hydrolysis of phospholipids. LH via PKA signaling regulates the phosphorylation/activation of acetyl-CoA carboxylase (ACACA) and ATP citrate lyase (ACLY), enzymes involved in *de novo* synthesis of fatty acids. Inhibition of ACLY and fatty acid transport to mitochondria suppresses LH-stimulated progesterone production. In summary, LH-sensitive metabolic pathways are essential for maintaining steroidogenesis in the corpus luteum.

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S6.3

Abstract Unavailable

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Workshops

Basic Physiology Workshop: New targets of GLP – 1 Receptor agonists

WS1.1

Abstract Unavailable

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WS1.2

Glucagon-like peptide 1 receptors as targets for addiction

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Addiction is a major health and socioeconomic burden for individuals and society. The need for new treatments is substantial, and peptides of the gut-brain axis, including glucagon-like peptide 1 receptor (GLP-1R) agonists, have been suggested as potential options. Early preclinical studies revealed that GLP-1R agonists attenuate both alcohol- and drug-associated behaviors. The newest generation of GLP-1R agonists, such as semaglutide and tirzepatide, have been tested in relation to addiction. The aim of our preclinical research aims to evaluate the role of the gut-brain axis in addiction. Acute or repeated administration of semaglutide substantially reduced alcohol intake and blocked relapse-drinking in male and female rats. Furthermore, semaglutide acutely suppressed the alcohol-induced locomotor stimulation and reduced the dopamine release in the nucleus accumbnes (NAc), a brain region central for addiction and were semaglutide was detected in alcohol-drinking rodents. On a similar note, semaglutide prevented the rewarding properties of cocaine and reduced the intake, motivation, and relapse to cocaine taking in male rats. Extensive experience then tested tirzepatide, an agonist with an even more profound affinity to the GLP-1R, and affinity to the GIP receptors. These studies show that tirzepatide, once or repeatedly, reduced the intake of alcohol across sexes in various alcohol drinking models. It blocked the rewarding properties of alcohol, which was suppressed, and electrophysiological studies pinpointed the lateral septum (LS) as an important region regulating the above-mentioned areas. In support, proteomics revealed a disruption of histones in LS by alcohol, and this effect was restored by tirzepatide. It should be further noted that GLP-1R in LS was also central in mediating the alcohol-mediated behaviors. In summary, these preclinical data suggest a central role for the gut-brain axis in regulating addiction in rodents deserving further clinical studies.

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WS1.3

Abstract Unavailable

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Clinical Workshop: Make it make sense – Interpreting discordant or complex dynamic hormone results

WS2.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.WS2.1

WS2.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.WS2.2

WS2.3

Low glucose, high stakes - investigation of spontaneous hypoglycaemia

Robert Semple
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Glucose is the central metabolic currency of life. Severe hypoglycaemia is both symptomatically frightening and life-threatening in the short term. The mechanisms that maintain normal, tight regulation of plasma glucose are thus crucial, and require preserved function of key metabolic and endocrine organs. These can go awry in myriad ways, yet the diagnostic focus of endocrinologists is often surprisingly narrow. This tends to focus on hypoglycaemia caused by insulin administration, hypoglycaemia caused by adrenal, liver or kidney failure, hypoglycaemia caused by neuroendocrine tumours, or the vague entity of postprandial hypoglycaemia. This talk will use a series of cases to illustrate other acquired or congenital causes of hypoglycaemia pertinent to the endocrinologist. These will range from the relatively frequent but under-recognised, to the exquisitely rare but mechanistically informative. The focus will be on combining clinical and biochemical evidence, often in collaboration with laboratory colleagues, in rational diagnostic decision making, and in use of specific diagnoses to guide precision therapy.

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How Do I...? Sessions

How do I...? 1

HDI1.1

Abstract Unavailable

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HDI1.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.HDI1.2

HDI1.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.HDI1.3

HDI1.4

Abstract Unavailable

DOI: 10.1530/endoabs.117.HDI1.4

HDI1.5

How do I...mainstream genomic testing from the endocrine clinic?

Anna Mitchell
Newcastle upon Tyne NHS Hospitals Foundation Trust, Newcastle upon Tyne, United Kingdom

The launch of the NHS Genomic Medicine Service in 2018 began the process of "mainstreaming" genomic testing in the NHS. Mainstreaming was introduced to firmly embed genomic medicine into all relevant clinical pathways and specialties, moving diagnostic genomic testing away from specialist Clinical Genetics services and into routine clinical care. The overarching aim is to improve equity of access to genomic tests and to ultimately streamline patient care. Ensuring that eligible patients are offered appropriate genomic testing should now form part of routine clinical care in endocrinology clinics within NHS. This "How do I" talk covers how to approach genomic testing in the general endocrinology clinic including: identifying eligible patients via the National Genomics Test Directory; aspects of consent around genomic testing; the logistics of requesting genetic panel tests; and a simple approach to interpreting panel test results.

DOI: 10.1530/endoabs.117.HDI1.5

How do I...? 2

HDI2.1

How do I induce puberty in congenital hypogonadotropic hypogonadism?

Sasha Howard
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Congenital hypogonadotropic hypogonadism (CHH) is an inherited disorder characterized by absent, incomplete, or arrested pubertal development during adolescence. The condition results from deficient secretion of gonadotropin-releasing hormone (GnRH) from the hypothalamus with impaired secretion of gonadotropins—luteinizing hormone (LH) and follicle-stimulating hormone (FSH)—from the anterior pituitary gland, leading to insufficient endogenous sex steroid production by the gonads. CHH may occur as an isolated (idiopathic) condition or in association with anosmia, known as Kallmann syndrome. It may also present as part of a broader syndromic disorder or in conjunction with additional pituitary hormone deficiencies. Puberty induction in adolescent or young adult males with CHH has traditionally involved the administration of low, gradually increasing doses of testosterone beginning from 12 years of age. While this approach effectively induces virilization, it does not stimulate testicular growth or support the potential for spermatogenesis. This limitation is particularly relevant in individuals with a history of cryptorchidism or prepubertal testicular volumes (<4 mL). In such cases, pretreatment with FSH may be beneficial to promote expansion of the Sertoli cell population and optimize future fertility potential. Current research advances include a UK-wide prospective randomised controlled trial (the PinG Study) comparing gonadotropin regimens and an international registry (I-HH) to enable lifelong follow-up to determine the impact of these interventions on fertility, physical and psychosocial well-being and quality of life.

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HDI2.2

Abstract Unavailable

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HDI2.3

Abstract Unavailable

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HDI2.4

Abstract Unavailable

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HDI2.5

Building back bone and improving fracture risk – what you can do for your patients, right now

Emma Duncan
King's College London, London, United Kingdom. Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

My talk will focus on the best use of the most effective medications for people with osteoporosis, and how we can be more sophisticated in our use of the many drugs now available for this common, disabling, and expensive disease. Unusually in endocrinology, bone is an area where there are multiple new therapeutics, both for rare disorders and for common diseases. For osteoporosis, this growth is going to continue, with the recent FDA decision to allow bone density to be used as an end point in trials for osteoporosis. Even just considering medications already available, the default of 'just start a generic oral antiresorptive' is over – as is magical thinking about calcium and vitamin D! This talk will highlight data from randomised controlled trials, head-to-head comparisons, and meta-analyses; and help the audience as specialists in this area not only to model best practice individually but also to educate our colleagues, both in primary care and in hospital management about the best way we can help our ageing population to age well.

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Meet The Expert Sessions

Congenital Adrenal Hyperplasia
MTE1

Managing Congenital Adrenal Hyperplasia - Optimising Treatment Strategies

Miguel Debono
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Congenital adrenal hyperplasia (CAH) is an inherited disorder most commonly caused by 21-hydroxylase deficiency, leading to impaired cortisol synthesis and excessive adrenal androgen production. Classic CAH presents in infancy with severe enzymatic deficiency and includes salt-wasting and simple virilizing forms, both of which may result in life-threatening adrenal crises if untreated. Females may present with virilized external genitalia, whereas males, except for occasional subtle changes, typically have normal genital appearance at birth. Lifelong glucocorticoid therapy, often combined with mineralocorticoid replacement, is required; however, treatment-related complications and chronic androgen excess can adversely affect growth, fertility, and metabolic health. Poor hormonal control is associated with precocious puberty, reduced adult height, and reproductive dysfunction in both sexes. Nonclassic CAH is a milder form that typically presents later in life with symptoms such as hirsutism, acne, or menstrual irregularities, particularly in females. Although advances in screening, diagnostic techniques, and treatment strategies have improved patient outcomes, significant challenges remain in long-term disease management. Emerging therapeutic approaches, including glucocorticoids that better mimic the physiological cortisol rhythm and androgen-lowering therapies independent of glucocorticoid action, show promise. Greater emphasis on mental health and individualized, life-stage–appropriate care is essential, with particular attention to ensuring a smooth transition from pediatric to adult healthcare services. Real life cases highlighting how we should approach patients suffering from congenital adrenal hyperplasia and related complications will be discussed.

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Belzutifan – VHL and beyond
MTE2

Abstract Unavailable

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Fertility preservation in male childhood cancer
MTE3

Meet the expert - fertility preservation in male childhood cancer

Rod Mitchell
University of Edinburgh, Edinburgh, United Kingdom. Royal Hospital for Children and Young People, Edinburgh, United Kingdom

Childhood cancer survival rates have increased dramatically over recent decades and currently >80% of children with cancer will survive over the long-term. This has resulted in a dramatic increase in the number of young adults experiencing late effects of treatment, including infertility. For girls, ovarian tissue cryopreservation and re-transplantation is an established method for fertility preservation and restoration. However, for prepubertal males due to receive gonadotoxic therapy there are currently no proven clinical options to preserve and restore fertility. Current approaches include removing testicular tissue from the patient prior to treatment for cryostorage and subsequent re-transplantation or in-vitro maturation of germ cells to generate sperm. Alternative approaches could involve co-administering treatments that can protect the testis from chemotherapy-induced damage. In 2015, the first UK clinical research programme to develop approaches to preserve fertility in prepubertal and adolescent males facing gonadotoxic therapies was established in Edinburgh. This session will discuss the current status of clinical research activity and describe a practical approach to fertility preservation in young males due to receive cancer treatment.

DOI: 10.1530/endoabs.117.MTE3

Nurse
MTE4

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE4

Functional imaging in tricky pituitary cases
MTE5

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE5

Advances in systemic therapy for thyroid cancer
MTE6

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE6

Hormone and risk management across the lifespan in transgender patients
MTE7

Hormone and risk management across the lifespan in transgender patients

Paul Connelly
Queen Elizabeth University Hospital, Glasgow, United Kingdom

Gender-affirming hormone therapy is a core component of care for many transgender and gender diverse adults, with endocrinologists increasingly responsible for managing long term cardiometabolic and skeletal health as treated cohorts age. This session will review contemporary principles for the safe use of gender-affirming hormone therapy across the lifespan, with particular emphasis on cardiovascular risk modification and bone health optimisation. The talk will examine patterns of sex steroid exposure from adolescence through older age, including the effects of oestrogen, testosterone and androgen suppression on lipid profiles, insulin sensitivity, blood pressure, body composition and thrombotic risk. Bone health considerations will be addressed across key life stages, including the impact of puberty suppression, gender-affirming hormone therapy and ageing. Practical approaches to fracture risk assessment, dual-energy X-ray absorptiometry (DXA) interpretation and intervention thresholds will be outlined. The session will emphasise individualised risk assessment, longitudinal monitoring and shared decision making, integrating gender-affirming hormone therapy into routine endocrine risk assessment.

DOI: 10.1530/endoabs.117.MTE7

Approaches to weight loss for people with obesity: Lifestyle, Surgery & Medications on quality of weight loss
MTE8.1

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE8.1

MTE8.2

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE8.2

MTE8.3

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE8.3

Blood and Bone

MTE9

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE9

Updates in diagnosis and management of POI

MTE10

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE10

Meet the Editor

MTE11

Abstract Unavailable

DOI: 10.1530/endoabs.117.MTE11

Other Sessions

What is New?

WIN1

What's new in clinical endocrinology?

Niamh Martin
Imperial College, London, United Kingdom

Over the past year, clinical endocrinology has seen important developments across a wide spectrum of subspecialty areas. In this annual conference update, I will review some of the recent key developments in endocrinology that are shaping both our scientific understanding and clinical practice.

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WIN2

What's new in basic science research in endocrinology?

Gabriela da Silva Xavier
University of Birmingham, Birmingham, United Kingdom

Last year, I took on the role of co-Editor-in-Chief of two of the journals of the Society for Endocrinology- the Journal of Endocrinology (JOE) and Journal of Molecular Endocrinology (JME). It is an enormous privilege to see so much fantastic work first hand. In this session I will draw on my more extensive than usual survey of basic science research in endocrinology in the past year to summarise some of the fantastic research that we have covered, and discuss how these topics could impact the field in the future.

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Cutting Edge Techniques: Trailblazing techniques driving new discoveries in endocrinology

CE1

What has single cell sequencing told us about the hypothalamus?

John Tadross
University of Cambridge Institute of Metabolic Science, Cambridge, United Kingdom

Single-cell and spatial genomics are reshaping hypothalamic biology by resolving molecular diversity at cellular resolution while preserving anatomical context. Our efforts to map the adult human hypothalamus through HYPOMAP integrate single-nucleus RNA sequencing with spatial transcriptomics to generate a reference of cell states, their organisation, and their relevance to the physiology & pharmacology of energy balance. Across ~430,000 nuclei, HYPOMAP delineates 452 transcriptionally defined clusters spanning neuronal and non-neuronal populations and maps their spatial distributions across the human hypothalamus. The results show broad conservation of major cell classes across species alongside notable divergence in neuronal subtypes and drug-relevant receptor programmes, underscoring why translation from rodent models can succeed in principle yet fail in detail. Within systems central to body-weight regulation, the atlas reveals species differences in the cellular and spatial organisation of key endocrine-relevant pathways, including the melanocortin and incretin systems, with direct implications for interpreting pharmacology and refining target biology. By anchoring human genetics to specific cell populations, the data further sharpen where, and in which cell types, BMI heritability is manifested. Common-variant BMI association signals are enriched in defined neuronal populations and nominate putative effector genes, while rare variant burden implicates genes with established links to BMI and highlights additional candidates for investigation. These convergent genetic signals provide a bridge from population studies to candidate circuits and mechanisms. A concrete example is DENND1B-mediated regulation of MC4R trafficking: integrating genetic evidence with cell-resolved expression and spatial localisation supports biological plausibility in the human hypothalamus and illustrates how atlases can move beyond cataloguing to enable hypothesis generation. Together, these results position human spatio-cellular atlases as enabling infrastructure for discovery—connecting anatomy, cell identity, and human genetics to accelerate mechanistic insight and therapeutic translation in endocrinology.

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CE2

What can mass spectrometry do for endocrinologists?

Angela Taylor
Birmingham, Birmingham, United Kingdom

More than a decade has passed since my 2015 article, Mass spectrometry and Immunoassay: How to Measure Steroid Hormones Today and Tomorrow (Euro J Endo (2015) 173:2), yet mass spectrometry has still not been widely (enough) adopted in endocrine research. Many laboratories continue to rely on immunoassays and ELISAs, which can suffer from cross-reactivity, limited sensitivity, and narrow dynamic ranges, potentially affecting accuracy. Barriers to adoption, include cost, workflow complexity, and researcher/clinician unfamiliarity. I will highlight the advantages of mass spectrometry, including accurate, multiplexed, and reproducible hormone measurements across diverse biological samples, such as serum, urine, saliva, tissue, hair, sweat and cell media. Using examples from steroid, thyroid, and vitamin D measurements I will demonstrate the potential to improve understanding of endocrine disorders using mass spectrometry. I will discuss my experiences at the Steroid Metabolome Analysis Core (SMAC), University of Birmingham, applying mass spectrometry to a wide range of both clinical and research questions. Through collaborative projects, SMAC has integrated mass spectrometry with both fundamental and clinical research to enhance precision, investigate metabolism, validate biomarkers, develop new diagnostics, and improve patient stratification. Demonstrating how mass spectrometry can translate directly into impactful accurate, evidence-based endocrine research including profiling hormones in adrenal cancer, hormone excess and deficiency, stress, trauma, recovery, and endocrine cancers. Therefore, the question is not what mass spectrometry can do for endocrinologists, but why aren't all endocrinologists demanding to use mass spectrometry?

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CE3

Abstract Unavailable

DOI: 10.1530/endoabs.117.CE3

SfE Guidelines

GL1

Abstract Unavailable

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GL2

Review of the new (2025) ESE Guidelines on Management of Chronic Hypoparathyroidism

Neil Gittoes
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Hypoparathyroidism is a rare disease that is mostly caused by inadvertent surgical removal of parathyroid glands. Historically, management of hypoparathyroidism has been by a 'workaround' utilising initially very high doses of native vitamin D and in more recent times, combinations of active vitamin D, sometimes with calcium supplementation (and thiazide diuretics). To date, there is no universally available hormone replacement therapy for this hormone deficiency state. Some of the long-term complications of hypoparathyroidism are mediated or exacerbated by the standard of care approaches. In particular, renal dysfunction in association with hypercalciuria is a frequent longer-term complication. Furthermore, from a patient experience perspective, many patients experience life-changing neurocognitive symptoms that cannot be addressed by simply normalising calcium homeostasis. The emergence of PTH replacement therapies that mimic physiology have allowed a more desirable approach to long-term management of hypoparathyroidism. Care for patients with hypoparathyroidism is variable, as highlighted in national GIRFT reports. On the backdrop of above, the European Society for Endocrinology have recently updated guidance on management of chronic hypoparathyroidism and propose a position for PTH replacement therapy, particularly in those cases that are not adequately controlled on conventional therapy. This talk will review those guidelines that are timely as later this year, we will learn from NICE the national position of the first new PTH replacement therapy.

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Oral Communications

Adrenal and Cardiovascular

OC1.1

Replacing the early morning cortisol rise reduces fatigue and improves qol in adrenal insufficiency: a double-blind study

Aled Rees[1], Alessandro Prete[2], Verena Theiler-Schwetz[2], Wiebke Arlt[3], Irina-Oana Chifu[4], Birgit Harbeck[5,6], Catherine Napier[7], John Newell-Price[8], Nicole Reisch[9], Günter Stalla[10], Helen Coope[11], John Porter[11], Jo Quirke[11] & Richard Ross[8]
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Background
Replacement therapy with immediate-release hydrocortisone in adrenal insufficiency (AI) fails to restore the early morning cortisol rise, and patients suffer from fatigue and an impaired quality of life (QoL). Plenadren, a once daily dual-release hydrocortisone, only replaces daytime cortisol levels whilst Chronocort, a twice daily delayed-release and sustained absorption hydrocortisone, replaces the cortisol circadian rhythm with an early morning rise in cortisol. Using Plenadren and Chronocort, we tested the hypothesis that waking with physiological cortisol levels will reduce fatigue and improve QoL.
Methods
Double-blind, double-dummy, two-period, two-sequence crossover, randomised study comparing 4 weeks' treatment with 25 mg Chronocort versus 25 mg Plenadren. Inclusion criteria were primary AI with morning pre-dose cortisol < 50 nmol/l. The primary endpoint was the difference in 07:00 h cortisol after 4 weeks of treatment. Key secondary outcome was the Multidimensional Assessment of Fatigue (MAF) score after 4 weeks. Other secondary and exploratory outcomes included AddiQoL, PROMIS 7b, SF36, EQ-5D-5L, GAD-7 and PHQ-9.
Results
Of 49 evaluable participants, 92% achieved a physiological 07:00 h cortisol >140 nmol/l with Chronocort compared with 4% on Plenadren, with median serum cortisol of 417 vs 6 nmol/l, ($P < 0.0001$). The disease specific questionnaire AddiQoL ($P = 0.03$), the fatigue questionnaire PROMIS 7b ($P = 0.02$), SF36 physical functioning ($P = 0.03$) and EQ-5D-5L QoL ($P = 0.02$) showed significant benefit for Chronocort compared to Plenadren. The MAF score was not significantly different between the two treatments; however, a sensitivity analysis showed that in the first period, before crossover, Chronocort reduced the MAF Score ($P = 0.008$) compared to Plenadren. Anxiety with GAD-7 scale showed no difference but the PHQ-9 depression scale revealed a significant difference in favour of Chronocort ($P = 0.017$). The safety profiles were similar for both treatments.
Conclusions
Chronocort provides physiological waking cortisol levels and is associated with reduced fatigue and improved QoL compared to Plenadren in AI patients.

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OC1.2

Validation of prognostic biomarkers in adrenocortical carcinoma through Next-Generation Sequencing and pyrosequencing in a real-life setting

Abubaker Mohamed[1], Lorenzo Tucci[2,3,4], Dario De Biase[5,6], Juliane Lippert[7], Lisa James[1], Nicola Chadderton[1], Alice Fair[1], Amina Mulla[1], Brendan O'Sullivan[1], Kassiani Skordilis[8], Antonio De Leo[4,6], Phillipe Taniere[1], Guido Di Dalmazi[3,4] & Cristina L Ronchi[2,9]
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Background
Adrenocortical carcinoma (ACC) is a rare malignancy with heterogeneous outcomes. We showed that somatic variants and *PAX5* CpG methylation assessed on paraffin-embedded (FFPE) samples can improve prognostic classification.
Aim
To investigate the real-life feasibility of a Next-Generation Sequencing (NGS) and *PAX5* pyrosequencing service for ACC prognostic classification in two European centres.
Methods
53 ACC patients (operated 2002-2025) were divided into a retrospective cohort with known genetic background, an independent validation cohort and a prospective cohort. Tumour DNA was extracted from FFPE tissue and sequenced using a validated NGS panel covering 10 ACC-specific genes. Variant allele frequency (VAF) thresholds were validated between 5%-10%. For *PAX5* methylation, 24 samples (2019-2024) were tested using bisulphite-pyrosequencing quantitative assay to assess 7 CpG sites in the promoter region ($>25\%$ indicating hypermethylation). Turnaround time (TAT) and cost-effectiveness were also assessed.
Results
After excluding 11 cases with low-quality DNA, 39 samples were analysed. In the retrospective cohort ($n = 6$), all somatic variants were confirmed, with two additional *TERT* promoter variants detected. In the validation cohort, 29 variants were found in 19/33 cases, including pathogenic/likely pathogenic variants (53.5% of total findings) in *CTNNB1* (9.3%, mean VAF 62.3%), *TP53* (23.3%, mean VAF 63.9%), *NF1* (16.3%, mean VAF 41.7%) and variants of uncertain significance in *TERT, APC, MEN1, NF1,* and *ZNRF3* (13.9%). In the prospective cohort ($n = 3$), a *TERT* promoter variant was identified (c.-124C>T, VAF 66.85%). For *PAX5* pyrosequencing, 9/24 samples (2022-2024) showed reliable results with one case being hypermethylated (mean methylation 68.5%). Average TAT was 21 days, with costs of €350-400/sample for NGS and €40/sample for pyrosequencing.
Conclusion
The ACC-specific NGS service was reliable, feasible, and cost-effective. *PAX5* pyrosequencing was only suitable for samples aged <2-years. Further investigations are required for prospective testing in view of implementation in clinical setting to improve prognostic classification and identify drug targets.

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OC1.3

Serum steroid metabolomics is inferior to urine steroid metabolomics in the detection of adrenocortical carcinoma

James Hawley[1,2], Angela Taylor[3], Roland Veen[4,1], Lida Abdi[1], Alessandro Prete[5], Vasileios Chortis[6], Vera Dosedelova[1], Carl Jenkinson[1], Conall Dennedy[7], Magalie Haissaguerre[8], Dimitra Vassiliadi[9], Urszula Ambroziak[10], Martin Fassnacht[11,12], Darko Kastelan[13], Irina Bancos[14], Alice Sitch[15], Michael Biehl[4,1] & Wiebke Arlt[1,16]
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Background
Differentiating malignant adrenocortical carcinoma (ACC) from benign adrenocortical adenoma (ACA) remains challenging. Diagnosis often relies on

multimodal imaging; however, this lacks specificity. Urine steroid metabolomics (USM), a combination of multi-steroid profiling by LC-MS/MS and machine learning, has been shown to significantly improve diagnostic accuracy over imaging only. LC-MS/MS analysis is more widely available for serum steroids than urinary steroid metabolites. However, to date, the comparative utility of serum steroid metabolomics (SSM) has not been investigated.
Objective
To compare the utility of SSM and USM for detecting ACC.
Design
We included paired 24-h urine and morning serum samples from 462 patients with confirmed ACC ($n = 78$) and ACA ($n = 384$), recruited in the prospective EURINE-ACT study. All samples were analysed by LC-MS/MS, measuring 14 serum steroids (androgens, glucocorticoids, core precursors) and 14 equivalent urinary steroid metabolites. ACA and ACC were randomly selected into training ($n = 157$) and test ($n = 305$) sets. Results from 157 patients (40 ACC, 117 ACA) were used to train serum- and urine-specific machine learning algorithms utilising generalised matrix learning vector quantisation (GMLVQ). The two locked algorithms were then applied to the serum and urine results, respectively, obtained in the prospective test cohort comprising 305 patients (38 ACC, 267 ACA). Diagnostic performance was assessed using Receiver Operating Characteristic curve analysis and chi squared tests.
Results
Applying the locked USM algorithm to the 24-h urine steroid profiling results of the test cohort produced an AUROC (Area Under the Receiver Operating Characteristic curve) of 0.90 (95%CI 0.84-0.96). By contrast, the SSM algorithm applied to the serum steroid profiling results of the test cohorts produced an AUROC of 0.78 (95%CI 0.69-0.87). Chi squared analysis revealed a significant difference between USM and SSM ($P = 0.02$).
Conclusion
SSM is diagnostically inferior to USM, which remains the test of choice for detecting ACC.

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OC1.4

Improved wellbeing and reduced cardiometabolic risks with once-daily low-dose prednisolone in adrenal insufficiency: interim results from the hyper-aid study

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Introduction
In adrenal insufficiency (AI), hydrocortisone in divided doses is recommended as first-line replacement therapy, with once-daily prednisolone (3–5 mg) as an alternative. Hydrocortisone's short half-life may affect adherence, whereas once daily prednisolone may better mimic the physiological diurnal cortisol rhythm.
Aim
To compare the effects of standard-dose hydrocortisone and low-dose prednisolone on cardiometabolic markers and wellbeing
Methods
This ongoing, prospective, open-label, multicentre crossover study includes adults with AI stable on glucocorticoid therapy for $\geq$4 months. Participants attended two visits: visit 1 before switching from hydrocortisone to prednisolone or vice versa and visit 2 after $\geq$4 months of switching.
Results
A total of 291 participants were enrolled nationally (mean age 57 years, 61% female, 73% with secondary AI); 205 completed the study, including 189 who switched from hydrocortisone to prednisolone (median dose was 4 mg [IQR 3–4 mg]). After $\geq$4 months on prednisolone, mean body weight decreased from 87.1 $\pm$ 20.6 to 85.3 $\pm$ 20.7 kg ($P < 0.001$), and systolic blood pressure fell from 135.6 $\pm$ 19.6 to 129.2 $\pm$ 18.3 mmHg ($P = 0.016$), with no change in diastolic blood pressure. Mean HbA1c improved from 42.0 $\pm$ 9.7 to 40.4 $\pm$ 8.3 mmol/mol ($P = 0.009$). Modified SF-36 scores improved in General Health ($+$ 4.2 $\pm$ 23.5, $P = 0.0478$), Energy ($+7.6 \pm 27.4$, $P = 0.0024$), and Well-being domains ($+4.3 \pm 21.9$, $P = 0.031$), with no change in nausea ($+2.2 \pm 17.4$, $P = 0.154$). In those who switched to hydrocortisone ($n = 16$), mean body weight increased from 77.5 $\pm$ 21.2 to 79.8 $\pm$ 20.8 kg ($P < 0.001$), with no change in blood pressure or HbA1c.
Conclusion
In this real-world study, once-daily low-dose prednisolone improved cardiometabolic markers and wellbeing compared with hydrocortisone, supporting its use in favour of hydrocortisone for patients with AI.

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OC1.5

Validating the utility of morning salivary cortisone in the assessment for adrenal insufficiency

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Adrenal insufficiency (AI) is associated with morbidity and premature mortality. The short Synacthen test (SST) is the reference diagnostic test for AI but requires repeated intravenous clinic-based sampling. Recently, waking salivary cortisone has been proposed as a convenient non-invasive alternative for initial screening. We sought to validate this approach and further define clinically useful cut-off values for morning salivary cortisone. We retrospectively analysed a real-world cohort of 543 patients who underwent an SST for suspected AI, with paired serum cortisol (SerF), salivary cortisol (SalF) and salivary cortisone (SalE) measurements. All patients attended our centre, a tertiary endocrine referral centre in Manchester. SerF was measured using immunoassay and salivary glucocorticoids using liquid-chromatography tandem mass spectrometry. Receiver operating characteristic (ROC) analysis was performed to determine sensitivity and specificity. Thresholds to exclude adrenal insufficiency were derived at ~97% and 100% sensitivity for baseline serF, salF and salE. Decision curve analysis (DCA) was then used to assess net clinical benefit at these thresholds. At baseline measurement, salivary cortisone achieved an area under the curve (AUC) of 0.93 (95% CI 0.91-0.95). This was comparable with baseline/morning serum cortisol (AUC 0.93, 95% CI 0.90-0.95) and significantly superior to baseline/morning salivary cortisol (AUC 0.87, 95% CI 0.83-0.91) for predicting SST outcome (DeLong: $Z = 3.419$; $P = 0.00063$). A salivary cortisone threshold of 19.9 nmol/l excluded adrenal insufficiency with 97% sensitivity and 59% specificity (LR-0.05), while 21.2 nmol/l achieved 100% sensitivity and 52% specificity (LR-0.00). DCA showed that a baseline/morning salivary cortisone threshold of 19.9 nmol/l provided the greatest net clinical benefit across relevant probability thresholds and was comparable to the NICE guideline morning cortisol cut-off of $>$300 nmol/l. Our threshold value is consistent with previous studies, lending support to adopting salivary cortisone as a first-line screening test for adrenal insufficiency.

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OC1.6

Childhood Androgen Excess and Metabolic Risk: A Case-Control Study in Premature Adrenarche and Adolescent Polycystic Ovary Syndrome

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Background
Idiopathic early onset androgen excess often presents in pre-pubertal children as premature adrenarche (PA) and in teenagers as adolescent Polycystic Ovary Syndrome (PCOS). There is inconclusive evidence on whether younger children with PA have higher risk of developing metabolic complications or progressing to PCOS in later life.
Aim
To describe the clinical, hormonal and biochemical phenotype of children with PA and adolescents with PCOS compared to healthy controls.
Design and Methods
Single-centre cross-sectional study (DUCHESS study). We report on auxology and body composition measured by dual-x-ray absorptiometry (DXA), fasting

serum hormone profiles (DHEAS, androstenedione, testosterone, SHBG, prolactin, IGF-1), biochemical surrogate markers of metabolic risk (lipid profile, HbA1c, glucose) and 24-hour urinary steroid profiling (gas-chromatography/mass spectrometry; in PA only).

Results

We recruited 68 children with PA (59 girls, 9 boys) and 39 healthy controls (21 girls, 18 boys), and 30 adolescent girls with PCOS and 16 controls; there were no significant age differences between cases and controls. Other causes of androgen excess were excluded. PA children, characterised by increased serum DHEAS, had higher weight, height, BMI z-score, total fat mass, IGF-1, and HDL cholesterol and lower SHBG than controls (median 61nmol/l [IQR 45.5] vs 88.6 [67.8]; $P = 0.002$). Adolescent girls with PCOS, characterised by increased serum androstenedione and DHEAS, had higher weight, BMI, and total fat mass and fasting triglycerides (1.06 mmol/l [0.46] vs. 0.65 [0.24]; $P = 0.0006$) and lower SHBG than controls. Urinary steroid profiling in PA revealed significantly higher excretion of DHEAS and 17-hydroxypregnenolone metabolites.

Summary and Conclusion

Children with early-onset androgen exposure have multiple differences from matched controls including higher stature, weight and BMI, lower SHBG, and altered urinary steroidogenesis. Ongoing work includes further recruitment and expanded biochemical characterisation, including fasting insulin and HOMA-IR assessments, serum multi-steroid profiling, and untargeted metabolomic analyses to identify metabolic risk signatures.

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Mechanisms and Management of Endocrine Disease

OC2.1

Peri-prostatic adipose tissue drives obesity-associated prostate cancer aggressivity via extracellular vesicles and Rho GTPase signalling

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Prostate Cancer (PC) affects 1-in-8 men in the UK, and obesity 1-in-3. Termed an epidemic by WHO, obesity will shortly overtake smoking as the largest modifiable cancer risk-factor. High-fat diet is linked with increased risk of PC death, and volume of peri-prostatic adipose tissue (PPAT) is associated with increased PC lethality and reduced therapy-response. Furthermore, weight-gain/central-obesity are major side-effects of mainstay androgen-deprivation therapy. Molecular mechanisms underpinning obesity-driven PC remain unknown. PPAT EVs from obese patients significantly increase proliferation, migration, epithelial-to-mesenchymal transition and invasion of PC cells. SNP analysis of RNA-seq data from PPAT EV-treated PC cells reveals EV phenotypic effects are not attributable to transferred long RNAs, but PPAT EVs contain distinct microRNA cargo compared to non-prostatic adipose (NPAT), with targets linked to Rho-GTPase signalling and cell-adhesion. PPAT EV proteomics identifies proteins involved in glycolysis, ATP-synthesis, and Rho-GTPase signalling, suggesting PPAT EVs may modulate metabolism and ECM-associations and metastasis in target PC cells. Consistently, RNA-seq of PPAT EV-treated PC cells revealed dysregulation of Rac/Rho, EGFR-signalling and cytoskeleton dynamics, with differential impacts in lean-*versus*-obese context. Top PPAT EV-dysregulated genes are increased in PC-*versus*-normal tissue, associate with reduced survival and significantly alter PC proliferation/migration. One such is TBX1, a developmental transcription-factor significantly elevated following treatment with PPAT-vs-NPAT EVs. TBX1 silencing significantly reduced PC cell proliferation/migration, but did not impact non-cancerous cells. Importantly, PPAT-enhanced TBX1 altered TGFB-mediated Rho-GTPase pathway-activation, leading to increased activity of Paxillin, a key regulator of focal adhesions (FAs) that promotes FA-turnover and motility. Indeed, TBX1 silencing increased PC cell ECM-adhesion and reduced expression of Rho-GTPase genes, whilst treatment with PPAT-vs-NPAT EVs increased this. We implicate Rho-GTPase signalling as a causal driver of PPAT-driven PC aggressivity through TBX1-mediated cell-adhesion changes, increasing PC motility/ migration. PPAT EV miR and protein cargo may be responsible for these phenomena.

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OC2.2

Imaging adrenal aldosterone synthase expression with [^{18}F]AldoView PET-CT in primary aldosteronism

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Primary aldosteronism (PA) results from dysregulated aldosterone secretion, leading to hypertension and cardiovascular, metabolic, and renal disease. Adrenalectomy benefits patients with "unilateral" PA, but it is challenging to identify those patients most likely to benefit. Adrenal venous sampling (AVS), the current reference standard for guiding treatment decision, is technically demanding, invasive, and only available at a few specialised centres. To simplify and improve treatment stratification, we developed [^{18}F]AldoView, the first highly selective aldosterone synthase (CYP11B2)-specific PET radioligand. We present results from the first-in-human study, which evaluated the potential of [^{18}F]AldoView PET-CT to detect aldosterone-producing lesions in 17 consecutive patients with PA who had lateralise on AVS and were scheduled for laparoscopic adrenalectomy. Specificity of tracer binding was assessed by autoradiography and immunohistochemical (IHC) staining for CYP11B1 and CYP11B2 in excised adrenal tissues. [^{18}F]AldoView PET-CT identified one or more focal lesions (total n = 22) in all 17 adrenals predicted to be dominant by AVS and additionally revealed microlesions (< 1 cm^3) in the contralateral glands of five patients. When corrected for lesion size, lateralisation on PET was concordant with AVS in all cases. IHC confirmed dense CYP11B2 expression consistent with aldosterone-producing adenomas in 15 patients and multiple micronodules in two. The binding pattern of [^{18}F]AldoView closely reflected aldosterone synthase expression in tissue sections from the resected adrenals.

Conclusion

[^{18}F]AldoView PET-CT demonstrates high specificity for macro- and microscopic aldosterone synthase-positive lesions. [^{18}F]AldoView may have the potential to transform diagnostic pathways and refine treatment stratification across the spectrum of aldosterone dysregulation. A phase II trial (IDEAL2) is underway to evaluate its performance in a broader population of patients with PA.

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OC2.3

Retrospective Review of the Management of Head and Neck Paragangliomas in a UK PPGL Centre of Excellence

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Head and neck paragangliomas (HNPGLs) are rare neuroendocrine tumours predominately arising from parasympathetic ganglia. HNPGLs can be sporadic or hereditary, rarely secrete catecholamines and have malignant potential. Herein we report a series of HNPGLs in a UK tertiary referral centre. A retrospective review of 79 patients (50 female) diagnosed between 2014-2025 was performed. Patients were excluded from data analysis if data sets were incomplete. The cohort's median age was 58 years (range 20-86). Tumour location was jugulotympanic for 65.8% (52/79), carotid body for 17.7% (14/79), vagal for 6.3% (5/79), multifocal within the head and neck in 8.8% (7/79) and one patient had a HNPGL and a synchronous abdominal paraganglioma. The median tumour size from radiological reports was 23x19mm. A pathogenic variant in the succinate dehydrogenase (*SDHx*) genes was identified in 38% (30/79) of these: 60% (18/30) *SDHB*, 30% (9/30) *SDHD*, 6.7% (2/30) *SDHA* and 3.3% (1) *SDHC*. Plasma metanephrines or plasma 3-methoxytyramine were elevated in 20.3% of cases (16/79). Of those with raised 3-methoxytyramine: 75% (9/12) had *SDHx* mutations (6/9 *SDHB*). Of the *SDHx* carriers, 70% (21/30) were probands and 30% (9/30) were gene carriers identified through screening programmes. Management included surgical excision in 18/79 (22.8%), surgery and radiotherapy in 3/79 (3.8%), radiotherapy alone in 19/79 (24.1%) and surveillance in 39/79 (49.4%). 11/79 (13.9%) patients developed local recurrence of their tumour or tumour growth. Of these: 36.4% (4/11) had local regrowth after partial excision ± radiotherapy treatment and 63.6% (7/11) had local recurrence after total

surgical excision. 10/12 (83.3%) patients who developed recurrent or progressive growth of HNPGLs harboured an *SDHx* mutation. This series produced results comparable to other reported cohorts with a ~15% rate of recurrent or progressive HNPGL growth and a similar prevalence of *SDHx* mutations and highlights the need for long term follow up and expert MDT input.

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OC2.4

Sphingosine kinase 2 (SPHK2) inhibition as a therapeutic strategy for adrenocortical carcinoma (ACC)

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Background
Sphingolipid metabolism plays a role in adrenal homeostasis, as evidenced by the association of sphingolipid enzyme deficiency with adrenal insufficiency. In contrast, high transcriptomic expression of several sphingolipid enzymes is associated with poor prognosis in adrenocortical carcinoma (ACC). This study is focused on SPHK2, high transcriptomic expression of which is associated with poor overall survival in ACC (analysis of the TCGA-ACC data).
Methods
Immunohistochemical staining of SPHK2 was undertaken in 125 ACC (where clinical data were available for correlation), 21 adrenocortical adenomas (ACA), and 5 normal adrenal tissues from University Hospital Würzburg. Lentiviral driven stable overexpression of SPHK2 was established in 3 ACC lines (H295R, TVBF-7, MUC-1) with cell proliferation, migration, response to mitotane treatment and selective SPHK2 inhibition assayed.
Results
SPHK2 expression was significantly higher in ACC compared to ACA but showed no correlation with established prognostic factors, clinical scores, or steroid production. Although there was a trend toward reduced overall survival with high SPHK2 expression, it did not reach statistical significance, and no impact was seen on progression or recurrence free survival. All three ACC cell lines (H295R, TVBF-7, MUC-1) express SPHK2. Overexpressing SPHK2 did not affect cell proliferation assayed at 72 hours in the 3 cell lines. SPHK2 overexpression did, however, promote cell migration in the H295R cell line. Opaganib (ABC294640), a selective SPHK2 inhibitor, reduced cell viability to a similar extent as mitotane in all three cell lines. Interestingly, SPHK2 overexpression in TVBF-7 cells induced mitotane resistance; this did not affect the susceptibility of the cells to SPHK2 inhibition.
Conclusion
SPHK2 inhibition, already in phase II clinical trials for other cancers, may present an alternative/adjunctive therapy in ACC. Further work is ongoing to identify the biological pathways disrupted by SPHK2 inhibition and determine how they differ from those targeted by mitotane.

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OC2.5

Rationalising the use of hypertonic saline-stimulated copeptin measurements in differentiating between AVP deficiency and primary polydipsia

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Polyuria-polydipsia syndrome, a relatively uncommon primary presentation to Endocrine services, is characterised by production of large volume of hypotonic urine. After excluding hyperglycaemia, hypercalcaemia, hypokalaemia and arginine-vasopressin resistance (diagnosed with elevated untimed serum copeptin levels), the main differentials are arginine-vasopressin deficiency (AVP-D) and primary polydipsia (PP). Hypertonic saline-stimulated copeptin (HSC) has emerged as the gold standard test to accurately differentiate between AVP-D and PP. HSC nevertheless requires intense monitoring, is not widely accessible and can predispose to seizures and thrombophlebitis. We reviewed our use of HSC from 2017 to 2020. AVP-D was excluded in 10 patients (defined as serum copeptin >4.9 pmol/L with concurrent serum sodium ≥ 150 mmol/L during HSC). In half of them, HSC was not necessary as AVP-D were ruled out by: 24hour urine output <2.5L(N = 2), fasted urine osmolality >700 mOsm/kg(N = 2) or hyponatraemia on random testing(N = 1). We therefore devised a diagnostic algorithm sequentially incorporating untimed serum/urine biochemistry and paired serum/urine fasted biochemistry after 2 days of fluid restriction (2L daily), with 24hour urine collection on day 2, in patients with a high pre-test probability of PP. Our re-audit data (2021 to 2024 period) reveals that the need for HSC was eliminated in six out of eight patients with PP. For the two patients who underwent HSC, one had Wolfram syndrome and declined fluid restriction for 2 days and the other patient requested further confirmatory testing despite evidence of PP on paired urine/serum fasted biochemistry after 2 days of fluid restriction. Our diagnostic algorithm to sequentially investigate patients with a high pre-test probability of PP can eliminate the need for HSC in at least 75% of cases, making it a more favourable and widely accessible approach.

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Bone and Reproductive Endocrinology

OC3.1

Investigating fertility and reproductive ageing in a Down syndrome mouse model

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Background
Down syndrome (DS) is caused by the triplication of chromosome 21 and is associated with several endocrine abnormalities including reduced fertility. While onset of puberty is unaffected in individuals with DS, fertility and reproductive lifespan are often diminished. We used the Dp1Tyb mouse model to investigate mechanisms underlying reduced fertility and reproductive ageing.
Methods
The Dy1Tyb mouse strain has an extra copy of 63% of Hsa21-orthologous mouse genes and was used as our *in vivo* model of DS. Breeding performance from Dp1Tyb and wild-type (C57BL/6J) colonies was analysed using in-house facility records and public data from the Mouse Phenome Database (Jackson Laboratory). Animals were sacrificed at the end of reproductive life, defined as >3 months without producing a litter. To evaluate female reproductive ageing, we determined the age of last litter as a proxy for menopause onset and quantified total follicular count at the end of reproductive life.
Results
Male and female Dy1Tyb breeders (crossed with wild-type mice) produced fewer litters per dam, with fewer pups per litter, compared to wild-type breeders, with female mutants producing less than males. Furthermore, female mutants exhibited a significantly earlier age of last litter, indicating premature reproductive decline, compared to wild-type controls. Histological analysis revealed similar ovarian weights but a reduction in total follicular count at the end of reproductive life in female mutants compared to wild-type controls.
Conclusion
Dp1Tyb mice replicate the subfertility observed in individuals with DS and reveal evidence of accelerated reproductive ageing in females, characterised by earlier cessation of reproduction and diminished ovarian reserve. These findings highlight the Dp1Tyb strain as a robust model to investigate mechanisms of infertility and reproductive senescence in DS.

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OC3.2

Kisspeptin challenge test reveals hypothalamic dysfunction in obesity-related hypogonadism

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Background
Male obesity-related secondary hypogonadism (MOSH) affects two-thirds of men with BMI $\geq$ 40 kg/m^2 and is associated with increased morbidity and mortality. Animal models suggest decreased hypothalamic function in obesity-related hypogonadism. Herein, we use kisspeptin for the first time to examine hypothalamic dysfunction in men with obesity, both with and without hypogonadism.
Methods
Men with MOSH (BMI $\geq$30 kg/m^2; $n = 21$) were identified by fasting total-testosterone $<$10nmol/l (SfE guidelines). We also enrolled healthy eugonadal controls both with (BMI $\geq$30kg/m^2, $n = 20$) and without obesity (BMI $<$30kg/m^2, $n = 80$). Endocrine profiling included LH-pulsatility assessment (10-minutely sampling for 8hrs), responses to intravenous kisspeptin and gonadotrophin-releasing hormone (GnRH) bolus to interrogate hypothalamic and pituitary function, respectively. Hormone concentrations were compared using Kruskal-Wallis test, and temporal endocrine profiles using mixed-effects models.
Results
Total-testosterone ($\beta = -0.47$), free-testosterone ($\beta = -0.01$), and dihydrotestosterone ($\beta = -0.04$) were inversely associated with BMI (all $P < 0.0001$). LH pulse-frequency [median, IQR] was increased with obesity (BMI 20–30kg/m^2: 3.00 [3.00,4.75] *vs* $>$40kg/m^2: 5.00 [4.00,6.00]) pulses per 8hrs; $P = 0.007$, but LH pulse-amplitude and GnRH responses did not differ. The early-phase LH response to kisspeptin was blunted in men with MOSH (median area-under-the-curve at 60mins: MOSH 38.78 [23.85, 78.26] *vs* lean controls 108.7 [78.56, 190.40] $p < 0.0001$, *vs* eugonadal men with obesity 124.1 [81.58, 163.90] IU•h/l, $P = 0.0011$). FSH responses to kisspeptin were higher in eugonadal men with obesity than lean controls (893.80 [596.10, 1104.00] *vs* 434.80 [292.70, 692.10] IU•h/l; $P = 0.003$).
Conclusion
Our data revealed increased LH pulse-frequency but no change in pulse-amplitude in men with obesity. Eugonadal men with obesity had an increased response to kisspeptin, but the early phase response to kisspeptin was reduced in men with MOSH. Our data demonstrates, for the first time in humans, that abnormal hypothalamic function plays a key role in the pathophysiology of obesity-related hypogonadism.

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OC3.3

Short-term oestradiol variability across HRT preparations in post-menopausal women

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Background
Variability in oestradiol profiles across hormone replacement therapy (HRT) preparations has clinical implications. However, short-term variability across preparations has not been examined previously. Herein, we assessed short-term reproductive hormone variability in postmenopausal women on different HRT preparations.
Methods
Reproductive hormone levels were measured in 35 postmenopausal women using gel, oral, patch, or spray HRT. For gel, oral, and spray users, serial venous sampling was performed every 15mins over 90mins. Variability was quantified using peak–trough changes and coefficient-of-variation (CV%), with the oestradiol assay CV $\leq$7.7%. Hormonal differences were assessed using Kruskal–Wallis test, and associations with Spearman's r.
Results
Age [mean (SD)] was 56.7 (4.1) years and BMI 24.0 (2.7) kg/m^2. Oestradiol-equivalent doses ranged from low–medium for oral ($n = 4$) and spray ($n = 3$), low–high for gel ($n = 15$), and medium–high for patch ($n = 15$). Baseline oestradiol was negatively correlated with FSH for gel ($r = -0.56$, $P = 0.03$) and patch ($r = -0.57$, $P = 0.04$), with weaker correlations for LH (gel: $r = -0.54$, $P = 0.06$; patch: $r = -0.50$, $P = 0.06$). Short-term oestradiol variability differed by preparation: peak–trough changes [median (IQR)] were 144.8pmol/l (80.7–324.6) for gel, 177.9pmol/l (115.8–280.1) for oral, and 395.9pmol/l (130.2–891.6) for spray. Spray also exhibited the highest oestradiol CV% [54.1% (36.7–78.3)], compared with oral [17.1% (10.7–24.2), $P = 0.04$] and gel [15.1% (2.8–17.0), $P < 0.01$] preparations. Oral and gel did not differ significantly ($P = 0.08$).
Discussion
In postmenopausal women, oestradiol negatively correlated with FSH and LH, consistent with negative feedback. Short-term oestradiol variability differed by HRT preparation. Spray exhibited the greatest fluctuations, followed by gel and oral preparations. Variability exceeded intra-assay CV% confirming pharmacokinetic rather than analytical effects. Our data shows that single time-point measurements may not represent prevailing oestradiol levels and may not be suitable for monitoring or adjusting HRT, which should instead be guided by symptoms.

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OC3.4

DNA methylation of gonadotropin-releasing hormone regulatory genes is altered in human delayed puberty

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Delayed puberty is frequently an inherited condition with a clear genetic basis, previously linked to variation in GnRH pathways genes. However, many patients do not have an identifiable genetic variant responsible for their delayed puberty and the role of epigenetic modifiers of human pubertal timing is underexplored. Robust evidence has been provided that the timing of puberty in animal models is regulated by an epigenetic mechanism of transcriptional repression. In view of the unique dynamic activity of the hypothalamic-pituitary-gonadal axis, changes in DNA methylation are highly likely to play a regulatory role in pubertal onset and timing. Genome wide DNA methylation was detected using the Illumina EPIC array, for patients ($n = 92$) with delayed puberty with no previously identified genetic cause, and related unaffected controls ($n = 20$). Analysis in R utilised dmpFinder and bumphunter packages. This revealed differentially methylated CpG sites linked to key genes involved in upstream regulation of GnRH signaling, including *TAC3, SIRT1, PDYN, KMT2A, NELL2, KAT2B*, *NOS1* and *ZNF573* which showed a difference in methylation between individuals with delayed puberty compared to controls. These differentially methylated CpG sites were identified in either enhancer or promoter regions of their corresponding genes. The top 5 CpG sites identified novel candidate genes for delayed puberty, including *CADPS2*. Over representation analysis identified multiple KEGG pathways previously associated with growth dysfunction as significantly altered. These included cAMP, neuroactive ligand-receptor interaction and growth hormone synthesis pathways. Differential methylation of genes related to BMI was observed, but it was not specific to patients with low or high BMI. Subsequently, pathogenic exonic variants in the genes associated with the top 10 CpG sites were identified in additional patients with delayed puberty. These findings support that changes in methylation of key GnRH regulatory genes contribute to the phenotype of delayed puberty.

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OC3.5

Improvements in Lower Extremity Alignment are Associated with Physical Functioning in Children with Achondroplasia Treated with Navepegritide: 52-Week Results from the ApproaCH Trial

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Genu varum is common in children with achondroplasia, and can lead to pain, impaired mobility, and a negative impact on health-related quality of life. In this post-hoc analysis from the pivotal ApproaCH trial we report the effects of navepegritide, a prodrug of C-type natriuretic peptide (CNP), on genu varum and its association with Achondroplasia Child Experience Measure-Physical Functioning (ACEM-PF), an achondroplasia-specific clinical outcome assessment. ApproaCH randomized 84 children (aged 2-11 years) 2:1 to receive once-weekly navepegritide (100 µg/kg/week) or placebo. Radiographs were collected at baseline and Week 52, with key features of skeletal dysplasia assessed by blinded central readers. Data are reported as least square (LS) mean differences versus placebo calculated by ANCOVA, and Pearson correlation coefficients (r). The primary endpoint—annualized growth velocity at Week 52—was greater in navepegritide-treated children versus placebo (LS mean difference 1.49 cm/year, $P < 0.0001$). Compared with placebo at Week 52, navepegritide significantly reduced tibial-femoral angle (TFA) (difference -1.81 degrees, $P = 0.0094$), significantly improved fibula-to-tibia ratio (difference -0.016, $P = 0.0001$), and improved ACEM-PF scores (difference -4.6, $P = 0.252$). Compared with the overall population, children with prominent genu varum at baseline (TFA ≥ 5 degrees) treated with navepegritide had greater improvements versus placebo in TFA (difference -3.99 degrees, $P = 0.0073$) and ACEM-PF (difference -8.2, $P = 0.048$). Changes in ACEM-PF were associated with improvements in TFA in children with more severe genu varum at baseline ($r = 0.31$; $P = 0.062$); the correlation was stronger in this subgroup aged <8 years ($r = 0.39$; $P = 0.035$). Navepegritide demonstrated superiority over placebo in AGV, and reduced TFA at Week 52 in the ApproaCH trial. Associations between improvements in genu varum and ACEM-PF support that changes in lower extremity alignment with once-weekly navepegritide positively impact physical functioning, and suggest that navepegritide may offer benefits beyond promoting linear growth that translate into meaningful improvements in children living with achondroplasia.

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OC3.6

Comparative Effectiveness of Bariatric Surgery vs. Pharmacologic Weight Loss on Bone Health and Fracture Risk in Asian Population

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Obesity management often needs significant weight loss, which can be achieved through bariatric surgery or pharmacologic therapies. This study compared the short-term impact of Roux-en-Y Gastric by pass surgery (RYGB) versus Pharmacologic therapy with liraglutide (GLP 1 A) on bone mineral density (BMD) and fracture risk in patients with severe obesity.

Methods

A 6-month prospective observational study from was conducted in 60 adults with BMI ≥ 35 kg/m2. Study participants were allocated into two groups: Surgery (RYGB, $n = 30$) and Pharmacotherapy (liraglutide 3.0 mg/day, $n = 30$ mg/day, $n = 30$). patients were followed over 6 months and along with prospective weight loss lumbar spine and femoral neck BMD were assessed by DEXA at baseline, 12, and 24 weeks. Serum markers of bone turnover (CTX, PINP) and fracture risk (FRAX score) were evaluated alongside weight changes.

Results

The surgical group achieved greater weight reduction (-22.5 kg) compared to pharmacotherapy (-10.2 kg). However, RYGB was associated with a more pronounced decline in hip BMD (-4.8% vs. -1.2%) and spine BMD (-2.5% vs. -1.5%). Bone turnover markers showed a marked rise in resorption (CTX +65%) post-surgery, whereas liraglutide was associated with significant suppression of both CTX (0.65 → 0.10 ng/mL) and PINP (0.25 → 0.05 ng/mL), with a greater relative decline in resorption. The FRAX score increased more in the surgical group (+1.5), indicating higher fracture risk.

Conclusion

RYGB provides greater weight loss but carries a greater risk of bone loss and increased fracture risk compared to pharmacologic therapy. Liraglutide shows a more bone-sparing profile, suggesting it may be preferable for patients at risk of osteoporosis. Long-term follow-up is guaranteed to confirm these findings.

Key works

CTX - C telopeptide, PINP (pro collagen type 1 pro peptide), DEXA (dual Xray energy bone absorptiometry), FRAX (fracture risk assessment tool)

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Thyroid

OC4.1

Functional characterization of two different NAH-associated activating TSHR mutations

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Activating germline mutations of the thyroid-stimulating hormone receptor (*TSHR*) are rare, and result in congenital nonautoimmune hyperthyroidism (NAH). Here we report the first functional characterization studies of two NAH-associated *TSHR* mutations. Firstly, a novel, maternally inherited mutation (p.Leu512Val) identified in a clinically-euthyroid female with TRAb negative thyrotoxicosis and a strong family history of NAH. Secondly, a previously reported *TSHR* mutation (p. Thr490Arg), in a male, with similar biochemistry and a maternal history of NAH. Transfection studies were performed in heterologous cells to compare expression and function of wild-type (WT) and mutant TSHR's. Western blotting, immunostaining and flow cytometric analysis demonstrated comparable total cellular and surface expression of WT and mutant receptors. TSHR is a G-protein coupled receptor activating both the Gs/adenylyl cyclase pathway (cAMP, predominant effect), as well as the Gq-phospholipase C pathway (Ca and PKC responsive). Compared with wild-type TSHR, two different cAMP responsive reporter assays, cAMP-RE-luc (indirect) and the Glosensor assay (direct), demonstrated elevated constitutive and TSH-stimulated Gs-coupled signalling for both mutant receptors. In contrast, a Nuclear Factor of Activated T-cells-RE reporter assay (Gq-pathway) did not show a difference. The effects of the TSHR mutations were analysed *in silico* using EM-structures (ref: https://doi.org/10.1038/s41586-022-05173-3 and https://doi.org/10.1038/s41586-022-05159-1). Substitution of L512, located in the middle of the transmembrane domain, with the smaller Valine is predicted to result in a more dense structure, resembling the active conformation. Replacement of Thr490, situated between the transmembrane and ligand binding domains, with the larger Arginine could, due to steric hindrance, alter the position of the ligand binding domain to a more upright position, similar to the ligand-bound active receptor. Collectively, our laboratory and *in silico* findings support increased constitutive Gs-signalling (cAMP), but not the Gq-signalling (Ca and PKC) pathway as a cause of NAH in individuals harbouring the T490R and L512V TSHR mutations.

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OC4.2

Neutrophil count and neutropenia in newly diagnosed hyperthyroidism: ethnic variation and TRAb-Free-T4 interaction

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Background
Hyperthyroidism is associated with reduced neutrophil counts. Whether thyroid autoimmunity (TSH-receptor antibodies; TRAb) modifies the relationship between free thyroxine (FT4) and neutrophils, and how ethnicity relates to neutrophil levels at diagnosis, remains unclear.
Methods
Results from 237 adult patients with newly diagnosed hyperthyroidism with diagnostic thyroid function tests and TRAb titre between August 2020 to July 2025 were retrospectively analysed. A univariate general linear model (ANCOVA) was used to assess the effects of FT4 and TRAb on neutrophil count, including their interaction. Low absolute neutrophil count (ANC) was defined as $<2.0\times10^9$/l. Neutrophil counts and neutropenia rates between Graves' disease (GD) (elevated TRAb) and non-GD, across self-identified ethnic groups, were compared.
Results
Of 237 patients, 152 had Graves' and 85 had non-Graves' aetiologies. Neutrophil counts were lower in Graves' (median [IQR] 3.44 [2.67–4.64]$\times$10^9/l) than non-Graves' hyperthyroidism (3.71 [2.92–5.12]$\times$10^9/l; $P = 0.045$).The TRAb$\times$FT4 interaction was significant, indicating that the association between FT4 and neutrophils differed by TRAb level ($P < 0.001$). Higher FT4 was linked to disproportionately lower neutrophils in patients with high TRAb, with little FT4 effect in TRAb-negative patients. Ethnicity was an important determinant of neutrophil count: Black GD patients had higher prevalence of low ANC (33.3%) than Asian (10%) and White patients (2.5%, $P < 0.001$). Mean ANC in GD was 1.14 x10^9 higher upon achieving euthyroid status than at diagnosis ($P = 0.002$). Seven individuals continued to have low ANC (5 of Black ethnicities, 1 White, 1 unspecified) and two remained neutropenic (both of Black ethnicities).
Conclusions
Both autoimmunity and ethnicity significantly influence neutrophil counts in newly diagnosed hyperthyroidism. Patients with high TRAb and high FT4 exhibited the greatest neutrophil reductions. Neutrophil counts and neutropenia risk vary by ethnicity, with Black patients disproportionately affected – perhaps reflecting thyrotoxic effect superimposed on the benign ethnic neutropenia. Our findings support individualised interpretation of neutrophil counts in hyperthyroid patients.

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OC4.3

Development of 3D thyroid follicles from primary human and murine thyrocytes

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Cell culture models are widely used to evaluate different facets of whole-organ biology, including mechanisms of organ function and consequences of genetic perturbation or pharmacological modulation. The thyroid is a complex organ, consisting of polarized thyrocytes organized into follicular structures with a clear distinction in membrane protein expression between the apical and basal aspect of the follicle. This cellular polarisation is essential for permitting uptake of Iodine and synthesis, storage and secretion of thyroid hormone. Under conditions of monolayer culture, primary thyrocytes may lose functional activity, and there is a lack of human thyrocyte cell lines that maintain sufficient differentiation for study of normal thyroid function. We have developed methodology for culturing three-dimensional, functionally active primary human thyroid follicles. Human thyrocytes are isolated from surgical thyroidectomy specimens by enzymatic digestion, these dissociated thyrocytes can then be suspended in a 3D-matrix. In this 3D culture system these cells spontaneously reorganise to form follicular structures, comparable to the organ niche, in contrast to a predominantly monolayer of cells in a 2D culture system. Direct comparison of the same cells cultured in 2D or 3D demonstrates increased mRNA expression of key indicators of thyroid function (*SLC5A5*, *TG*, *TSHR)* with appropriate response to TSH, preserved polarised expression of key thyroidal proteins and an increased cellular uptake of ^{125}I in the 3D cell culture system. Additionally, we have established that these structures are amenable to viral transduction and therefore future applications of this model can include genetic manipulation. Human thyrocytes also tolerate cryopreservation and recovery. Moreover, this methodology is equally applicable to culturing freshly isolated murine thyroid follicles. Thus, our paradigm represents an exciting tool for future evaluation of thyroid biology and function through manipulation of gene expression, pharmacological modulation and comparison of primary thyroid follicular cultures from relevant murine models and human primary cells.

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OC4.4

Evaluating levothyroxine cessation and thyroid status: a city-wide population record analysis

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Introduction
Hypothyroidism is conventionally viewed as a lifelong condition requiring continuous Levothyroxine (LT4) therapy. However, some patients discontinue treatment. Understanding the clinical outcomes of these patients, especially those on low doses, can inform whether lifelong therapy is always necessary for milder disease. This study used the Greater Manchester Care Record (2010–2024) to evaluate this.
Methods
We analysed primary care data for patients with a diagnosis of hypothyroidism or no diagnosis code who started LT4 after 2012. We included only patients on a low-dose regimen (average daily dose $<80\%$ of full replacement, calculated by BMI) who remained on therapy for at least three months. Inclusion was conditional on having TSH/FT4 results available before starting/during/after stopping LT4. We compared median serial TSH/FT4 values.
Results
Of 52,676 patients who started LT4 during the study, 12.3% (6,470) stopped medication. We focused on the 1,870 patients who met the 3-month treatment and were clinically monitored (had a post-cessation TFT). Patients who stopped had pre-treatment a slightly lower median TSH (6.4mIU/l) FT4 (11.7pmol/l) than those who continued, TSH (7.3mIU/l) and FT4 (11.0pmol/l), suggesting milder initial dysfunction. Crucially, in the 407 patients with post-cessation TSH and FT4 values, the median TSH after stopping LT4 was 3.1mIUL/l (IQR 2.1–4.3) and FT4 was 13.0 pmol/l (IQR 11.5–15.6). This means post-discontinuation at 3+months, TSH and FT4 remained in the euthyroid range.
Conclusion
A significant subset of patients, primarily those started on LT4 for milder indications (low dose), successfully discontinue treatment and maintain thyroid hormone levels within the therapeutic range. The sustained normalisation of TSH/FT4 post-cessation suggests the initial dysfunction may have been transient. This finding raises important questions about the rationale of lifelong LT4 for the large, increasing population on low doses while supporting the need to evaluate supervised withdrawal trials.

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OC4.5

Batoclimab Induces Very Rapid and Sustained Post-treatment Euthyroidism in Graves' Disease

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Objectives
To report post-treatment outcomes among hyperthyroid patients with Graves' disease (GD) who received batoclimab, a neonatal fragment crystallizable receptor blocker, in a phase 2a, proof-of-concept open-label study.
Methods
Overtly hyperthyroid GD patients with elevated thyrotropin receptor autoantibodies (TSH-R-Ab) despite ≥12 weeks on moderate-to-high dose antithyroid drugs (ATD) were eligible. Participants received weekly subcutaneous injections of batoclimab for 24 weeks (Weeks 0-11, 680 mg; Weeks 12-23, 340 mg). At Week 24, participants with FT3/FT4 ≤upper limit of normal (ULN) entered a 24-week batoclimab-free follow-up period (Weeks 24-48).
Results
By Week 2, 15/25 (60%) patients achieved FT3/FT4 ≤ULN without increasing ATD dose. This increased to 20/25 (80%) patients at Week 12 or end of high-dose treatment, including 15 (60%) who were off ATD, and to 18 (72%) patients at Week 24 or end of treatment (EOT), including 10 (40%) who were off ATD. Six months following EOT, 17/25 (68%) patients had FT3/FT4 ≤ULN; of these, 8 were off ATD and 5 were on ≤2.5 mg ATD/day. Mean (SD) TSH increased from 0.01 (0.01) mIU/l at baseline to 0.32 (0.61) and 0.77 (0.85) mIU/l at Weeks 24 and 48, respectively. Mean (SD) TSH-R-Ab levels decreased from 17.96 (12.12) IU/l at baseline to 8.13 (8.82), 6.16 (8.85), and 9.94 (12.03) IU/l at Weeks 2, 24, and 48, respectively ($P < 0.0001$ vs baseline for all). Total IgG rebounded after treatment stopped, with a mean (SD) level of 11.72 (2.64) g/l at baseline compared to 4.10 (1.76) g/l at Week 24 ($P < 0.001$) and 11.14 (2.78) g/l at Week 48 ($P = 0.42$). Batoclimab was well tolerated with no new safety signals.
Conclusions
Batoclimab resulted in rapid and sustained normalization of FT3/FT4. Six months after stopping treatment, 52% of patients remained euthyroid either off ATD or on ≤2.5 mg ATD/day.

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OC4.6

Mapping the mutational landscape of thyroid carcinoma using whole-exome sequencing

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Background
The molecular landscape of thyroid carcinoma (TC) is characterised by diverse somatic alterations, most prominently affecting the MAPK and PI3K-AKT pathways. This study applied whole-exome sequencing (WES) to characterise the spectrum of driver mutations in archival tumour tissue from a TC cohort and to explore inter-tumour heterogeneity across different histological subtypes.
Methods
Archival formalin-fixed paraffin-embedded (FFPE) tumour DNA from 23 patients with histologically confirmed TC (papillary= 12, follicular= 5, medullary= 3, anaplastic= 3) underwent WES. Somatic single-nucleotide variants (SNVs) and small insertions/deletions (INDELs) were identified using Mutect2, Strelka, and VarDict. Variants passing all high-confidence filters (depth ≥ 30, tumour allele depth ≥ 5, allele frequency ≥ 1 %) were annotated through the Cancer Genome Interpreter and cross-referenced with the COSMIC Cancer Gene Census (v99). Selected driver variants were validated using droplet digital PCR (ddPCR).
Results
Across the cohort, 4639 high-confidence somatic variants were detected, all of which were SNVs; no INDELs passed filtering thresholds. Of these, 116 variants were classified as putative driver mutations. The most frequently altered genes were *BRAF*, *NRAS*, *HRAS*, *TP53*, *ARID1B*, and *KMT2A*, implicating the MAPK and PI3K-AKT pathways as dominant oncogenic axes. *BRAFV600E* occurred in 41.7 % of papillary cases, lower than TCGA (59.7 %), whereas *NRASQ61R* appeared in 60 % of follicular cases, exceeding published averages (38 %). Only three variants, *BRAFV600E*, *NRASQ61R*, and *HRASQ61R*, were shared across 13 patients, reflecting pronounced molecular heterogeneity. ddPCR validation confirmed these alterations with strong correlation between WES-derived VAF and ddPCR FA ($r = 0.76$, $P < 0.05$).
Conclusion
WES of TC tumours revealed a heterogeneous mutational profile dominated by SNVs, with limited inter-tumoural overlap even within histological subtypes. The predominance of *BRAF* and *RAS* mutations supports their central role in TC, while extensive molecular diversity highlights the need for personalised, mutation-guided surveillance and therapeutic strategies in TC.

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Metabolism, Obesity and Diabetes

OC5.1

Integrative multi-omics analysis reveals epigenetic regulation of placental genes associated with maternal B12 deficiency

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Obese mothers during pregnancy have been linked with complications of metabolic diseases and long-term health outcomes. Maternal nutrition plays a pivotal role in fetal development and *in-utero* programming events. Among key micronutrients, vitamin B12 is essential for DNA synthesis and neurological development. Its deficiency has been associated with adverse outcomes, including neural-tube defects, intrauterine growth restriction, and increased risk of metabolic disorders in offspring potentially through epigenetic mechanisms affecting placental function and fetal metabolism. In this study we aim to identify epigenetically regulated genes and miRNAs due to B12 deficiency through comprehensive integrated multi-omics in placental tissues. Human placental tissues ($n = 50$) from pregnant women (PRiDE Cohort) were profiled for differentially methylated regions (RRBS-seq), differentially expressed genes (RNA-seq) and differentially expressed miRNAs (sRNA-seq) in mothers with sufficient (>150 pmol/l) and deficient B12 (<150 pmol/l) levels adjusting for maternal age, fetal-sex and body mass index. Mothers with vitamin B12 deficiency exhibited higher BMI, lower folate, and elevated fasting glucose and homocysteine levels compared to those with sufficient B12, while gestational age and neonatal characteristics didn't differ significantly. Integration of placental multi-omics identified extensive molecular alterations, including 14,219 differentially methylated regions, 208 differentially expressed genes, and 46 miRNAs. Forty-three genes were both differentially methylated and expressed, 24 of which were also targeted by 5 miRNAs; an additional 145 genes were miRNA-regulated independently of methylation. qPCR validation confirmed upregulation of ZBTB16 and downregulation of AGPAT5, both correlating with maternal B12 levels. Pathway enrichment highlighted neuronal differentiation, IL6 production, lipid metabolism, complement cascades, and cytoskeletal organization, suggesting a key regulatory role of maternal B12 in placental gene expression and metabolic programming. Our findings reveal epigenetically regulated targets associated with maternal B12 deficiency, highlighting placental epigenomic and transcriptomic changes, with ZBTB16 and AGPAT5 suggesting potential mediation of effects on neurodevelopment and offspring metabolic outcomes.

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OC5.2

Identifying high-risk women after GDM: multivariate analysis of routine clinical metrics for postpartum dysglycaemia

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Background
Women with gestational diabetes (GDM) have a ≥6-fold increased risk of developing type 2 diabetes, with highest risks observed in women with postpartum dysglycaemia (PPD) on an oral glucose tolerance test (OGTT) performed 6-12 weeks postpartum. This study aims to identify predictors of PPD in women with a history of GDM.
Methods
From 01/10/2023-31/07/2025, we prospectively assessed women prior GDM who completed a 75-g OGTT 6-12 weeks postpartum. The primary outcome was PPD (2-hr glucose ≥5.6mmol/l). Univariate and multivariate logistic regression were performed, with multiple imputation for missing data and multicollinearity checks. Model performance was evaluated using AUC and Brier score with 1,000 bootstrap iterations for internal validation. Predictor importance was evaluated via dominance analysis. Optimal thresholds for continuous variables were identified using Youden's index.
Results
40/409 women (34.2%) developed PPD. Predictors included higher maternal age (OR 1.05, 95% CI 1.00-1.10, $P = 0.048$), higher antepartum 2-hr OGTT glucose

(OR 2.03, 95% CI 1.31-3.20, $P < 0.001$), higher HbA1c at GDM diagnosis (OR 3.08, 95% CI 1.95-4.99, $P = 0.002$), and family history of diabetes (OR 2.29, 95% CI 1.55-3.42, $P < 0.001$). Compared to Malay women, Chinese women had increased odds of PPD (OR 1.77, 95% CI 1.07-2.95, $P = 0.026$). *In-vitro* fertilisation (OR 0.19, 95% CI 0.07–0.47, $P < 0.0001$) and pre-pregnancy BMI (OR 0.95, 95% CI 0.92–0.99, $P = 0.011$) were associated with decreased risk of PPD. Model performance was acceptable (AUC 0.77, 95% CI 0.72–0.81; Brier 0.17, 95% CI 0.16-0.19). Dominance analysis identified 2-hr OGTT as the strongest contributor to model variance (32.5%) followed by family history (16.3%), ethnicity (15.4%) and HbA1c (13.0%). The Youden-optimised HbA1c threshold for predicting postpartum dysglycaemia was 5.5% (36mmol/mol).
Conclusions
Antepartum parameters may identify women at highest risk of PPD and could inform targeted intervention within postpartum diabetes care pathways.

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OC5.3

Beneficial effect of protein-induced glucose tolerance is independent of protein-induced insulin release

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Acute protein ingestion is suggested to improve glucose tolerance through secretion of glucoregulatory hormones such as glucagon-like peptide-1 (GLP-1), insulin and glucagon upon sensing of amino acids. Calcium sensing receptor (CaSR), known for regulating calcium homeostasis, also functions as an amino acid sensor and is expressed in key glucoregulatory tissues including vagal afferent neurons, enteroendocrine cells, and pancreatic islets. We investigated the role of CaSR signalling in the vagus, enteroendocrine L-cells and pancreatic α- and β-cells in mediating protein's effect on glucose tolerance and hormone secretion. To understand the role of CaSR, pharmacological antagonists, surgical vagal CaSR knockdown, and tissue-specific CaSR knockout mice (PPG-Cre x CaSR-flox for enteroendocrine L-cells and α-cells and Ins1Cre x CaSR-flox for β-cells) were used. Pdx1CreERT x GLP-1R fl/fl mice were used to investigate the role of GLP-1 receptor signalling in β-cells. Our results suggested a vagal CaSR pathway mediating protein-induced insulin secretion, while a separate NMDA-dependent central pathway modulates glucose tolerance independently of insulin. Pharmacologically inhibiting central glutamate NMDA receptors prevented the effects of protein on glucose tolerance without affecting insulin secretion, whereas inhibition of major vagal efferent pathways to the pancreas via peripheral injection of a M3-muscarinic receptor antagonist inhibited both insulin and glucose tolerance effects. Vagal CaSR knockdown prevented only the effect on insulin. Protein's effect on glucose-stimulated insulin secretion (GSIS) was blunted in mice with CaSR knocked out in both L-cells and α-cells but unaffected when CaSR was deleted in α- or β-cells alone, suggesting that protein does not act directly on CaSR in these pancreatic cells to mediate its effects. Furthermore, protein-enhanced GSIS was lost in mice with β-cell-specific GLP-1R knockout, highlighting the role of gut-derived GLP-1. In summary, protein improves glucose tolerance via a central, insulin-independent pathway, while its insulinotropic effect involves vagal CaSR signalling and pancreatic GLP-1R signalling.

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OC5.4

High fracture rates in obesity despite normal bone mineral density

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Background
Obesity has been traditionally considered protective against fragility fractures due to associated higher bone mineral density (BMD). However, recent studies challenge this by reporting high fracture rates in obese individuals. Therefore, we comprehensively studied obesity parameters in fragility fracture patients and hypothesised that obesity does not protect against fragility fractures.
Methods
This retrospective observational study included 1,007 patients aged ≥50y with fragility fractures from the Imperial NHS Trust Fracture Liaison Service Database. Primary outcome was obesity prevalence. Secondary outcomes included BMD/T-scores (lumbar spine, femoral neck, total hip) from dual-energy X-ray absorptiometry (DEXA), fracture sites, and comorbidities in obese versus non-obese patients. Body mass index (BMI) was categorised using ethnic-specific cut-offs.
Results
Obesity prevalence (22%) was higher than the London average (20%) ($P = 0.03$). Obese patients fractured at a younger age than non-obese patients (median 72 vs. 77 years, $P < 0.0001$), despite normal BMD at total hip and spine (median T-score –0.8 and –0.9 respectively). Obese patients were more likely to experience upper limb fractures (OR 1.47, $P < 0.05$) and less likely to sustain hip fractures (OR 0.47, $P < 0.001$). Bone-related comorbidities were more prevalent among obese patients, including type 2 diabetes/prediabetes (50% vs. 35% in non-obese, $P = 0.0001$).
Discussion/Conclusion
High obesity prevalence and younger fracture age in obese patients suggest obesity does not protect against fragility fractures in this large cohort. These findings highlight obese individuals may have weakened bones despite normal BMD. This may be due to impaired bone quality (not captured by DEXA), driven by multiple factors including comorbidities. Biomechanical factors, such as greater hip padding and higher impact forces on the arms during falls, may explain the predominance of upper limb fractures in obese patients. Fracture risk assessment in obese individuals should consider bone quality, comorbidities, and nutritional factors alongside BMD to better identify those at fracture risk.

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OC5.5

A targeted epi-drug screen identifies HDAC6 inhibition as an enhancer of beta cell function and immune evasion

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The destruction or dysfunction of pancreatic beta cells is central to the aetiology and pathogenesis of type 1 and type 2 diabetes (T1D/T2D), respectively. Human genetic approaches have indicated that the immune system is a key primary driver in T1D, and beta cells display inherent vulnerability to cytotoxic T lymphocytes vs other islet cells. We and others have demonstrated the importance of epigenetic pathways, including CpG methylation and modification to histone proteins, as drivers of beta cell functional maturation and/or function. We therefore screened for epigenetic molecules with potentially beneficial effects on beta cell adaptation using a library of 'epi'-drugs. Our drug screen uncovered a novel role for a cytosolic histone deacetylase (HDAC) 6 whose inhibition increased insulin content and release in immature human beta cells, primary islets and stem cell-derived islet clusters. Meta-analysis of previously defined islet scRNA-seq datasets as well as pseudo-timing analysis also suggested that HDAC6 expression is aberrantly expressed at high levels in immature vs mature beta cells, consistent with an inverse relationship between HDAC6 expression and beta cell function. We have previously shown that HDAC6 inhibition mediates an anti-inflammatory response in beta cells via maintenance of STAT1 acetylation, thereby attenuating STAT1 phosphorylation. Consistent with these findings, RNA-seq analysis following HDAC6 inhibition in human beta cells revealed an enrichment for immune response pathways, increased expression of survival genes, as well as increased beta cell identity markers and diminished expression of beta cell 'disallowed' genes. HDAC6 inhibition also attenuated STAT3 activity and reduced beta cell surface expression of HLA class I proteins in response to pro-inflammatory cytokines, the latter a major hallmark of T1D. Overall, our findings demonstrate that HDAC6 inhibition in human beta cells may have therapeutic potential early in T1D to prevent/slow the autoimmune attack.

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OC5.6

Decoding the obese duodenal cell atlas

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The duodenum is an active regulator of metabolic homeostasis, shown by rapid glycaemic improvements after procedures altering proximal nutrient flow even before weight loss, yet the obesity associated cellular, molecular, and microenvironmental changes that drive barrier, hormonal, and immune dysfunction remain poorly defined. To define cellular pathology of the obese human duodenum, we conducted a pilot single-cell RNA-sequencing study in 28 individuals: 14 with obesity (BMI $\geq$ 35) and 14 lean (BMI $<$ 25). Duodenal biopsies were collected over 6 months. Freshly dissociated cells underwent magnetic-activated cell sorting (MACS) to enrich epithelial and immune compartments, followed by fixation to preserve RNA integrity for downstream processing. MACS-enriched samples yielded greater cellular diversity. In contrast, non-enriched samples showed marked depletion of total epithelial cells and loss of key epithelial subsets, including stem cells, transit-amplifying (TA) cells, and Paneth cells. Sequencing data were processed in Trailmaker and visualized using Scanpy. 47,744 high-quality cells were retained after quality control, including mitochondrial read-content filtering ($>$50%) and doublet removal (scDblFinder). The retained cells were then normalized, batch-corrected/integrated (Harmony), and clustered using Leiden (resolution 1.5). The epithelial compartment comprised five enterocyte subtypes, goblet, tuft, BEST4+ enterocytes, microfold cells, Paneth, TA, stem, and enteroendocrine cells. Immune populations included cytotoxic T cells, CD8+ and CD4+ T cells, NKT cells, B cells, T- and B-memory cells, Tregs, exhausted T cells, macrophages, mast cells, and dendritic cells. Cluster proportions were broadly comparable between females and males; however, cytotoxic T cells, memory T cells, CD8+ T cells, and enterocytes exhibited potential sex-associated differences. Collectively, this pilot establishes technical feasibility for duodenal biopsy acquisition and processing compatible with longitudinal sampling and downstream multi-omic profiling. The full study will expand the atlas to $\sim$600k cells, enabling mapping of cellular and transcriptomic remodelling at the epithelial interface and revealing how they shape the obesity-related metabolic responses.

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Neuroendocrinology and Pituitary

OC6.1

Predictive value of day-7 serum cortisol for hypothalamic–pituitary–adrenal axis recovery following transsphenoidal surgery

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Background
Transsphenoidal surgery (TSS) for pituitary disease can impair hypothalamic–pituitary–adrenal (HPA) axis function, necessitating peri-operative glucocorticoid replacement. At our centre, serum cortisol is measured seven days post-operation. Patients with values above 350 nmol/l discontinue hydrocortisone and undergo a short Synacthen test (SST) at six weeks to confirm recovery. The value of this confirmatory test is uncertain. We evaluated whether the day-7 cortisol concentration predicts subsequent adrenal sufficiency, aiming to inform a more efficient postoperative pathway.
Methods
A retrospective cohort study was conducted in adults undergoing TSS between July 2021 and July 2024. Adrenal sufficiency was defined as baseline cortisol $>$ 225 nmol/l and peak stimulated cortisol $>$430 nmol/l on six-week SST. Day-7 cortisol was evaluated as a predictor of SST success using receiver operating characteristic (ROC) analysis, with Youden's J statistic identifying the optimal threshold. Internal validation was performed with 2000 bootstrap replications. Pre-specified thresholds of $>$300 nmol/l and $>$350 nmol/l were also assessed.
Results
Ninety-eight patients were included; 45.9% achieved SST-defined adrenal sufficiency. Day-7 cortisol demonstrated excellent discrimination for SST success (AUC 0.862, 95% CI 0.788–0.937). The optimal threshold (328.5 nmol/l) achieved sensitivity 75.6% (61.3–85.8) and specificity 88.7% (77.4–94.7). The $>$ 300 nmol/l and $>$350 nmol/l thresholds yielded sensitivities of 77.8% and 60.0%, and specificities of 81.1% and 90.6%, respectively. Bootstrap validation confirmed robustness (median optimal threshold 325.5 nmol/l, 95% CI 237.5–330.5; AUC 0.866, 0.781–0.930).
Conclusion
A single day-7 serum cortisol measurement accurately predicts recovery of the HPA axis after TSS. A threshold $>$328 nmol/l provides optimal test performance, while 300 nmol/l and 350 nmol/l cut-offs offer flexibility depending on whether clinical priorities favour sensitivity or specificity. Adoption of a data-informed day 7 cortisol threshold could reduce unnecessary follow-up SSTs.

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OC6.2

Defective nitric oxide pathway signalling - a link between premature birth and altered mini-puberty?

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Mini-puberty is the period of transient hypothalamic-pituitary-gonadal (HPG) axis activity shortly after birth, before the axis is 'switched-off' until puberty. The amplitude of mini-puberty is exaggerated in preterm babies, with potential consequences for neuronal maturation, pubertal disorders, behavioural and metabolic conditions. Nitric oxide (NO) is a key player in regulation of mini-puberty and reproductive development, with Nitric oxide synthase 1 (NOS1) deficiency causing abnormal mini-puberty in mice and congenital hypogonadotropic hypogonadism in humans. We interrogated 63 patient samples from the Finnish mini-puberty cohort ('miniNO' project, grant 847941), for variants in genes associated with NO signalling pathways. Whole genome sequencing was filtered for rare, predicted pathogenic variants. We identified two preterm infants with variants of interest. One female patient, born at 24.7 weeks, carried a rare missense heterozygous variant (c.1855A$>$T, p.M619L) in *NOS1*. She displayed a very exaggerated mini-puberty. At 14.8 years the patient was pre-menarchal, suggesting pubertal delay. The variant is in the highly conserved oxygenase domain of NOS1. *In vitro*, the NO output from cells transiently expressing the p.M619L mutant was significantly attenuated compared to wild-type NOS1, suggesting decreased NOS1 activity. Additionally, the p.M619L variant dimerised with wildtype NOS1, suggesting impaired functional homodimer formation, potentially underlying pathogenicity. A second female patient, born at 32.1 weeks had a missense heterozygous variant (c.296G$>$A, p.S99N) in NOS1 associated protein 1 (*NOS1AP*). The variant has gnomAD European frequency of 0.57%. The patient demonstrated a flat mini-puberty profile and pubertal delay. NOS1AP is expressed in GnRH neurons and co-expressed with NOS1. Ongoing functional characterisation thus far suggests no impact on NO output. Measurement of GnRH is ongoing. Here we identify rare exonic variants in genes within the NO synthesis pathway in patients with preterm birth and abnormal mini-puberty, providing potential human evidence for the role of NO signalling in prematurity and HPG axis regulation.

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OC6.3

Charting the clinical course of immune checkpoint inhibitor-related endocrinopathies amongst 833 ICI-treated patients in north wales

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Background
Immune checkpoint inhibitors (ICIs) are a rapidly expanding therapeutic class that act by restoring T-cell anti-tumour activity via PD-1/PD-L1 and CTLA-4 inhibition. Yet whilst ICIs have notably improved cancer survival, they are associated with endocrine toxicities often requiring lifelong management. Among these, immune-mediated hypogonadism remains an overlooked yet relatively common toxicity that may reflect central dysfunction. Recently, the MHRA and EMA have approved additional ICIs – atezolizumab, durvalumab, dostarlimab, tremelimumab – and a novel LAG-3 inhibitor, relatlimab. However, real-world data on incidence, onset, and associations of these newer agents are limited.
Objective(s)
To investigate associations between ICI-related endocrinopathies and patient demographics, ICI regimen, and cancer type.

Methods
Following HRA approval (IRAS ID: 360494, REC reference: 25/HCRW/0013), this retrospective cohort study included adults treated with ICI at Glan Clwyd Cancer Centre between 01/01/2022 - 31/01/2025. The endocrinopathy cohort ($n = 123$) comprised those with persistent biochemical endocrine abnormality, or imaging suggesting gland dysfunction. Controls ($n = 710$) included subclinical, transient, or confirmed steroid/radiotherapy-related endocrinopathies. Binary logistic regression was performed.
Results
Cohort mean age was 64.0 (SD: 12.0); 54.5% were male. Age, sex, and ICI agent showed no significant overall associations. Breast (OR 2.51, $P = 0.016$*) and renal cell cancer (OR 1.989, $P = 0.050$*) were associated with increased odds of ICI-related endocrinopathy. The overall incidence was 14.8%; predominantly thyroid dysfunction (61%) and rarely insulin-dependent diabetes (0.8%). Thyroid toxicity also predominated among the newer agents. Longer ICI treatment increased risk (OR 1.002/day, $P < 0.001$). Generally, ICI-related endocrinopathies developed early (<250 days) but onset varied markedly ($P < 0.001$): median 26.5 days [10.5–102.5] for hypogonadism versus 208 days [78–307] for adrenal insufficiency.
Conclusions
ICI-related endocrinopathies are common, affecting 14.8% of ICI-treated patients. Longer ICI exposure confers greater risk, supporting ongoing monitoring beyond initial treatment cycles. Marked differences in endocrinopathy onset indicate distinct immune mechanisms and diagnostic windows that warrant timely detection.

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OC6.4

Peripartum increases in serum prolactin and differential mammary prolactin receptor isoform expression are associated with human secretory activation

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The onset of lactation, termed 'secretory activation', occurs within 96 hours after childbirth and is mediated by physiological hyperprolactinaemia, which stimulates the mammary prolactin receptor (PRLR) to induce milk synthesis. However, the precise serum prolactin concentration required and effect of maternal factors such as age, parity, body mass index (BMI) and type of delivery remain to be elucidated. Moreover, the contribution of different mammary PRLR isoforms, which include the full-length PRLR and several shorter isoforms, to secretory activation is unknown. We investigated this in $n = 226$ healthy breastfeeding women (mean age = 35 years, range 24-46) recruited following informed consent at 36 weeks' gestation and followed up during postpartum days 1-5. All participants initiated milk secretion by postpartum day 4. Serum was obtained for prolactin measurements and mammary RNA isolated from milk samples for PRLR isoform analysis. Our findings showed that mean ± SEM serum prolactin increased from 4082 ± 102 mU/l at 36 weeks' gestation to 5113 ± 183 mU/l on postpartum day 1 ($P < 0.0001$) with prolactin values peaking at 5359 ± 169 on postpartum day 2 and decreasing thereafter. However, delivery involving the use of forceps, suction or emergency c-section, all of which may delay secretory activation, abrogated the rise in prolactin; whilst maternal age, parity and BMI were not associated with serum prolactin. In addition, RNA-sequencing conducted in $n = 56$ participants showed that the full-length isoform is the most abundant type of mammary PRLR with its expression >40-fold higher than other shorter isoforms. Furthermore, mammary full-length PRLR expression significantly increased by >8-fold during postpartum days 1-5 ($P < 0.0001$). In summary, this study demonstrates that secretory activation is associated with a significant peripartum increase in serum prolactin and marked increase in mammary full-length PRLR expression. Moreover, assisted deliveries and emergency c-section impaired the prolactin rise, which may explain why these factors cause delayed secretory activation.

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OC6.5

Insights into Somatostatin Analogue Response: Alterations in SSTR and Ki-67 Expression in LCC-18 Neuroendocrine Tumour Cells

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Introduction
Neuroendocrine neoplasms (NENs) represent a heterogeneous group of tumours with variable clinical behaviour and prognosis. Somatostatin analogues (SSAs) are central to NEN management through modulation of somatostatin receptors (SSTRs), yet the molecular mechanisms underlying receptor regulation and therapeutic resistance remain poorly defined. This study investigated the effects of octreotide acetate (OA), lanreotide acetate (LA), and pasireotide (P) on the expression of SSTR subtypes 2, 3, 4 and 5, and the proliferation marker Ki-67, in LCC-18 neuroendocrine tumour cells.
Material and Methods
LCC-18 cells, derived from grade 3 NEN, were exposed to increasing concentrations (6.25-100 μM) of OA, LA and P for 2 hours. Expression of SSTR subtypes and Ki-67 was evaluated using immunocytochemistry (ICC) and quantitative real-time PCR (qRT-PCR). Apoptosis was assessed using an Annexin V assay to determine potential cytotoxic effects.
Results
Preliminary findings revealed no significant apoptotic induction with OA or LA treatment, whereas P elicited a mild apoptotic response at 100 μM ($P = 0.032$). The qRT-PCR analysis showed distinct, dose-dependent modulation of SSTR expression: OA and LA upregulated SSTR2 and SSTR5 at moderate concentrations, while P induced broader activation of SSTR3 and SSTR4 accompanied by reduced Ki-67 expression, suggesting an antiproliferative effect. These results indicate that each analogue exerts a unique receptor-specific regulatory profile that may influence treatment responsiveness and receptor internalisation dynamics.
Conclusion
Each molecular profiling of SSTR and Ki-67 expression following SSA exposure may help identify biomarkers predictive of therapeutic efficacy. Understanding these regulatory mechanisms could guide more personalised therapeutic strategies and improve clinical outcomes for patients with NENs.

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OC6.6

Long-term and sustained biochemical control of acromegaly and improved quality of life with CAM2029 octreotide subcutaneous depot: final analysis of the core phase of ACROINNOVA 2

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Biochemical control is crucial to reduce morbidity and improve quality of life (QoL) for patients with acromegaly. CAM2029, a long-acting, octreotide subcutaneous depot, is conveniently self-administered via an autoinjector pen with small-gauge needle. In the 24-week (W), Phase 3 ACROINNOVA 1 trial (NCT04076462), CAM2029 achieved superior biochemical control versus placebo and improved QoL from standard of care (SoC) in patients previously biochemically controlled. ACROINNOVA 2 (NCT04125836) assessed long-term

(52W) safety and efficacy. ACROINNOVA 2, a Phase 3, open-label trial (with 52W extension), directly enrolled (DE) patients with insulin-like growth factor I (IGF-I) $\leq 2\times$ upper limit of normal (ULN; per age and sex) on SoC, and patients completing ACROINNOVA 1 (prior-CAM2029; prior-placebo). Patients received CAM2029 20 mg every 4W ($\pm$1W) for 52W (prior-placebo, W24–52). The primary objective was to evaluate safety. Secondary endpoints included the proportion of patients with biochemical control (IGF-I $\leq$ULN; W50/52 mean), Acromegaly Index of Severity scores (symptom severity) and patient-reported outcomes (PROs) including the Acromegaly QoL Questionnaire and treatment satisfaction. 135 patients were enrolled: 81 DE, 36 prior-CAM2029, 18 prior-placebo; 127 patients completed treatment. CAM2029 was well tolerated with no new safety signals. IGF-I control among DE patients improved from 14.8% at baseline to 36.5% at W50/52. At W50/52, IGF-I control was sustained in 88.6% of prior-CAM2029 patients; prior-placebo patients regained IGF-I control with CAM2029 (94.4% had IGF-I control at W50/52). In the overall population, symptoms and multiple PROs, including QoL and treatment satisfaction, were progressively improved from baseline to W52; results indicated some further improvements from W24 to W52. CAM2029 had a long-term safety profile comparable to SoC and offered sustained biochemical and symptom control of acromegaly, with improvements in QoL and treatment satisfaction versus SoC baseline. These results support CAM2029 as a promising treatment option for acromegaly with tangible improvements in PROs.

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Oral Poster Presentations

Neuroendocrinology and Pituitary

OP1.1

Immune Checkpoint Inhibitor-Related Hypophysitis and Pituitary Dysfunction: A Systematic Review of Clinical Presentation, Diagnosis, and Management

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Objective
To review the clinical presentation, diagnosis, and management of immune checkpoint inhibitor (ICPi)-associated hypophysitis and pituitary dysfunction.
Method
A systematic review of studies published from 2005 to 2025 was conducted to evaluate pituitary immune-related adverse events (irAEs) linked to CTLA-4 inhibitors, PD-1/PD-L1 inhibitors, and combination regimens. Eighty-four eligible studies comprising 7,259 patients were included. Extracted data included ICPi type, demographics, cancer type, treatment duration, imaging findings, type of pituitary dysfunction, clinical presentation, and management.
Results
The weighted average proportion of male patients was 68.3%, with a pooled mean age of 63.9 years. Common symptoms included fatigue, headache, hyponatraemia, nausea, anorexia, and neuropsychiatric changes. While MRI is a key diagnostic tool, it may not always detect subtle or early-stage pituitary involvement. In the CTLA-4 group, patients received ipilimumab for 2–12 cycles (mean: 3.3) before hypophysitis onset. In the PD-1/PD-L1 group, median time to onset was 28 weeks (range: 10–46 weeks). Hypophysitis induced by CTLA-4 inhibitors—particularly ipilimumab and CTLA-4-based combination therapies—is more commonly associated with hypopituitarism than that caused by other ICPi classes. In contrast, isolated ACTH deficiency, more frequently observed with PD-1 and PD-L1 inhibitors, typically presents as secondary adrenal insufficiency, often without distinct abnormalities on early MRI imaging. Reported MRI abnormalities included radiological evidence of hypophysitis, pituitary stalk abnormalities, pituitary enlargement, microadenoma, pituitary atrophy, and empty sella. Some patients showed no radiological abnormalities. The most common biochemical abnormalities in the combination group were hypopituitarism and secondary adrenal insufficiency. High-dose glucocorticoid initiation, careful tapering, and tailored long-term hormone replacement remained the mainstays of management.
Conclusion
Our systematic review demonstrates that hypopituitarism and secondary adrenal insufficiency are common and often persistent sequela of ICPi-associated hypophysitis. Prompt recognition through integrated clinical, biochemical, and radiological evaluation is crucial to minimise long-term endocrine morbidity and improve patient outcomes.

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OP1.2

MECP2 as a regulator of transcription and chromatin conformation in GnRH neurons: implications for puberty

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Whilst several key genetic contributors to the phenotype of central precocious puberty (CPP) have been recognized, many familial cases remain without clear genetic aetiology. We have identified Methyl-CpG-binding protein 2 (*MECP2*), a chromatin-associated transcriptional regulator with known roles in neuronal maturation, as a candidate gene for CPP. Located on chromosome Xq28, *MECP2* is highly expressed in hypothalamic nuclei (arcuate, suprachiasmatic, and paraventricular) and co-localises with GnRH within GnRH neurons, suggesting a role in puberty onset through regulation of the GnRH neuronal axis. Furthermore, MECP2's known role as an epigenetic regulator of chromatin compaction makes it an attractive candidate as a key player in the delicate regulation of pubertal onset. We have demonstrated differential expression of CPP- and Rett syndrome-associated *MECP2* variants in a GT1-7 mouse neuronal GnRH-producing cell line, compared to wildtype *MECP2*. Studies in a GnRH reporter system demonstrated differential ability of *MECP2* variants to supress GnRH promoter activity, suggesting a possible regulatory role in the GnRH neuronal network. To understand the role of MECP2 in transcriptional and epigenetic regulation of GnRH secretion, we utilised a multi-omics approach, carrying out RNAseq and ATACseq on wildtype and *Mecp2*-knockout GT1-7 cell lines. Analyses identified 4552 chromatin regions with differential accessibility upon loss of *Mecp2* expression *in vitro* (3530 increased accessibility, 1022 reduced accessibility). Combination of ATACseq and RNAseq analysis identified two subsets of genes differentially regulated in *Mecp2* knockout GT1-7, compared to wild-type: 487 genes appeared in both datasets, regulated by MECP2 through chromatin accessibility, and 495 were unique to RNAseq analysis, upon which MECP2 may act as a direct transcriptional regulator. Importantly, several genes identified in both datasets, including *Sox11, Igsf10 and Lgr4* have known vital roles in regulation of puberty and GnRH, strongly suggesting that MECP2 contributes to regulation of pubertal onset through regulation of GnRH.

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OP1.3

HypoMap3D: a reference spatio-cellular atlas of the mouse hypothalamus for studying neuroendocrine biology and disorders

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The hypothalamus is a main neuroendocrine organ that plays multiple roles in orchestrating physiological functions in the body such as somatic growth, circadian rhythm, sexual reproduction and energy homeostasis. In order to better understand the cellular architecture of this brain region, we integrated single-cell sequencing data from multiple studies and released harmonised cell atlases of the mouse hypothalamus, aka HypoMap in 2022, and human HYPOMAP later in 2025 to the research community. Here we are presenting the second iteration of our mouse atlas, HypoMap3D, which has ~4X more cells and better regional coverage than its predecessor. In this version we have also included four spatial transcriptomics studies of coronal sections at 100µm intervals to reconstruct a comprehensive spatio-cellular map of the mouse hypothalamus in 3D. To demonstrate the use of this new resource, we examine the molecular and spatial heterogeneity of different hypothalamic Kisspeptin (*Kiss1*) neurons, which are crucial for controlling the hypothalamic-pituitary-gonadal axis, and investigate sexual dimorphism of gene expression in these neurons.

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OP1.4

Autistic spectrum disorders and heterogenous pituitary phenotype in patients with AIP- variants

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Background
AIP codes for the aryl hydrocarbon receptor-interacting protein which is a co-chaperone protein with numerous binding partners. *AIP* acts as a tumour suppressor gene within the pituitary and heterozygous pathogenic germline *AIP* variants (*AIP*var) result in apparently isolated pituitary disease. However, a recently described multi-system syndrome in *AIP*var homozygotes raises potential, previously unobserved phenotypic consequences of *AIP*var heterozygosity.
Aims
1) To characterise the phenotype of *AIP*-related pituitary disease 2) To investigate for possible additional *AIP*-associated disease.
Methods
Prospective, international observational study of individuals with likely pathogenic and pathogenic germline *AIP* variants.
Results
Four hundred and eighteen *AIP*var heterozygotes were identified. Two hundred and twelve had pituitary disease, with 31 diagnosed prospectively after cascade genetic testing. A slight majority diagnosed prospectively had non-functioning tumours (55%). The majority of non-prospectively diagnosed patients had acromegaly or gigantism (85%), 13% developed prolactinoma and 2% clinically non-functioning tumour. In patients with growth hormone excess, the phenotype

varied from radiological pituitary hyperplasia with subtle growth hormone excess to young onset, proliferative tumours with florid growth hormone excess. Prolactinomas showed a similar pattern, ranging from microadenoma to giant, invasive tumours. Six percent of *AIP*var heterozygotes had autistic spectrum disorder (6%), showing a range of autistic spectrum phenotypes including attention-deficit/hyperactivity disorder. This phenotype was independent of pituitary lesions, hormone excess/deficiencies and the use of cabergoline therapy. This prevalence is higher than that observed in the general population, where prevalence is about 1%.

Conclusions

*AIP*var result in heterogeneous pituitary disease which is not always classically aggressive. *AIP*var heterozygotes appear to have a higher prevalence of autistic spectrum disorders. These findings require validation and mechanistic studies to investigate the potential molecular biology of such an association.

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Metabolism, Obesity and Diabetes

OP2.1

miR-10b-5p promotes brown adipocyte differentiation and the thermogenic program in white adipose tissue

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Obesity results from the excess accumulation of energy in white adipocytes (WAs), leading to metabolic disorders such as diabetes. In contrast, beige and brown adipocytes (BAs) generate heat through non-shivering thermogenesis. Since brown adipose tissue (BAT) dissipates energy and counteracts fat accumulation, stimulating BAT activation and white adipose tissue (WAT) browning may provide an effective approach to treat obesity. MicroRNAs (miRNAs), small non-coding RNAs that regulate gene expression, have emerged as key modulators of adipogenesis and metabolic function. Here we found that miR-10b-5p plays an essential role in adipogenesis in BAT and WAT. Small RNAseq analysis of primary mouse BAs and WAs identified miR-10b-5p to be upregulated in mature BAs. MiR-10b-5p depletion severely compromised differentiation into mature BAs as judged by lack of lipid droplet accumulation and decreased expression of adipogenic markers. RNA sequencing revealed a significant increase in genes related to G Protein signalling associated with elevated Tubby (Tub). Consistent with transcriptomic findings, Tub mRNA and protein levels increased with miR-10b-5p inhibition in BAs. Next, we investigated the effects of miR-10b-5p upregulation on WA differentiation. Elevated abundance of miR-10b-5p in WAs significantly enhanced white adipogenesis as judged by the increased production of lipid droplets and elevated expression of adipogenic markers. We also observed increased Ucp1 and Ppargc1a levels during white adipogenesis, indicating an increase in the expression of the thermogenic gene program. The miR-10b-5p mimic during WA differentiation instigated a substantial increase in maximal respiration, ATP production coupled respiration and proton leak, indicating a higher mitochondrial uncoupling, which could potentially contribute to thermogenesis. Upon activation of β-adrenergic signalling, a robust increase of Ucp1 and Ppargc1a was detected. Our research work demonstrates that miR-10b-5p modulates adipocyte differentiation and fat browning. These findings strengthen the therapeutic possibility of using miRNAs to control obesity and its associated diseases in humans.

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OP2.2

Loss of 11β-HSD1 attenuates skeletal muscle atrophy during glucocorticoid therapy in experimental kidney injury

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Background

Therapeutic glucocorticoids (GCs) are anti-inflammatory steroids that remain a cornerstone in the treatment of inflammatory kidney disease. However, off-target side effects including muscle atrophy and metabolic dysfunction limit their application. The enzyme 11β-HSD1 regulates the pre-receptor metabolism and amplification of GCs, influencing their peripheral side effects in tissues such as muscle. This study investigated the influence of 11β-HSD1 on muscle wasting related to GC therapy in the specific context of a murine model of kidney disease.

Methods

Male wild-type (WT) and 11β-HSD1 global knockout (11βKO) transgenic mice received 0.15 % adenine diet over 5 weeks to produce sustained renal injury. At week three, animals were additionally treated with the GC corticosterone in drinking water (100 mg/l) or vehicle control (0.6% ethanol) for a period of two weeks. Animals were culled at week 5, and serum, kidney, and muscle (quadriceps, tibialis anterior, soleus) collected. Renal impairment was assessed via serum markers (urea, creatinine) and histopathology. Lean muscle weight and fibre size were assessed, and markers of catabolic metabolism determined by qRT-PCR.

Results

The adenine diet resulted in comparable renal impairment in both WT and 11β-HSD1 KO mice. This was characterised by tubular damage and fibrosis, and elevated levels of serum urea and creatinine. Corticosteroid treatment improved renal inflammation and function in adenine-fed WT animals, but resulted in reduced quadriceps and tibialis-anterior weights and fiber size, with a marked increase in catabolic mediators such as Foxo1 and Fbxo32. In contrast, 11β-HSD1 KO mice were protected against corticosteroid-induced muscle atrophy.

Conclusion

These data indicate that targeted inhibition of 11β-HSD1 KO has the potential to ameliorate off-target side effects in muscle caused by therapeutic glucocorticoids in the setting of experimental renal injury. Further research will focus on muscle-specific targeting of 11β-HSD1 inhibition and validating translational potential in humans.

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OP2.3

Efficacy of GLP-1 Receptor Agonists in Patients with Prader–Willi Syndrome: A Retrospective Cohort Study

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Background

Prader–Willi syndrome (PWS) is a neurodevelopmental disorder characterised by hyperphagia, obesity, and increased risk of type 2 diabetes. Glucagon-like peptide-1 receptor agonists (GLP-1) are prescribed for weight management and glycaemic control. This study evaluated their efficacy in a PWS cohort.

Methods

We retrospectively reviewed outcomes of 28 patients with PWS (aged 17–33 years) attending a specialist PWS clinic between June 2023 – July 2025. Demographic, anthropometric, glycaemic (HbA1c), and treatment data were obtained from electronic health records. Patients were categorised by GLP-1 therapy (Saxenda, Ozempic, Mounjaro, Rybelsus) versus no GLP-1 use. Primary outcomes were changes in weight and BMI; secondary outcome was HbA1c change.

Results

Of 28 patients, 8 were excluded due to unavailable follow-up data, leaving 20 for analysis. At baseline, 5 patients were receiving GLP-1 therapy (80% diabetic [$n = 4$]) and 15 were not (46.67% diabetic [$n = 7$]). During $\leq$1 year of follow-up, the GLP-1 cohort experienced a mean weight gain of 2.38 $\pm$ 3.83 kg and BMI increase of 0.95 $\pm$ 1.22 kg/m^2 but achieved a substantial reduction in HbA1c 21.60 $\pm$ 30.54 mmol/mol. In contrast, the non-GLP-1 group gained 2.75 $\pm$ 9.09 kg with a BMI increase of 0.84 $\pm$ 3.70 kg/m^2, alongside a rise in HbA1c 1.08 $\pm$ 2.37 mmol/mol. Over the study period, 7 additional patients commenced GLP-1 therapy (Mounjaro), raising the treated group to 12 (60%). Extended follow-up data for 4 patients (all GLP-1) demonstrated mean weight reduction of 1.45 $\pm$ 2.63 kg and BMI reduction of 0.285 $\pm$ 0.76 kg/m^2.

Conclusion

In patients with PWS, GLP-1 receptor agonists were associated with significant HbA1c improvement but no short-term benefit in weight or BMI compared with non-GLP-1 patients. Uptake of GLP-1 therapy increased during follow-up, reflecting its growing role in clinical management. Longer-term studies are required for assessing metabolic and anthropometric effects in this population.

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OP2.4

Biased agonism can modulate response to GLP-1R therapy through altered surface availability in the CNS

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Introduction
Glucagon-like peptide-1 receptor (GLP-1R) agonists are highly effective anti-obesity therapeutics that are thought to primarily enact appetite suppression via action on central nervous system (CNS) appetite centres. However, their therapeutic potential can be limited by side effects and variable efficacy. Biased agonism, which selectively modulates downstream signalling pathways such as G-protein activation versus β-arrestin-mediated receptor internalisation, offers a promising strategy for refining these therapies. We hypothesised that biased GLP-1R agonists may cause differential receptor desensitisation in key CNS regions, providing a mechanism for improving therapeutic outcomes.
Methods
To investigate this *in vivo*, mice were pre-treated with vehicle or one of two biased GLP-1R agonists: ExD3, which promotes receptor internalisation, or ExF1, which is internalisation-resistant. The functional consequence of this pre-treatment was assessed by measuring the physiological response to a subsequent challenge with the conventional GLP-1R agonist Exendin-4 (Ex-4). To visualise the underlying mechanism, we used light-sheet microscopy on cleared brains to quantify available surface GLP-1R in pre-treated mice via injection of a fluorescently conjugated agonist, Ex-4-Cy5.
Results
Pre-treatment with the pro-internalisation agonist ExD3 significantly attenuated the response to the Ex-4 rechallenge compared to vehicle controls. In contrast, pre-treatment with the internalisation-resistant agonist ExF1 preserved the physiological response to Ex-4. Light-sheet imaging data directly corroborated these findings, revealing that ExD3 pre-treatment caused a marked reduction in available surface GLP-1R in key appetite-regulating nuclei. Conversely, ExF1 pre-treatment did not reduce surface receptor availability.
Conclusion
These findings provide direct *in vivo* evidence that biased agonism at neuronal GLP-1R critically modulates receptor surface availability and functional desensitisation. This mechanism likely contributes to the differential efficacy observed among new GLP-1R therapeutics. Targeting GLP-1R bias to minimise receptor internalisation presents a key strategy for developing more potent and sustained therapies for obesity.

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Adrenal and Cardiovascular

OP3.1

A Role for Non-Muscle Myosin IIA in Adrenocortical Carcinoma

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Adrenocortical carcinoma (ACC) is a rare but aggressive endocrine malignancy with limited therapeutic options and poor prognosis. Complete surgical resection is the only curative treatment, with 5-year survival reaching 80% in early-stage disease (1). However, 25–30% of patients present with metastatic disease, where survival falls below 15% despite radiotherapy and mitotane-based chemotherapy (1,2). 5-year survival across all patients is less than 40% (3). Deeper understanding of ACC pathophysiology is vital to enable advances in management. Recently our group identified the transmembrane protein, delta-like non-canonical Notch ligand 1 (DLK1) to be highly expressed in ACC, where it maintains tumour cells in an undifferentiated state and is associated with worse recurrence-free survival (4,5). Using proteomic screening, we discovered that Non-Muscle Myosin IIa (NMIIa), an actomyosin motor protein coded for by the MYH9 gene with known roles in regulating division, adhesion, and mechanotransduction (6), is the predominant interactor of DLK1 in ACC cells. While NMIIa is reported as a tumour promoter in several cancers including oesophageal and pancreatic (7,8), in head and neck squamous cell carcinoma it exerts tumour-suppressive effects by enhancing nuclear shuttling of p53 (9). This suggests NMIIa function in cancer is context-dependent and mediated by interacting partners. We also show that higher NMIIa expression enhances the negative prognostic effect of higher DLK1 expression in ACC. Additionally, NMIIa inhibition with the specific small molecule inhibitor blebbistatin in H295R cells unexpectedly promotes proliferation in a dose-dependent manner, suggesting that NMIIa motor activity normally restrains proliferation. These findings highlight NMIIa as a context-dependent regulator in ACC: while its motor activity suppresses proliferation, we hypothesise that the NMIIa-DLK1 interaction supports maintenance of a less differentiated cell type. Further studies are ongoing to interrogate this further.

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OP3.2

Redox modulation enhances the metabolic efficacy of SGLT2 inhibition

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Sodium-glucose co-transporter 2 (SGLT2) reabsorbs up to 180 g of glucose daily in the kidney. SGLT2 inhibitors have transformed the treatment of type 2 diabetes and cardiovascular disease and are now being explored for non-metabolic indications, including cancer and neurodegeneration. Beyond glycaemic regulation, SGLT2 has emerging roles in immune-metabolic signalling. We previously showed that SGLT2 knockout (KO) mice exhibit reduced IL6 expression and restored adrenal corticosterone secretion, independent of glycosuria or body weight. To investigate underlying mechanisms, we performed data-independent acquisition mass spectrometry on plasma and eight metabolic organs (heart, liver, kidney, spleen, muscle, adrenal glands, white and brown adipose) from obese SGLT2 KO, chronically dapagliflozin-treated, and control mice. Across groups, differentially expressed proteins (DEPs) were enriched for oxidative stress and glutathione-related pathways, with greatest DEP overlap observed between plasma and adrenal glands in SGLT2 KO mice (113 DEPs). Dapagliflozin-treated mice exhibited a similar number of DEPs, predominantly in plasma and muscle. To assess glutathione's functional relevance *in vivo*, high-fat diet-fed mice were treated with dapagliflozin ± buthionine sulfoximine (BSO), a glutathione synthesis inhibitor. In male mice, BSO co-treatment significantly improved glucose clearance across intraperitoneal and oral glucose tolerance tests (AUC reduced by ~20%) compared to dapagliflozin alone, despite a 40–50% reduction in total glutathione and no change in body weight. IL6 and TNFα levels were reduced by 30–50% in dapagliflozin and combination groups. In females, BSO caused ~15% weight loss, and glucose tolerance was similar to that of males. Notably, females showed increased glutathione secretion in response to dapagliflozin—an effect not observed in males. These findings reveal a redox-sensitive, sex-specific mechanism whereby glutathione depletion enhances SGLT2 inhibitor efficacy, supporting a novel hormetic interaction. This has important implications for repurposing SGLT2 inhibitors in cardiometabolic and immune-mediated diseases.

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OP3.3

Salivary hybrid steroids and the sub-classification of primary aldosteronism: a pilot study

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Introduction
Recent primary aldosteronism (PA) guidelines recommend screening all hypertensive patients using the aldosterone-to-renin ratio (ARR). With a 10–13% prevalence of PA in the hypertensive population, PA case detection and subclassification of patients would overwhelm endocrine services. Surgical outcomes at two years are highly variable with the greatest likelihood of complete clinical success (by PASO criteria) seen in those with the *KCNJ5* mutated aldosterone-producing adrenal adenomas (APAs). Early identification of *KCNJ5*-mutant cases could help select those who will benefit the most for invasive

treatments. Plasma hybrid steroid profiling—namely the 18-hydroxycortisol:cortisol ratio—can distinguish *KCNJ5*-mutant APAs from others. This pilot study evaluated whether salivary hybrid steroid measurement could replicate plasma findings, exploring its potential as a simple, non-invasive screening tool to stratify PA patients early in the diagnostic pathway.

Methods

Early morning and late-night saliva samples collected onto Sarstedt Salivette® collection devices, and venous EDTA plasma samples, were collected from 51 patients who satisfied the Endocrinology Society criteria for diagnosis of PA, 3 non-PA controls were also included. Aldosterone, 18-hydroxycortisol, 18-oxocortisol and cortisol were measured by LC-MS/MS. Paired analysis was conducted between the collection modalities.

Results

Patients with raised concentrations of hybrid steroids in plasma also exhibited raised concentrations in early morning saliva (R-squared 0.70/0.66 for 18-oxocortisol/18-hydroxycortisol respectively). Early morning hybrid steroid concentrations were approximately five-fold higher than the corresponding late-night sample. Correlation of plasma with late-night saliva samples was variable (R-squared 0.37/0.66 for 18-oxocortisol/18-hydroxycortisol respectively).

Discussion

Hybrid steroids in saliva correlate well with those found in plasma in this pilot study, indicating potential for large-scale use in screening the hypertensive population. The comparison of saliva samples taken at two different time points highlights the probable impact of ACTH on the production of hybrid steroids. Further work in demonstrating sensitivity and specificity for *KCNJ5* mutant detection is necessary.

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OP3.4

Weight loss induced by bariatric surgery impacts significantly on serum and urinary mineralocorticoid metabolism in men and women

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Obesity is a risk factor for hypertension and perturbations in mineralocorticoid metabolism have been implicated. Weight loss reduces aldosterone concentrations without parallel changes in renin activity, implicating renin-independent mechanisms. Adipocytes express aldosterone synthase (CYP11B2) and secrete aldosterone, providing a potential mechanism linking adiposity to mineralocorticoid metabolism. Robust data exploring this association using highly sensitive liquid chromatography–tandem mass spectrometry (LC-MS/MS) methods are lacking. Baseline anthropometric and metabolic data were collected in a cohort of patients undergoing bariatric surgery for obesity. Serum and urine samples were collected for multisteroid profiling by LC-MS/MS pre-operatively. Clinical and biochemical assessments were repeated after a defined postoperative interval. Data are reported as median and interquartile range. Sixty-two patients were included [n = 41 female; median BMI 49.3kg/m^2 (45.1–54.6); median age 50.5 years (43.3–56.6)]. Median weight loss after surgery was 17.6% (13.7–21.2) after 18 weeks (16–20). Blood pressure improved [systolic 140 ± 14 mmHg to 132 ± 13mmHg; diastolic 83 ± 11 mmHg to 77 ± 12 mmHg, $P < 0.05$ for each]; antihypertensive medication use fell in study participants from 53.2% to 32.3%. Weight loss significantly reduced serum aldosterone [300pmol/l (200-500) to 175pmol/l (115–328), $P = 0.002$] and deoxycorticosterone concentrations [100pmol/l (0.00–100) to 85pmol/l (53–127), $P = 0.05$], with a non-significant reduction in urinary tetrahydroaldosterone concentrations. Serum corticosterone increased following weight loss [5.5nmol/l (3.2–9.95) to 9.3nmol/l (4.5–16.8), $P = 0.001$]. Postoperative increases were observed in urinary tetrahydrocorticosterone [136 (86–208) to 167 (120–279) mg/24h, $P = 0.0123$] and tetrahydrodeoxycorticosterone [148 (55–269) to 222 (83–380) mg/24h, $P = 0.0004$]. The concurrent fall in aldosterone and rise in corticosterone may indicate altered CYP11B2 activity, with increased urinary tetrahydro-metabolites suggesting enhanced hepatic clearance from higher substrate availability. These data suggest mineralocorticoid excess contributes to obesity-related hypertension and is potentially ameliorated by weight loss.

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Endocrine Cancer and Late Effects

OP4.1

Computer-assisted cytopathological diagnosis in pancreatic tumours: a systematic review and meta-analysis

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Background

Pancreatic malignancies, including pancreatic neuroendocrine tumours (PNETs), present major diagnostic challenges. The gold standard for diagnosis is endoscopic ultrasound-guided fine-needle aspiration or biopsy (FNA/B), assessed by a cytopathologist. However, workforce shortages have prompted interest in computer-assisted diagnosis (CAD) to ease these pressures and improve diagnostic efficiency. Despite this, the collective diagnostic impact of CAD in pancreatic cytology has not been quantified. We aimed to evaluate the accuracy of CAD in this setting.

Methods

We conducted a systematic review and meta-analysis; five databases were searched for studies published between January 2010 and May 2025 applying any CAD technique to pancreatic FNA/B cytology. Two reviewers independently screened records, with risk of bias assessed using QUADAS-2. Random-effects bivariate models generated pooled sensitivity, specificity and summary receiver-operating-characteristic (SROC) curves. Studies were analysed separately depending on whether the CAD tool evaluated multiple cytopathological images per case (multi-image level) or a single image from each case (single-image level).

Results

Ten studies met eligibility criteria and provided quantitative data. At the multi-image level, pooled sensitivity and specificity were 91% [95% confidence interval: 86–94] and 92% [87–96], respectively. At the single-image level, pooled sensitivity and specificity were 85% [69–93] and 91% [73–97], respectively. The SROC area under the curve was 0.945. Heterogeneity was high (I^2 = 65–93%), driven by retrospective designs and variable reference standards.

Conclusion

CAD tools achieved near-expert diagnostic accuracy and could reduce indeterminate reports and staffing demands. In endocrine oncology, they may enhance diagnostic precision for pancreatic cancers, such as PNETs, enabling earlier hormonal evaluation and surgical planning. However, selection bias, single-centre training and inconsistent thresholds limit generalisability. Prospective multi-centre validation with whole-slide workflows and consistent reporting is warranted, and integration with telepathology may expand access in low-resource regions.

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OP4.2

SGK3 and lipid remodelling: a key player in androgen-mediated metabolic dysregulation in endocrine-resistant breast cancer

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Introduction

Cancer cells often undergo significant metabolic reprogramming to meet the demands of rapid growth, adaptation to stress, evasion of cell death, and the development of therapeutic resistance. Our group previously demonstrated that an androgenic steroid environment arising post-aromatase inhibitor (AI) therapy correlates with unsustained response to therapy in breast cancer (BC). Notably, androgens upregulate serum-and-glucocorticoid-regulated kinase 3 (SGK3), a

recognised functional substitute for AKT that is implicated in second-line treatment resistance. Here, we investigate the role of SGK3 in regulating lipid metabolism in BC cells under androgenic conditions and the impact on cell survival
Methodology
Using in-house isogenic models of endocrine-resistant breast cancer (MCF7/MCF7-Aro-LetR and ZR75.1/ZR75.1-Aro-LetR) and a novel SGK3 protein degrader (SGK3-PROTAC1), we assessed the effects of SGK3 degradation on lipid accumulation and metabolism through Seahorse Mito Stress assays, lipidomic assays, flow cytometry, protein analysis, and fluorescence imaging under androgenic conditions.
Results
AI-resistant cells exhibited enhanced metabolic plasticity, reflected by increases in mitochondrial mass, membrane potential, respiratory activity, and glycolytic capacity. These cells also displayed significantly higher fatty acid uptake and lipid droplet accumulation. Notably, SGK3 degradation disrupted both lipid accumulation and intracellular lipid distribution. This metabolic perturbation sensitised AI-resistant cells to ferroptosis, a lipid-dependent form of cell death, which was rescued by ferroptosis inhibitors. Furthermore, SGK3 loss stabilised 17βHSD4, a key enzyme involved in peroxisomal β-oxidation and androgen inactivation, underscoring a critical link between SGK3, lipid metabolism, and ferroptotic vulnerability.
Conclusions
An androgenic steroid microenvironment induces marked metabolic reprogramming in BC cells, reminiscent of metabolic dysregulation observed in disorders of androgen excess such as PCOS. SGK3 emerges as a critical regulator linking androgen signalling, lipid metabolism, and ferroptosis sensitivity. Targeting this pathway may offer new therapeutic avenues to overcome endocrine resistance in breast cancer.

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OP4.3

Optimising glucocorticoid replacement in adrenocortical cancer: the role of ACTH monitoring

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Background
Mitotane is an adrenolytic drug used in the treatment of adrenocortical carcinoma (ACC). It accelerates steroid metabolism and increases corticosteroid binding globulin (CBG), necessitating higher doses of glucocorticoid replacement. At Imperial College Healthcare NHS Trust prednisolone is preferred over hydrocortisone for its once-daily dosing and stable pharmacokinetics. However, biomarkers to guide glucocorticoid dosing in mitotane-treated ACC patients remain undefined.
Methods
From 25 ACC patients, 6 met the inclusion criteria: mitotane therapy, once-daily prednisolone replacement, and available prednisolone and ACTH day curves. Clinical and treatment data were collected. Descriptive statistics explored prednisolone and ACTH trends. ACTH measurements at 2, 4, 6, and 8 hours post-dose were compared using Friedman and paired Wilcoxon tests. Spearman's correlation assessed the relationship between prednisolone and ACTH. The ACTH reference range (10-20 ng/l) was based on optimally replaced primary adrenal insufficiency patients.
Results
Median mitotane exposure was 13 months (range 8–20). Prednisolone doses ranged from 4–20 mg once daily. CBG was elevated in 85% of patients. ACTH values were stable and highly correlated between 4–8 hours post-dose (Rs > 0.85, $P < 0.0001$), but differed significantly at 2 hours. No consistent correlation was found between ACTH and prednisolone levels. ACTH trends aligned more closely with clinical dose adjustments than prednisolone concentrations: median ACTH was 21.8 ng/l when doses were increased and 2.5 ng/l when decreased. No adrenal crises occurred.
Conclusion
ACTH appears to be a reliable biomarker for prednisolone dose adjustment in ACC patients on mitotane. Its stability between 4–8 hours post-dose provides a practical window for glucocorticoid titration.

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OP4.4

GloBE-Reg: A Global Registry for Evaluating the Safety and Effectiveness of Growth Hormone Therapy Across The Age Span

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Introduction
The Global Registry For Novel Therapies In Rare Bone & Endocrine Conditions (GloBE-Reg, https://globe-reg.net/) project was launched in 2022 with the aim of supporting studies that focus on effectiveness and long-term safety of specific therapies in adults and children. The project's initial focus has been on recombinant human growth hormone therapy (rhGH).
Methods
GloBE-Reg consists of three dataset layers: (1) core data elements applicable to any rare condition; (2) the selection of a specific therapy and diagnosis; (3) a therapy- and diagnosis-specific minimum dataset, which collects longitudinal data including clinician-reported outcomes and adverse events. The fields within GloBE-Reg are developed following guidance from short-life expert working groups.
Results
Since its launch, 40 centres from 23 countries in 5 continents had enrolled 4,944 cases with a median current age of 12.5 (6.1, 18.0; 10^{th}, 90^{th} centile). Of these, 513 (10%) were above the age of 18 yrs and of these adults, 323 (63%) were on daily rhGH, 163 (32%) on long-acting rhGH, and 23 (4%) had stopped rhGH. In these cases, 12 different brands of rhGH were in use and the most common indications included GH deficiency in 378 (74%) and Turner syndrome in 61 (12%) with the remaining 14% including idiopathic short stature, small for gestational age and Prader-Willi syndrome. The first GloBE-Reg study that is currently open for recruitment in adults is focussing on safety and effectiveness of rhGH (daily or long-acting) in cancer survivors. Further information is available at https://globe-reg.net/studies/.
Conclusion
GloBE-Reg has demonstrated its versatility for collecting data to support long-term safety and effectiveness studies for multiple drugs and conditions. The preliminary data collected on rhGH underscore the platform's long-term utility in evaluating the safety and effectiveness of a wide range of drugs.

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Innovation in Teaching and Assessment

OP5.1

Postgraduate Educational Methods in Diabetes, Endocrinology and Metabolism (PEMDEM): A Systematic Review of Training Approaches and Their Impact on Clinical Competence and Patient Care

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Background
There is a paucity of evidence regarding which educational methods best enhance clinical competence and patient outcomes in diabetes, endocrinology and metabolism.
Objective
To systematically review and qualitatively synthesise evidence on educational approaches used in postgraduate training for diabetes, endocrinology, and metabolism, assessing their effectiveness on knowledge, skills, engagement, and patient care delivery.
Methods
Following PRISMA guidelines, seven databases (PubMed, MEDLINE, EMBASE, Web of Science, ERIC, CINAHL, and Scopus) were searched from inception to January 2025. All studies in which postgraduate healthcare professionals participated in structured educational interventions related to diabetes, endocrinology, or metabolism were included. Data was synthesised narratively and thematically. Methodological quality was assessed using RoB 2 and ROBINS-I tools.

Results
Of 12,676 studies screened, 25 met the inclusion criteria. Notably, 88% ($n = 22$) of studies focused on diabetes, with limited evidence in endocrinology ($n = 3$) and none in metabolism. Four overarching themes emerged: (1) **Knowledge, Skills, Confidence, and Competency:** 92% of studies reported improved knowledge, skills, and confidence, particularly in diabetes care. Virtual, didactic, and workshop-based approaches all enhanced learning, with interactive and applied models showing the strongest, most sustained effects. **(2) Attitudes, Perceptions, and Satisfaction:** Case-based and virtual learning were highly rated for relevance, accessibility, and engagement. Interprofessional and blended approaches further improved satisfaction and collaboration. **(3) Application to Patient Care and Clinical Outcomes:** 44% of studies demonstrated improved clinical practice, safer prescribing, and greater adherence to evidence-based care. (4) **Engagement, Implementation, and Learning Processes:** Flexible, learner-centred, and feedback-informed designs achieved higher engagement and satisfaction than rigid formats.
Conclusions
Blended virtual and case-based learning approaches emerged as the most effective educational method. However, the literature reveals a striking gap in endocrinology and metabolic education research. Future studies should prioritise large-scale, longitudinal, and mixed-method evaluations to inform an evidence-based model of postgraduate training in endocrinology and diabetes care.

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OP5.2

EndocrineDigiSim: A Pilot Study of Digital Endocrine Consultation Simulation for Postgraduate Medical Training

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Background
Simulation-based training has become an established component of postgraduate medical education and is now recognised as a curricular standard. Traditional simulation learning, however, predominantly involves practical skill training and often require extensive onsite infrastructure, significant resourceful setup.
Objective
We aimed to adapt the core principles of simulation-based learning to a digital format, enabling accessible training of general clinical skills in resource-efficient postgraduate training in endocrinology.
Methods
We developed and piloted *EndocrineDigiSim*, a series of digital endocrine consultation simulations for postgraduate students enrolled in the MSc Endocrinology and Diabetes program at Queen Mary University of London. Each session involved an active participant, a real-life patient, peer observers, an invigilator, and a feedback reviewer. Simulated consultations, both new patient and follow-up, focused on various presentations of acromegaly and were conducted remotely via Microsoft Teams. Sessions aimed to recreate realistic clinical encounters in a non-procedural specialty, fostering the development of clinical reasoning and communication skills. Feedback was provided verbally, in writing, and via recorded summaries to encourage reflective practice. Knowledge was assessed pre- and post-session, and participants completed structured feedback forms.
Results
Participants reported high satisfaction with the digital simulation format, citing enhanced engagement, learning retention, and accessibility. Preliminary assessments indicated knowledge improvement following participation. Patients involved in the simulations also provided positive feedback regarding the experience.
Conclusion
EndocrineDigiSim demonstrates that digital simulation training is a feasible, effective, and resource-efficient approach to postgraduate endocrine education. Accessible technology enables the delivery of high-quality experiential learning to broader audiences, reducing the financial and logistical demands of conventional onsite simulation.

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OP5.3

Hormone hype and health misinformation: social media marketing of cortisol and testosterone

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Social media is a powerful but often unregulated space for health communication, with platforms including TikTok, Facebook, X and Instagram, playing a growing role in shaping public understanding of steroid hormones. This study investigates how cortisol and testosterone are represented in popular TikTok videos, with a focus on scientific accuracy, marketing strategies, and the promotion of dietary supplements. We conducted a content analysis of the most interacted-with posts (likes, shares, and views) using the keywords "cortisol" and "testosterone." Posts were evaluated against 11 criteria, including scientific accuracy, use of biohacking language, marketing tactics, influencer affiliations, and algorithmic amplification. Our analysis revealed widespread misinformation and oversimplification. Cortisol was frequently described as the root cause of belly fat, fatigue, and poor performance, while testosterone was portrayed as a panacea for masculinity, energy, and muscle growth. These narratives were commonly used to promote unproven supplements through emotionally charged, fear-based, and aspirational marketing techniques. Many creators offered testimonials or linked to affiliate products, despite lacking robust scientific evidence. Though most platforms have misinformation policies, enforcement was inconsistent, with little flagging of medical inaccuracies. This study highlights the urgent need for improved regulation of online health claims, increased transparency in influencer marketing, and public education on endocrine health. In the era of algorithm-driven misinformation, protecting consumers from pseudo-scientific narratives is vital for evidence-based medicine and public trust.

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OP5.4

Enhancing endocrine training through virtual simulation: addressing social determinants of health, health inequities and multiple long-term conditions

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Introduction
Patients with endocrine disorders often present with multiple long-term conditions (MLTCs), influenced by social determinants of health (SDOH) and health inequities. These factors significantly affect both acute and long-term management. Endocrine disorders frequently present with complex and overlapping cardiometabolic and systemic symptoms. Trainees are often not formally taught how to manage and balance these complex clinical and non-clinical factors. To address this, we developed a virtual simulation-based teaching programme using Simulation via Instant Messaging – Bedside Application (SIMBA). The programme integrated elements of non-clinical diagnosis and management into clinical case transcripts. Two sessions were delivered: SIMBA-MODY (Maturity-Onset Diabetes of the Young) and SIMBA-Pituitary, focusing on common presentations in endocrine practice.
Methods
Two virtual simulation sessions were conducted for postgraduate healthcare professionals. Eight anonymised patient cases were simulated across two sessions using instant messaging platforms. Each session was followed by expert-led case-based discussions highlighting clinical reasoning, social determinants, and key learning points. Participants completed pre- and post-session questionnaires assessing self-reported knowledge and confidence using five-point Likert scales. Data were analysed using the Wilcoxon Signed Rank Test.
Results
For SIMBA-MODY, 27 participants completed pre- and post-session surveys. Self-reported confidence in managing MODY presentations improved significantly (16.7% vs 74.1%, $P < 0.05$). For SIMBA-Pituitary, 22 participants completed both surveys, with self-reported confidence increasing significantly from 39.8% to 90.9% ($P < 0.05$). Most participants agreed that simulation was an engaging learning method (85.2% in SIMBA-MODY; 86.4% in SIMBA-Pituitary). Participants also reported improved understanding of SDOH, health inequities, and the management of MLTCs following both sessions.
Conclusion
Virtual simulation using SIMBA is an effective educational tool for enhancing postgraduate healthcare professionals' confidence in managing endocrine disorders within the broader context of MLTCs, SDOH, and health inequities. As patient complexity increases, SIMBA offers a scalable, interactive approach to teaching these non-clinical competencies, to improve patient care.

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OP5.5

Inpatient hyponatraemia diagnosis and management

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Background
Hyponatraemia is one of the most common electrolyte abnormalities in hospitalised patients and is associated with increased morbidity, mortality, and length of stay. It affects approximately 15–20% of inpatients and often reflects underlying systemic illness or inappropriate fluid or medication management. Accurate diagnosis and timely, guideline-directed treatment are essential to improve outcomes. This quality improvement project aimed to evaluate and enhance the inpatient diagnosis and management of hyponatraemia across eight adult medical wards in a District General Hospital.
Method
A retrospective two-cycle clinical audit was conducted over a 14-day period. Adult inpatients with confirmed hyponatraemia (serum sodium $<$135 mmol/l) were included. Data were collected on five key parameters: (1) sodium level at diagnosis, (2) biochemical work-up (serum/urine osmolality, urine sodium, cortisol, thyroid, liver, and lipid profiles), (3) assessment and documentation of volume status, (4) referral to the Endocrinology team for moderate to severe cases, and (5) initiation of treatment according to Trust guidelines.
Interventions
Following Cycle 1, targeted interventions were implemented, including educational sessions delivered during AMU teaching, on-take/post-take ward rounds, and clinical meetings. Posters summarising the Trust's hyponatraemia management algorithm were displayed across all medical wards and medical take office. Audit findings were also presented at Endocrinology departmental and AMU teaching sessions to raise awareness and promote standardised care.
Results
In Cycle 1, 272 patients were screened, identifying 66 (24%) with hyponatraemia (60 analysed). In Cycle 2, 252 patients were screened, identifying 59 (23.2%) cases (48 analysed). Documentation of volume status improved from 43% to 88%, Endocrinology referrals from 17% to 34%, and adherence to treatment guidelines from 50% to 92%.
Conclusion
Educational and awareness interventions significantly improved fluid status documentation, adherence to guidelines, and multidisciplinary collaboration in hyponatraemia management. Continued education and re-audits will sustain and further enhance these improvements in patient care.

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Bone and Calcium

OP6.1

CCN family member 3 (CCN3) is a potential human osteoanabolic lactation hormone

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CCN family member 3 (CCN3) is reported in mice to be an osteoanabolic peptide secreted by hypothalamic kisspeptin-expressing neurons, and protects the maternal skeleton from excess resorption during lactation. However, its role in breastfeeding women is unknown. We investigated whether maternal CCN3 concentrations increase after childbirth and are associated with: 1) changes in prolactin, which regulates kisspeptin-expressing neuronal activity; and 2) bone formation, measured using pro-collagen type 1 N-terminal pro-peptide (P1NP). This study included $n = 30$ healthy pregnant women intending to breastfeed and aged $>$18 years. Blood samples were obtained following informed consent at 36 weeks' gestation (baseline), postpartum day 4 (start of lactation), and during postpartum days 14-28 (established lactation). Biochemical values were compared with $n = 22$ age-matched healthy female volunteers who were neither pregnant or lactating. Mean+/-SEM plasma CCN3 concentrations were significantly higher during pregnancy (12.0+/-1.2 ng/mL) compared with healthy volunteers (5.9+/-0.6 ng/mL, $P < 0.001$). However, CCN3 values decreased to 7.3+/-0.7 ng/mL by postpartum day 4 and then significantly increased to 13.0+/-1.0 ng/mL, $P < 0.001$) by postpartum days 14-28. Serum prolactin showed a significant increase from 36 weeks' gestation (3897+/-292 mU/l) to postpartum day 4 (4984+/-279 mU/l, $P < 0.05$) and this rise significantly correlated with the postpartum increase in CCN3 ($r = 0.45$, $P < 0.05$). Plasma P1NP concentrations were significantly higher at postpartum days 14-28 (80+/-5.5 ng/mL) compared with healthy volunteers (50+/-2.6 ng/mL, $P < 0.001$). Moreover, plasma P1NP correlated with CCN3 during pregnancy ($r = 0.71$, $P < 0.001$) and at postpartum days 14-28 once lactation was established ($r = 0.48$, $P < 0.01$). In summary, maternal plasma CCN3 shows a biphasic longitudinal pattern with an increase during pregnancy, decreased concentrations following childbirth and subsequent postpartum increase once lactation is established. Furthermore, the significant associations with prolactin and P1NP indicate possible regulation by prolactin and highlight CCN3 as a potential novel osteoanabolic hormone in breastfeeding women.

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OP6.2

Characterisation of human sulfotransferases involved in vitamin D metabolite sulfation and population-level variation in sulfation

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Introduction
Vitamin D metabolites are key biomarkers for bone health, immune function, and chronic disease risk. Recent evidence indicates that phase II metabolites of vitamin D, may act as reservoir forms rather solely excretory products. However, the specific human sulfotransferases (SULTs) responsible for sulfating individual vitamin D metabolites remain poorly defined. Furthermore, population-level differences in sulfation capacity, potentially influenced by genetic differences, has not been systematically examined.
Methods
Vitamin D metabolites were incubated with 11 different recombinant human SULT isoforms to assess their sulfation activity. Resulting sulfate conjugates were quantified using LC-MS/MS. In parallel, 150 different human serum samples were analysed by LC-MS/MS to evaluate inter-individual and potential population-based differences in 25OHD3 sulfation.
Results
SULT2A1, *SULT1A1*1*, *SULT1A1*2*, and *SULT1E1* displayed sulfation activity towards vitamin D metabolites, with variation in sulfation activity between SULTs and mono and di-hydroxy forms of vitamin D. In the human cohort, no age-based or sex-based differences were observed in 25OHD3 sulfation. However, ethnic-based differences were observed with African-Americans displaying higher proportions of sulfated 25OHD3 (52.1%; median) compared to Hispanics (51.5%; median) and Caucasians (49.5%; median). Seasonal-based differences were also observed in 25OHD3 sulfation where samples collected in autumn and winter months having a higher proportion of sulfated 25OHD3.
Discussion
This study identifies the human SULTs involved in vitamin D conjugation metabolism and highlights factors that influence sulfation in humans. The observed ethnic and seasonal differences in 25OHD3 sulfation imply that both individual and environmental factors may regulate vitamin D conjugation and availability. Together, these findings enhance understanding of phase II vitamin D metabolism. Further studies will investigate the potential role of these sulfated vitamin D metabolites as storage forms, and its potential role in defining a more accurate assessment in vitamin D status.

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OP6.3

An endocrine nurse led cinacalcet clinic? saving money, avoiding admissions and keeping patient safe!

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Background
Primary hyperparathyroidism is a progressive condition causing multiple symptoms and complications including: hypercalcaemia, polyuria, bone pain, constipation, confusion, osteoporosis and kidney stones. Incidence rises with age and many patients with significant hypercalcaemia are not appropriate surgical candidates or may be awaiting surgery and require Cinacalcet a medication to manage hypercalcaemia. In Merseyside, Cinacalcet prescription is secondary care retained, requiring biochemical monitoring a week after commencement or dose adjustment and 3-monthly thereafter. Secondary care prescriptions rely on patient-initiated requests. In a cohort of elderly patients at risk of confusion, this can lead to reduced concordance and subsequent hypercalcaemia.
Aim
This project aimed to assess the safety of our current management with Cinacalcet therapy.
Method
Pharmacy identified all patients prescribed Cinacalcet between 1/4/22 and 27/9/23. Using electronic records, each case was reviewed, identifying hypercalcaemia associated hospital admissions and frequency of outpatient contact. The total cost of these hospital stays was calculated to assess the financial impact using the NHS National Tariff for inpatient care 2022-2023.
Results
21 patients identified on Cinacalcet, of which 13 conservatively managed and 8 awaiting surgery. 6 patients experienced 11 admissions due to hypercalcaemia, with an average admission of 9.4 days (range 3-23), totalling 85 bed-days. Causes for hypercalcaemia, requiring hospitalisation included: running out of medications, infrequent monitoring, illness and unknown. This resulted in an estimated combined cost of £66,814 (up to £6,074 per admission for electrolyte disorders, with interventions).
Conclusion
We concluded current practice was not adequate to effectively manage patients on Cinacalcet. We proposed a dedicated band 7 endocrine nurse led monthly Cinacalcet clinic, with a database for prescriptions, biochemistry monitoring and review of calcium related admissions if they occur. 12 sessions would cost an estimated £1,141/year, saving approximately £65,673/year. This clinic will start in January 2026, saving money, avoiding admissions, and keeping patients safe.

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OP6.4

Efficacy and Safety of Palopegteriparatide Treatment in Adults With Hypoparathyroidism: 3-Year Results From the Phase 3 PaTHway Trial

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Introduction
Palopegteriparatide is a prodrug of PTH(1-34), administered once daily, designed to provide active PTH within the physiological range for 24 hours/day. It is approved in the US, EU, UK and several other countries.
Methods
This analysis evaluated the long-term efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 156 of PaTHway, a phase 3 trial with a 26-week randomized, double-blind, placebo-controlled period, followed by an open-label extension.
Results
At week 156, 89% (73/82) of participants remained in the trial; of those, 96% were independent from conventional therapy (no active vitamin D and $\leq$600 mg/day elemental calcium) and 88% had normal albumin-adjusted serum calcium (2.07-2.64 mmol/l) with mean (SD) of (2.2 (0.2) mmol/l). Mean (SD) serum phosphate (1.1 (0.2) mmol/l) and calcium x phosphate product (2.5 (0.4) $mmol^2/l^2$) remained within normal ranges. Mean (SD) eGFR was 78.0 (14.5) mL/min/1.73 m^2, reflecting a mean (SD) increase of 8.8 (11.9) mL/min/1.73 m^2 from baseline ($P < 0.0001$); 59% and 43% of participants had an increase in eGFR of $\geq$5 mL/min/1.73 m^2 and $\geq$10 mL/min/1.73 m^2, respectively. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide treatment, remaining below the upper limit of normal ($\leq$250 mg/day) through week 156 (162.1 [117.8] mg/day). TEAEs were mostly grade 1 or 2, with no new safety signals identified.
Conclusion
Through year 3 of the PaTHway trial, retention rate was high and palopegteriparatide demonstrated consistent longer-term safety and efficacy, which included the maintenance of serum and urine biochemistries within normal levels and sustained improvement in renal function.

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Reproductive Endocrinology

OP7.1

Adaptive metabolic plasticity defends body reserves during reproduction

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Background
Reproduction is among the most energetically demanding stages in mammals, yet how energy balance is maintained during pregnancy and lactation remains unclear. Functional hypothalamic amenorrhea in women highlights the sensitivity of fertility to energy availability, but the metabolic strategies that buffer reproduction under energetic stress are poorly defined.
Methods
We quantified reproductive energy cost by treating the mother and offspring as a single metabolic unit. Female C57BL/6J mice were monitored in metabolic cages (CLAMS) from mating to postnatal day 18 at room temperature or thermoneutrality. Feeding behaviour was assessed using BioDAQ, fat distribution by micro-CT, and pair-feeding compared ad libitum and intake-restricted pregnant mice to test whether additional calories were required for gestation.
Results
Pregnancy modestly increased total energy expenditure (EE) by ~12% ($P = 0.03$) but reduced EE per gram of fat-free mass, indicating metabolic downregulation in late gestation. BioDAQ analysis showed food intake rose only slightly during pregnancy, whereas lactation induced marked hyperphagia consistent with a 2.2-fold greater energetic demand ($P < 0.0001$). Micro-CT revealed preferential lipid accumulation in visceral adipose tissue (VAT) during pregnancy, while subcutaneous adipose tissue (SAT) changed little. During lactation, VAT expanded further (2-fold vs GesD1, $P = 0.01$) as SAT declined (-43%, $P = 0.37$), reflecting lipid redistribution and mobilisation for milk synthesis. Under thermoneutrality, basal metabolism declined in both stages, but only lactation efficiency—the conversion of maternal energy into pup biomass—was impaired. Pair-fed pregnant mice still accumulated fat ($+36\%$, $P = 0.03$) and produced normal litters ($P = 0.46$), showing that pregnancy proceeds through metabolic reallocation rather than overfeeding.
Conclusions
Pregnancy conserves energy, while lactation mobilises these reserves to raise offspring. Even under caloric restriction, females reproduced normally, demonstrating a remarkable metabolic flexibility that safeguards maternal reserves and reproductive success, and may provide insight into functional hypothalamic amenorrhea.

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OP7.2

Low Protein Diet Alters Embryo Morphology and 1-Carbon Metabolism in Mice

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Periconceptional low-protein (LPD) intake has been linked to altered developmental trajectory of offspring, increasing their risk of developing non-communicable diseases in adulthood. These effects have been attributed to changes in the parental 1-Carbon metabolism. Until now, effects of poor maternal or paternal diet have been investigated individually and not in combination, despite being of higher clinical relevance. This study aimed to investigate the combined impact of maternal and paternal LPD on parental 1-C metabolism and preimplantation embryo development. Eight-week-old C57BL/6 mice were fed either a normal protein diet (NPD; 18% casein) or LPD (9% casein) for 8 weeks. Mice were mated in a 2×2 factorial design, resulting in four dietary groups: NN (NPD female, NPD male), NL (NPD female, LPD male), LN (LPD female, NPD male) and LL (LPD female, LPD male). Females were culled at embryonic day 1.5 (E1.5) for preimplantation embryo collection and culture in a time-lapse system (EmbryoScope). Liver 1-C metabolites were analysed using a novel LC-MS/MS method. A significant interaction between maternal and paternal diets was observed for blastocyst morphology, with embryos from group LL (both parents on LPD) showing a 20% decrease in survival rate. Maternal livers showed reduced ADMA, betaine, glycine, and serine, with increased cysteine and SAM, while methionine remained unchanged. Paternal livers exhibited lower choline and methionine, with no change in SAM. Branched-chain amino acids (valine, leucine) were significantly reduced in both maternal and paternal tissues. These findings indicate that parental LPD disrupts key metabolic pathways in both maternal and paternal tissues, particularly amino acid availability and methylation-related metabolites, which likely contribute to impaired blastocyst morphology and reduced embryo survival. The results highlight the synergistic impact of maternal and paternal nutrition on early embryonic development and emphasise the critical importance of adequate parental protein intake for reproductive success and developmental programming.

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OP7.3

A Single Centre Study to Describe the Changes in Serum Testosterone Concentration Following Application of Testosterone Gel in Post-Menopausal Women with Hypoactive Sexual Desire Disorder (HSSD) Already Receiving this as Part of Usual Care in Conjunction with Oestrogen Containing Hormone Replacement Treatment (HRT)

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Introduction
Hypoactive Sexual Desire Disorder (HSDD) is characterized by a persistent reduction in sexual desire causing personal distress, commonly affecting post-menopausal women or those who are post-oophorectomy. Although testosterone therapy may alleviate symptoms, evidence in women remains limited. Testosterone, licensed for men, has been used off-label at modified doses for women. This study assessed serum testosterone levels in post-menopausal women with HSDD treated with testosterone gel (Testogel 16.2 mg/g, Besins Healthcare UK Ltd).
Methods
Twenty-four post-menopausal women using Testogel 16.2 mg/g via pump every 3–4 days for 6 months, in addition to oestrogen +/- progesterone -based HRT, were included. Participants applied 20.25 mg of Testogel following a baseline blood sample. Blood samples were collected every two hours for 10 hours and at 24 hours post-application. Testosterone concentrations were measured by mass spectrometry. The Female Sexual Function Index (FSFI) assessed sexual function. Pharmacokinetic parameters—Cmax, Cavg, Tmax, AUC and t½—were calculated with and without baseline testosterone adjustment.
Results
Mean age was 53.7 ± 6.8 years; mean BMI 27.4 ± 4.3 kg/m^2; mean blood pressure 126/75 mmHg. Unadjusted median Cmax was 6.25 nmol/l (range 1.3–26.1) and Cavg 4.51 nmol/l (range 0.93–20.21). Median AUC was 121.8 nmol•h/l (range 35.9–458). Baseline-adjusted median Cmax was 3.55 nmol/l, Cavg 1.64 nmol/l, and AUC 39.45–181.8 nmol•h/l. Median FSFI score was 26.5/36 (IQR 18–30), with highest domain scores for arousal and satisfaction. All women reported subjective improvement in sexual function, with no androgenic side effects.
Conclusion
Marked variability was observed in testosterone pharmacokinetics among women applying Testogel 16.2 mg/g every 3–4 days. Despite this, all reported clinical benefit and no adverse effects. Development of a licensed daily testosterone formulation for women would provide a consistent, evidence-based therapeutic option for managing HSDD.

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OP7.4

Disentangling the impact of obesity on reproductive, metabolic and adipokine profiles in women with or without PCOS

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Background
Obesity and polycystic ovary syndrome (PCOS) frequently co-exist, however whilst PCOS is associated with increased hypothalamic GnRH neuronal pulsatility, animal models suggest that obesity is associated with reduced hypothalamic function. Dissecting the impact of obesity on reproductive, metabolic and adipokine pathways is essential to understand reproductive dysfunction in women.
Methods
We investigated reproductive, metabolic and adipokine profiles in 131 women. Overall, 25 of 76 women with PCOS had obesity, and 9 of 55 healthy eugonadal women with regular menstrual cycles had obesity. Follicular-phase bloods were analysed for reproductive hormones (LH, FSH, oestradiol, AMH, SHBG, total and free testosterone), metabolic markers (insulin, HOMA-IR, HbA1c, lipids) and adipokines (leptin, adiponectin, ghrelin). Group differences were assessed using Mann–Whitney U tests. Regression analyses (adjusted for age and ethnicity) evaluated associations between BMI and hormonal or metabolic outcomes.
Results
Adjusted models in women with PCOS revealed that BMI was inversely associated with LH ($P = 0.03$, $R^2 = 0.16$), SHBG ($P < 0.0001$, $R^2 = 0.38$) and AMH ($P = 0.04$, $R^2 = 0.13$), but positively associated with free testosterone ($P < 0.0001$, $R^2 = 0.34$), fasting insulin ($P = 0.0002$, $R^2 = 0.35$), HOMA-IR ($P = 0.0012$, $R^2 = 0.23$) and lipids ($P = 0.0001$, $R^2 = 0.24$). Leptin showed the strongest association with BMI ($P < 0.0001$, $R^2 = 0.82$ in PCOS vs $R^2 = 0.48$ in controls) while adiponectin and ghrelin declined with increasing BMI (both $P = 0.001$).
Conclusion
Obesity has a negative impact on reproductive hormone secretion including LH consistent with a mechanistic role in obesity-related hypogonadism. Reasons for the reduction in LH with obesity are multifactorial but include leptin resistance leading to decreased hypothalamic function and increased LH clearance. Increased GnRH neuronal activity in women with PCOS was most pronounced in those without obesity. These data support the independent impact of obesity on reproductive dysfunction in women with obesity that is distinct from PCOS.

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Featured Clinical Case Posters

CC1

Macrophage polarisation and metabolic reprogramming in cortisol-producing adenomas

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Background

Endogenous Cushing's syndrome (CS) is characterised by chronic cortisol excess, profoundly altering immune responses and host defence mechanisms. However, its direct effects on tissue macrophage phenotype and metabolism remain undefined. The impact of mild autonomous cortisol secretion (MACS) in cortisol-producing adrenocortical adenomas (CPA) without clinical CS features is unclear. We hypothesised that macrophage polarisation, activation, and bioenergetic function are altered in both CPA-CS and CPA-MACS.

Methods

Human macrophages were polarised into M1-like inflammatory state using TNFα (10 ng/ml) and IFNγ (20 ng/ml) and co-treated with 10% patient serum. Samples were obtained from 18 patients (12CPA-MACS [8 women], 6CPA-CS [4 women]) and 10 age- and sex-matched controls with endocrine-inactive adenomas (EIA). Cytokine levels and gene expression were analysed by ELISA and RT-qPCR. Mitochondrial viability (MTT assay) and phagocytosis were assessed after 48 hours. Data were correlated with cortisol secretion and tumour characteristics.

Results

Pro-inflammatory IL6 secretion was reduced in macrophages treated with CPA-MACS (0.72-fold,$P = 0.071$) and CPA-CS serum (0.50-fold, $P = 0.004$) compared with EIA, while IL6 mRNA showed a similar trend. The M2 marker CD163 modestly increased in CPA-CS (1.32-fold,$P = 0.258$) but not in CPA-MACS, correlating with post-dexamethasone cortisol levels and tumour size. TGFβ concentrations were significantly elevated in CPA-CS ($P = 0.012$), and IL6/CD163 ratio increased (2.41-fold,$P = 0.003$), indicating a cortisol-dependent shift toward an anti-inflammatory phenotype. Mitochondrial viability increased in CPA-MACS ($P = 0.059$) and CPA-CS ($P = 0.005$), accompanied by reduced ATP production and maximal respiration ($P < 0.05$) and enhanced glycolytic activity ($P < 0.01$) in CPA-CS. Phagocytosis was impaired in both CPA-MACS ($P = 0.014$) and CPA-CS ($P = 0.076$). Glucocorticoid receptor blockade partially restored mitochondrial respiration, spare capacity, and bioenergetic balance.

Conclusions

Both CPA-MACS and CPA-CS sera suppress M1-like macrophage activation and promote M2-like polarisation, impairing phagocytosis and altering mitochondrial metabolism. Even mild cortisol excess in MACS significantly modulates macrophage function, potentially contributing to systemic immune dysregulation and altered tissue homeostasis.

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CC2

Severe catecholamine-induced cardiomyopathy improved after adrenalectomy without surgical complications: case report

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Introduction

Catecholamine-induced cardiomyopathy (CIC) is a stress-induced heart dysfunction caused by excessive catecholamines. It often presents insidiously, as left ventricular dysfunction without significant obstructive coronary artery disease. Patients presenting with dilated cardiomyopathy and heart failure should be screened for phaeochromocytoma. Adrenalectomy remains the gold standard treatment in patients with CIC with intraoperative mortality of 4% versus 22% with conservative management.

Case details

A 57-year-old man with established hypertension and dilated cardiomyopathy presented following a fall and was noted to have a heterogenous 4 cm adrenal lesion on CT imaging. Biochemical testing revealed plasma metadrenaline 7 times upper normal limit (3379pmol/l) consistent biochemically with phaeochromocytoma, later confirmed by MIBG. Cardiac assessment revealed significant systolic and diastolic dysfunction with ejection fraction (EF) of 10%. Reversing Atrial Fibrillation (AF) with amiodarone allowed adequate alpha-blockade using doxazosin, though EF remained unchanged. The profound cardiac impairment initially led the first adrenal multiple multidisciplinary team (MDT) to deem him unfit for adrenalectomy. However, this decision was challenged by the endocrinologist prompting further MDT discussions including Cardiology, Surgery, ITU, Anaesthesiology and Endocrinology, which ultimately supported proceeding at a tertiary centre. Surgery was preplanned by cardiac intensivists and anaesthetists with extracorporeal membrane oxygenation (ECMO) on standby and potential escalation to cardiac transplant. He underwent open adrenalectomy with complete pheochromocytoma resection without surgical complications. At eight weeks post-surgery catecholamines normalised and EF improved to 20%. Six-month follow-up ECHO is awaited. Genetic testing for causes of cardiomyopathy/phaeochromocytoma were negative.

Summary

Surgery remains the definitive treatment for pheochromocytoma, though often limited by frailty, comorbidities, and surgical risk. This case showed improvement in CIC following adrenalectomy. Surgery should be pursued when feasible, even with severe cardiac impairment, utilising an MDT approach at a specialised tertiary centre. Even in the absence of post operative improvement in cardiac function, adrenalectomy may enable cardiac transplantation.

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CC3

CT-Guided Radiofrequency Ablation as a Novel Treatment for Adrenal Cushing's Syndrome in a High-Risk Surgical Candidate

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A 44-year-old female with a history of left hepatectomy for a hydatid cyst was referred following an incidental finding of a 2.8 cm right adrenal adenoma on MRI liver imaging. She had recently developed hypertension and pre-diabetes, accompanied by a one-year history of symptoms consistent with Cushing's syndrome. Initial investigations showed biochemistry consistent with a diagnosis of adrenal Cushing's syndrome without evidence of co-secretion. Medical therapy with metyrapone was tolerated well and the patient reported a marked improvement in her symptoms with a return of menstruation. She was referred to the endocrine surgical team for consideration of a right adrenalectomy. On review of imaging, there was concern that the adrenal gland had adhered to the liver at the site of the previous surgery and a surgical approach was not without significant risk. Emerging evidence from the FABULAS trial supports the use of radiofrequency ablation (RFA) for aldosterone-secreting adrenal adenomas[1]. However, its application in cortisol-secreting lesions remains underreported. Given the patient's surgical risk, CT-guided percutaneous RFA was performed under general anaesthesia in January 2025. The procedure was uncomplicated, and the patient was discharged on hydrocortisone. A 9 a.m. cortisol measured four days post-procedure (off hydrocortisone) was 28 nmol/l, confirming biochemical remission. Apart from transient infective complications, she has remained well on 7 mg prednisolone once daily. This case demonstrates the potential role of CT-guided RFA as a safe and effective alternative to surgery for functioning adrenal adenomas in patients unsuitable for surgical intervention. Further research is warranted to define its efficacy and long-term outcomes in cortisol-secreting adrenal tumours.

Reference

1. Argentesi *et al* (2025) 'Endoscopic, ultrasound-guided, radiofrequency ablation of aldosterone-producing adenomas (FABULAS): a UK, multicentre, prospective, proof-of-concept trial' The Lancet. 405, 10479 p637-647.

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CC4

A decade of experience using mifepristone to treat 'Primary Pigmented Nodular Adrenocortical Disease' in Carney Complex'

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Carney Complex (CC) is a rare autosomal dominant genetic disorder, caused by a PRKAR1A gene mutation. Multiple endocrine neoplasia syndromes, and primary pigmented nodular adrenocortical disease (PPNAD) are common features. PPNAD is characterised by normal to enlarged adrenal glands, containing multiple pigmented nodules with surrounding adrenal atrophy, and can cause ACTH-independent hypercortisolism. Recommended PPNAD management is bilateral adrenalectomy, which carries a high risk of morbidity and mortality. Mifepristone is a glucocorticoid receptor antagonist, which blocks the effects of endogenous hypercortisolism. In 2013, a 38-year-old female, already diagnosed with CC, presented with hirsutism, mood changes, central fat distribution, and disrupted sleep, on a background of other manifestations of CC - dermal schwannomas and breast adenomyoepitheliomas. Tests to evaluate ACTH-independent Cushing's syndrome yielded the following results and, in summary, revealed an elevated 24-hour urinary free cortisol (UFC), positive low and high dose dexamethasone suppression tests, and loss of salivary cortisol diurnal variation.

Investigation		Result (nmol/l) [reference range]
24-hour UFC		176 [<120]
Dexamethasone suppression test: serum cortisol	Low-dose	Baseline: 292 48hr: 357 [<50]
	High-dose	Baseline: 321 48hr: 457 [<50]
Salivary cortisol (3 consecutive days)	Morning	4 4 3 [5-46]
	Night	4 4 4 [<2.6]

She was diagnosed with PPNAD and trialled on 200 mg mifepristone, with a slight dose increase a few years later. A normal sleep pattern was restored, positively impacting energy, mood, and weight. Important to note is an incidental finding of endometrial adenosarcoma 3 years after initiation of mifepristone, suspected to have caused endometrial hyperplasia. She underwent a hysterectomy and salpingo-oophorectomy. A decade later, her condition remains well-controlled, and she lives an active and fulfilling life. This case report explores a decade of novel use of mifepristone to restore circadian rhythm and reduce effects of hypercortisolism in PPNAD in CC, advocating for its use and for regular screening with transvaginal ultrasounds.

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CC5

Spontaneous haemorrhage of a functioning parathyroid carcinoma presenting with refractory hypercalcaemia: a rare case report

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Parathyroid carcinoma is a very rare cause of primary hyperparathyroidism (<1% of cases). Spontaneous intralesional haemorrhage is exceptionally uncommon but may present as a life-threatening neck emergency. We describe a diagnostically and therapeutically complex case of functioning parathyroid carcinoma complicated by spontaneous haemorrhage and refractory hypercalcaemia. A 67-year-old man with hypertension, chronic kidney disease and bladder calculus was diagnosed with primary hyperparathyroidism in August 2024. By November, renal imaging was normal, DEXA confirmed osteoporosis, and he was referred for surgery. Calcium rose to 3.42 mmol/l (2.2–2.6), prompting cinacalcet 30 mg twice daily, later 60 mg twice daily. In January 2025 he presented with abdominal pain, fatigue and reduced oral intake; corrected calcium 4.27 mmol/l, PTH 111 pmol/l (1.6–6.9), eGFR 55 mL/min. On day two, he developed suprasternal ecchymosis and neck swelling. CT neck showed a large 6.7 cm right inferior parathyroid lesion with intralesional haemorrhage and oedema. MDT initially advised conservative management due to high surgical risk in acute bleeding. Despite hydration and cinacalcet 60 mg tds, calcium remained >3.0 mmol/l, requiring repeated intravenous bisphosphonates. Repeat imaging confirmed a persistent lesion with mediastinal extension. He underwent right parathyroidectomy and ipsilateral hemithyroidectomy; intra-operative PTH fell from 157 to 1.2 pmol/l. Post-operatively he developed a cervical haematoma requiring evacuation. Histology showed T1 N0 M0 R1 low-grade parathyroid carcinoma (Ki-67 <1%), positive for CK7, GATA3, chromogranin and vimentin; genetic testing was negative. Follow-up showed calcium 2.44 mmol/l, PTH 17 pmol/l (mildly raised, felt CKD-related), recovery of vocal cord function and no recurrence on imaging. This case highlights spontaneous haemorrhage as a rare presentation of parathyroid carcinoma. Severe hypercalcaemia, very high PTH and poor medical response should prompt malignancy consideration. Early imaging, airway assessment, MDT coordination and surgery are vital, with long-term surveillance recommended.

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CC6

Persistent hypercalcaemia secondary to suspected silicone-induced granulomatous disease: a diagnostic challenge

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Background
Hypercalcaemia has a broad differential diagnosis, including malignancy, primary hyperparathyroidism, and granulomatous diseases. Silicone-induced granulomatous disease is a rare cause of hypercalcaemia that poses diagnostic challenges. This report highlights a case of hypercalcaemia secondary to silicone granulomas following cosmetic injections.
Case Presentation
A 41-year-old lady was admitted with severe sepsis, acute kidney injury, and left pyelonephritis complicated by multiple renal stones. During her admission, persistent hypercalcaemia was identified. Her history included cosmetic gluteal silicone injections performed ten years earlier in Brazil and prolonged use of anabolic steroids. There was no history of malignancy, sarcoidosis, or autoimmune disease. Laboratory tests showed suppressed parathyroid hormone (PTH), normal PTH-related peptide (PTHrP), elevated serum angiotensin-converting enzyme (ACE) at 117 U/l, and calcitriol at the upper limit of normal (124 pmol/l). Vitamin D was 77 pmol/l. Urinary calcium was elevated, with worsening renal function. Vitamin A levels were high. Serum electrophoresis revealed mildly increased kappa and lambda light chains with a normal ratio. Imaging excluded malignancy or sarcoidosis. CT scan showed bilateral gluteal fat stranding and fat-density lesions consistent with silicone injections, while PET scan confirmed bilateral silicone deposits without neoplastic activity. A diagnosis of silicone-induced granulomatous disease causing calcitriol-mediated hypercalcemia was made.
Management and Outcome
Hypercalcemia was resistant to intravenous fluids and bisphosphonates. Oral prednisolone (40 mg daily) was initiated, leading to a rapid decline in serum calcium. Multidisciplinary input from endocrinology, nephrology, plastic surgery and radiology guided management. The patient's calcium remains mildly elevated on steroids, requiring ongoing monitoring.
Conclusion
Silicone granulomas are a rare cause of non-PTH-mediated hypercalcemia. A history of cosmetic silicone injections combined with elevated ACE and calcitriol should prompt consideration of this diagnosis. Corticosteroids are the primary treatment, with bisphosphonates and surgery reserved for refractory cases.

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CC7

Post-bariatric hypoglycaemia in pregnancy: Lessons learnt from a case series

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Introduction
Post-bariatric hypoglycaemia (PBH) is an increasingly recognised complication presenting in patients post-bariatric surgery. With >80% of patients who underwent bariatric surgery between 2020 and 2024 being female, and the majority of patients being of childbearing age, it is fundamental to understand potential risks of this complication during pregnancy. PBH is diagnosed with confirmation of Whipple's triad, and usually presents 2-4 hours after the ingestion of food. Medical management of PBH is not recommended in pregnancy, thus effective treatment options need to be explored.
Case Series
We present six patients diagnosed with PBH during pregnancy. 4/6 patients had sleeve gastrectomy and 2/6 Roux-en-Y gastric bypass. Duration between bariatric surgery and pregnancy varied between 8 and 44 months. Multidisciplinary team approach was adopted for all patients, involving specialist dieticians,

obstetricians, diabetic midwives and diabetologists. Mainstay management was dietary modification. Continuous glucose monitoring was utilised in addition in 4/6 patients for early correction of hypoglycaemia. 4/6 cases had greatly improved symptoms with dietary modification alone, however 2/6 cases had persistent hypoglycaemic severity and frequency. All patients had successful neonate delivery, with no complications noted. Post pregnancy, one case continues to suffer with severe hypoglycaemia resulting in multiple hospitalisations, and after multiple failed attempts with medical management, is awaiting thoracic outlet reduction surgery.
Discussion
PBH is an increasing complication recognised in pregnancy. It holds significant risk to both foetus and mother, including small for gestational age, intrauterine growth restriction, reduced quality of life and increased risk of mortality. Management during pregnancy is dietary modification alone. No randomised controlled trials have been conducted on safety and efficacy of medical management in pregnancy and no national/international guidelines exist on management of PBH in pregnancy. Both are urgently needed given the increasing prevalence of this significant complication.

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CC8

Hook effect in a giant infiltrating macroprolactinoma: a diagnostic pitfall with therapeutic implications

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Background
Giant macroprolactinomas (>4 cm) are rare pituitary adenomas associated with markedly elevated prolactin levels, often exceeding 5300 mIU/l, and can extensively invade adjacent skull base structures. Unlike most skull base tumours requiring surgery or radiotherapy, prolactinomas usually respond dramatically to dopamine agonists such as cabergoline. Accurate preoperative identification is essential, as misdiagnosis may lead to unnecessary invasive treatment. The Hook effect, an immunoassay artefact, can falsely lower prolactin readings in the presence of very high serum concentrations, masking the true diagnosis.
Case Presentation
A 23-year-old man presented with bilateral proptosis and papilloedema, incidentally detected during an optometrist visit. He had no headache, diplopia, or visual field defect. MRI revealed a large skull base mass replacing the sphenoid bone and extending into the orbits, nasal cavity, and temporal fossae, encasing the optic nerves and internal carotid arteries. The initial serum prolactin level was 3873 mIU/l, suggesting a chordoma with mild stalk-effect hyperprolactinaemia. Trans-sphenoidal biopsy demonstrated a pituitary neuroendocrine tumour (PitNET) of Pit-1 lineage, showing strong prolactin expression with scanty growth hormone staining, consistent with a lactotroph adenoma; however, a mammosomatotroph or mixed somatotroph–lactotroph adenoma could not be excluded. On repeat prolactin testing after serial dilution (1:200), the true concentration exceeded 855,932 mIU/l, confirming a giant macroprolactinoma with a marked Hook effect. MEN1 genetic testing was negative. Treatment with cabergoline and lanreotide achieved normalisation of prolactin within nine months, with follow-up imaging showing marked tumour regression and improved proptosis.
Discussion
- This case illustrates an unusual presentation of a giant macroprolactinoma manifesting solely with proptosis.
- Recognising the Hook effect enables timely dopamine agonist therapy, avoiding unnecessary surgery.
- The tumour's size and extensive local invasion poses ongoing challenges in decision making for debulking surgery/radiotherapy, requiring ongoing multidisciplinary guidance and monitoring for CSF leakage while on medical therapy.

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CC9

Airway emergency from acute parathyroid adenoma haemorrhage: A case presentation

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Background
Spontaneous haemorrhage of a parathyroid adenoma or hyperplastic gland can cause retropharyngeal haematoma. This rare but potentially life-threatening condition may present with acute neck pain, dysphonia, dysphagia, and in severe cases, airway obstruction. Fewer than 50 cases have been reported, with only a minority progressing to airway compromise -8.8% required emergency intubation and 4.4% required a tracheotomy.
Case Presentation
We report a case of a 65-year-old female patient with end-stage renal disease and tertiary hyperparathyroidism. She presented with acute neck pain, hoarse voice, and dysphagia. Contrast-enhanced Computed Tomography (CT) demonstrated an ill-defined retropharyngeal hyperdensity with significant narrowing of the pharyngeal airway. Differential diagnoses included malignancy and atypical infection. She underwent pre-emptive intubation to secure the airway and proceeded to a surgical tracheostomy. Initial fine needle aspiration was non-diagnostic; open exploration with repeat biopsy identified an infarcted left retropharyngeal parathyroid gland. Histology confirmed a parathyroid adenoma with hyperplasia and organising haematoma, consistent with recent acute haemorrhage.
Discussion
Retropharyngeal haemorrhage from parathyroid adenoma or hyperplasia is rare but potentially life-threatening. This case highlights the need to consider acute haemorrhage as a differential for equivocal imaging in acute presentations. This is particularly relevant in patients with hyperparathyroidism, alongside commoner causes such as malignancy and infection. In suspected upper airway compromise of unknown cause, early ENT and anaesthetic input with airway assessment, plus prompt CT imaging help guide management and confirm diagnosis.
Conclusion
We describe a rare case of parathyroid adenoma and hyperplasia complicated by acute haemorrhage, presenting as a retropharyngeal mass with airway compromise. Recognition of this entity is critical for timely diagnosis and intervention.

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CC10

Thyroid nodule rupture – an uncommon complication following radiofrequency ablation

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Radiofrequency ablation (RFA) is an emerging minimally invasive treatment for benign thyroid nodules, offering effective volume reduction with an acceptable safety profile. However, the rare complication of nodule rupture can occur in up to 2.5%. We report a case of thyroid nodule rupture complicated by infection following RFA, highlighting clinical presentation, diagnostic approach, management, and outcomes. A 34-year-old woman with a history of a euthyroid multinodular goitre presented with progressive painless neck swelling 2 months after a second RFA procedure. She had previously undergone uncomplicated initial RFA 12 months prior, with 50% nodule size reduction. Ultrasound imaging revealed a thyroid nodule rupture through the thyroid capsule and infection along the percutaneous tract. Over days, the swelling increased, later exhibiting erythema, tenderness, and fluid drainage. The patient was managed conservatively with antibiotics, local wound care, and close clinical and radiological monitoring. Over subsequent months, clinical and radiological improvements were observed, with the reduction of swelling size, resolution of the tract, and no further infectious signs. The patient (a co-author on this abstract) was highly involved in her own care, carefully cataloguing changes in her neck (photos, descriptions) in conjunction with other patients worldwide who had experienced this complication; this collaborative approach helped the clinicians in their management. Overall, there was a reduction in the size of her nodule from over 6 cm (prior to second RFA) to 3.3 cm (8 months following second RFA). Although RFA is generally safe, clinicians must remain conscious about rare but potentially serious complications such as nodule rupture and infection. Early recognition and tailoring of management strategies, ranging from conservative therapy to surgical intervention, are crucial. The patient's favourable outcome with conservative management reinforces the role of close follow-up and shared decision-making.

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Poster Presentations

Adrenal and Cardiovascular

P1

Physiological dose tapering promotes hypothalamic-pituitary-adrenal axis recovery in glucocorticoid-induced adrenal insufficiency

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Background
Glucocorticoid (GC) discontinuation is hindered by risk of GC-induced adrenal insufficiency (GC-AI). Guidelines discourage tapering below physiological doses (prednisolone 3-6 mg) when morning cortisol is $\leq$300 nmol/l, with values $<$150 nmol/l thought to indicate low likelihood of hypothalamic-pituitary-adrenal (HPA) axis recovery, though this assumes no axis suppression from such doses. We aim to evaluate how HPA axis function evolves during physiological dose tapering and assess whether current cortisol thresholds restrict successful discontinuation.
Methods
This retrospective cohort study evaluated 65 adults with long-term GC use for inflammatory disease undergoing prednisolone tapering at our tertiary endocrine centre between 2019 and 2024. Linear mixed-effects modelling was used to assess serial short Synacthen tests ($n = 52$) on reducing prednisolone doses ($\leq$5 mg).
Results
Mean age at referral was 55.4$\pm$16.4 years, with median prednisolone dose and duration of therapy being 5 [3.5-5] mg and 23 [6.5-66.5] months, respectively. For each 1 mg dose reduction, morning and post-Synacthen cortisol rose by 48.8 nmol/l and 57.5 nmol/l (both $P < 0.001$), respectively, with reductions $>$2 mg producing larger cortisol increases than 1 mg reductions (both $P < 0.05$). Among completed taper attempts ($n = 47$), 81% ($n = 38$) successfully weaned. Sixteen patients with a nadir morning cortisol $<$150 nmol/l while on a prednisolone dose $\leq$5 mg, including six with undetectable ($<$28 nmol/l) values, safely and successfully discontinued prednisolone. No adrenal crises occurred. All three patients who failed to wean due to insufficient HPA axis recovery had adequate 8-hour prednisolone replacement levels on 2 mg, suggesting this dose constituted full physiological replacement.
Conclusion
HPA axis function in GC-AI improves with dose reduction, even at physiological doses, and structured, symptom-led tapering is safe and effective. Pharmacokinetic variability may explain why some experience persistent axis suppression. Future guidelines should consider the suppressive effects of physiological doses, with HPA axis recovery following, rather than preceding, successful weaning.

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P2

Bridging the safety gap: implementing electronic health record alerts for patients with adrenal insufficiency

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Introduction
Adrenal insufficiency requires timely emergency treatment during adrenal crises. Previously, a robust information-sharing system with local ambulance services ensured that paramedics were aware of patients at risk of adrenal crisis, but this was withdrawn, creating a safety gap. We developed mechanisms including new electronic patient record (EPR) adrenal insufficiency alerts to address this safety concern. We also retrospectively reviewed the care of all patients with adrenal insufficiency under our care against the recently published NICE NG243 guidelines.
Method
We analysed EPRs of all patients with adrenal insufficiency managed between April 2023 and March 2025. Patient records and laboratory results were reviewed for retrospective compliance with NICE recommendations.
Results
From the documentation of our 180 patients with adrenal insufficiency, 94% had been counselled on sick-day rules, 91% given parenteral hydrocortisone education, 91% had renal function checked, 86% had blood pressure measured. New electronic adrenal insufficiency EPR alerts were introduced for all patients.
Conclusion
Most patients were managed in line with NICE guidance. Our Trust previously had a robust information sharing arrangement with our local ambulance services for patients with adrenal insufficiency as a crucial safety net for emergency pre-hospital parenteral steroid administration. Following the withdrawal of these alerts by the ambulance services we felt the need to introduce other reliable safety measures. We developed and implemented a specific 'Adrenal Insufficiency' alert in our Careflow® EPR system, referencing Trust guidelines for adrenal insufficiency emergency management. We also developed a GP template letter with all relevant information for primary care from the NICE NG243 guidelines, which requests GPs to insert an adrenal insufficiency alert in the Summary Care Record, making it visible to paramedic teams. These measures go beyond NICE guidance, which does not explicitly mandate electronic alerts, but they align with its intention of making the diagnosis visible across care settings.

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P3

Steroids, suppression, and specialist care: lessons from a severe asthma cohort

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Introduction
Adrenal insufficiency (AI) is a recognised complication of prolonged corticosteroid use in severe asthma, where multi-route exposure is common. Although guidelines recommend precautions for high-dose inhaled corticosteroid (ICS) use, it's unclear if ICS dose alone predicts AI. This study examined patients to assess the role of cumulative steroid exposure and evaluate the predictive value of ICS dose for adrenal suppression
Method
A retrospective review was conducted on patients seen at a Severe Asthma Clinic (March 2023–March 2024). Data included demographics, inhalers, cortisol levels, BMI and HbA1c. Possible AI was defined as morning cortisol $<$133nmol/l or afternoon $<$100nmol/l.
Results
156 patients (63% female, mean age 52$\pm$16.5 years, 88% Caucasian) were reviewed. Comorbidities included diabetes (11) and hypertension (21). 51 patients had low random cortisol levels, indicating possible AI, while 105 patients showed no AI.

Table 1. Comparison of clinical characteristics of AI and non-AI group

	Possible-AI ($n = 51$)	Non-AI ($n = 105$)	*P*-value
Mean BMI	31 $\pm$ 6.8	29 $\pm$ 6.6	0.14
Mean HbA1c (mmol/mol)	39 $\pm$ 11.2	36 $\pm$ 6.9	0.19
Mean Eosinophils (10^9/l)	0.84 $\pm$ 0.91	0.63 $\pm$ 0.53	0.13
High Dose ICS Exposure (2000 mg/day)	78%	73%	
Patients on Maintenance OCS (n)	24 (47.0%)	8 (7.6%)	–
Patients on Nasal Steroid (n)	16 (31.0%)	24 (22.8%)	–
Mean Nasal Steroid Exposure (mg)	13.82+/- 3.29 mg	8.96 +/- 1.58 mg4	0.813
Acute Prednisolone Courses per year	4.8 $\pm$ 3.3	3.2 $\pm$ 2.8	0.0089

Conclusion
Similar rates of high-dose ICS use across both groups suggest that ICS dose alone may not reliably predict possible adrenal suppression. In contrast, greater systemic/cumulative steroid exposure, including nasal steroids and indicators of more complex disease were more strongly associated with possible AI. Increased steroid burden also correlated with higher mean BMI and HbA1c. These findings support the need for broader risk assessment strategies beyond ICS dosing and underscore the value of multidisciplinary evaluation.

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P4

Adrenal suppression after local steroid injection in a patient on cobicistat-based antiretroviral therapy

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Potent drug–drug interactions between corticosteroids and pharmacokinetic boosters used in antiretroviral therapy (ART) are well recognised but often overlooked. Cobicistat, a strong CYP3A4 inhibitor, markedly reduces steroid

clearance, predisposing to iatrogenic Cushing's syndrome and adrenal suppression even after a single local injection.
Case Presentation
A 44-year-old woman with HIV, diagnosed in 2012 and on ART since 2015, had sequential regimen changes due to intolerance and resistance. In 2021 she was switched to Symtuza® (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) plus dolutegravir. She experienced chronic gastrointestinal side effects on multiple regimens. The hand pain team consulted about corticosteroid injection for musculoskeletal symptoms. Potential risks of adrenal suppression with concomitant cobicistat therapy were highlighted; however, the patient proceeded with injection. Subsequently, she developed symptomatic adrenal insufficiency. A short Synacthen test confirmed inadequate adrenal reserve, necessitating endocrine referral and hydrocortisone replacement.
Discussion
This case emphasises the significant clinical impact of cobicistat–steroid interactions. Local corticosteroid administration can result in prolonged systemic steroid exposure in patients on boosted ART, leading to adrenal suppression and crisis risk. Management requires endocrine involvement, hydrocortisone replacement, and patient education regarding stress dosing. Preventive measures include avoidance of CYP3A4-metabolised corticosteroids and consideration of safer alternatives, such as beclometasone.
Conclusion
Cross-specialty awareness of ART–steroid interactions is essential. Proactive communication between HIV, endocrine, and other specialist teams can prevent iatrogenic harm in this vulnerable population.

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P5

Audit of FH identification and management in a UK lipid clinic: are we meeting NICE standards CG71 and TA393?

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Familial Hypercholesterolemia (FH) is an autosomal dominant genetic disorder characterised by elevated LDL-C, with a UK prevalence of 1 in 250–500. It significantly increases the risk of myocardial infarction, stroke, and early cardiovascular disease (CVD). This audit evaluated whether FH identification and PCSK9 inhibitor (PCSK9i) prescribing at the lipid clinic align with NICE guidelines CG71 and TA393. A retrospective review of electronic medical records of patients attending lipid clinic was conducted, and it was found that 201 patients with 96 genetically confirmed and 105 clinically possible FH. Among the patients with suspected FH, 96% had documented Simon Broome or DLCN criteria in the electronic medical record. The 8 patients (4%) who didn't have it mainly were referred from different hospitals with confirmed FH genetic testing reports. Genetic testing was offered to 99% of eligible patients, aligning closely with the 100% standard. Therapeutically, 91% (20/22) of those prescribed PCSK9i met NICE eligibility criteria. One patient was incorrectly prescribed based on secondary prevention targets, and another had a clinical decision due to a strong family history of premature CVD. The overall mean LDL-C reduction was 45%, and 51% achieved a $\geq$ 50% LDL-C reduction from baseline. The audit shows strong adherence to diagnostic documentation and genetic testing, reinforcing good clinical practices. However, PCSK9i prescribing fell slightly short, highlighting the importance of compliance due to the high cost (£4,383 per patient annually) and the need for cost-effective prescribing. While the hospital covers around 1.5 million population, an estimated 3,000–6,000 individuals may have FH, underscoring the need for enhanced community screening and genetic testing availability at national level. Key recommendations include improving documentation, ensuring stringent PCSK9i prescribing in line with NICE criteria, optimizing referral pathways, and re-auditing within 12 months.

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P6

Evaluation of Evening Salivary Cortisone vs 48-hour Low Dose Dexamethasone Suppression Test in the Investigation of Cushing's Syndrome

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Introduction
Cortisol secretion follows a circadian rhythm, and loss of this diurnal variation with sustained hypercortisolaemia is strongly suggestive of Cushing's syndrome. While serum cortisol day curves are informative, they are impractical for routine clinical use. Salivary cortisone, a stable and non-invasive biomarker reflecting circulating free cortisol, may offer a convenient and patient-friendly alternative for assessing cortisol dynamics outside hospital settings. This study evaluated the diagnostic performance of salivary cortisone in patients investigated for suspected Cushing's syndrome.
Aim
To compare the diagnostic accuracy of evening salivary cortisone with results from the Low-Dose Dexamethasone Suppression Test (LDDST) in patients with Cushing's syndrome or mild autonomous cortisol secretion (MACS).
Methods
Patients attending a tertiary endocrine centre with confirmed or suspected Cushing's syndrome or MACS were included. Late-night salivary cortisone samples (9 pm–midnight) were analysed using tandem mass spectrometry and compared with 48-hour serum cortisol results following LDDST. Receiver operating characteristic (ROC) analyses assessed diagnostic accuracy and identified optimal salivary cortisone thresholds for hypercortisolism.
Results
The cohort included four patients with pituitary Cushing's, four with adrenal Cushing's, eleven with MACS, and thirteen without biochemical evidence of hypercortisolism. For Cushing's syndrome, the area under the ROC curve (AUC) was 0.974 $\pm$ 0.041 (95% CI 0.894–1.000; $P < 0.001$), indicating excellent diagnostic accuracy. The optimal late-night salivary cortisone threshold was 17.4 nmol/l (sensitivity = 0.875, specificity = 0.958, Youden's J = 0.833). For MACS, a threshold of 7.0 nmol/l yielded an AUC = 0.983 $\pm$ 0.029 (95% CI 0.925–1.000; $P < 0.001$), with sensitivity = 0.933, specificity = 0.917, and Youden's J = 0.850. Salivary cortisone correlated strongly with post-LDDST serum cortisol ($r = 0.86$, $P < 0.001$).
Conclusion
Evening salivary cortisone demonstrates excellent diagnostic accuracy and may provide a practical, reliable alternative to the LDDST for evaluating hypercortisolism.

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P7

Adrenal adenomata displaying mild autonomous cortisol secretion:a service evaluation of cardiometabolic profile routinely screened patients

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Introduction
The increasing use of high-resolution imaging has led to rising detection of adrenal incidentalomas (AIs), with a proportion of these exhibiting autonomous cortisol secretion, now termed Mild Autonomous Cortisol Secretion (MACS), is defined biochemically by a post-1 mg overnight dexamethasone suppression test(ONDST) cortisol between 51 and 137nmol/l with some variation in relation to assay platforms. Our primary objective was to identify the group of individuals with adrenal adenomata and associated MACS, and comprehensively to characterize their cardiometabolic profile
Methods
We undertook service evaluation of the cardiometabolic profile of adrenal adenomata presenting over a period of 3-years at a single centre. All subsequently

evaluated had a 0900 post-midnight dexamethasone of >50 nmol/l which was deemed a 'fail' on basis of ONDST serum cortisol level on our assay. A subcategorization into MACS1 (ONDST cortisol of 50-137nmol/l) and MACS2 (ONDST cortisol of >1387nmol/l was created to take account of those individuals with ONDST cortisol of >137nmol/l and no diagnosis of Cushing's syndrome. on subsequent evaluation.

Results

The diagnosis of MACS1 was associated with a higher diagnosis rate of cardiovascular disease (CVD) (17.7% in MACS 1) vs non-MACS = non-functioning adenoma (NFA) (3.7%)($P = 0.009$) and higher rates of prescription of lipid lowering agents (51.6%) vs (29.6%) ($P = 0.01$). ONDST cortisol levels in MACS1 patients correlated with a more adverse lipid profile (for higher LDL-cholesterol r2 = 0.404, $P = 0.007$; HDL-cholesterol r2 = -0.346, $P = 0.023$ for; for higher serum triglycerides r2 = 0.282, $P = 0.02$) in spite of higher rates of statin prescribing. Dunn's post hoc analysis indicated an overall more adverse lipid profile in MACS1.

Conclusion

The positive direction of association observed between serum cortisol and lipid measures, highlights that MACS carries a metabolically adverse lipid profile. The question remains as to whether a specific directed treatment of MACS should be offered over and above risk factor mitigating management.

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P8

Once-Daily Low-Dose Prednisolone Improves Cardiometabolic Profiles in Adrenal Insufficiency Versus Multiple-Daily Dose Hydrocortisone in a Double-Blind Randomised Crossover Trial

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Background

Once-daily low-dose prednisolone and multiple-daily dose hydrocortisone are options for management of adrenal insufficiency (AI). This is the first double-blind trial comparing these two treatments.

Methods

This is a double-blind randomised crossover study. Patients with AI received 4 months of low-dose prednisolone (2-4 mg) with matching placebo at noon and in the afternoon, or 4 months of standard-regimen hydrocortisone (10 / 5 / 2.5 mg) in the first study period. They were then crossed over to the alternative medication for the second study period. Anthropometrics, biochemical data for cardiometabolic and bone health, and subjective health survey data were collected at Day 1, 30 and 120 of each study period.

Results

There was a significant reduction in body weight at 4 months, with a treatment difference of -1.87 Kg ($P = 0.002$) favouring prednisolone treatment. Waist circumference and HbA1c reduced by -2.26 cm ($P = 0.010$) and -1.23 mmol/mol ($P = 0.001$) on prednisolone. Short-term and medium-term bone formation markers were suppressed on prednisolone with a treatment difference of -1.22 µg/l ($P = 0.035$) in osteocalcin and -13.8 ng/l ($P < 0.001$) in Procollagen 1 N-Terminal Propeptide. Urinary N-telopeptide levels, a resorption marker was also suppressed by -9.34 nmol/mmol ($P = 0.002$), associated with prednisolone. Other cardiovascular markers such as blood pressure, high-sensitivity troponin and CRP, did not show significant differences between prednisolone and hydrocortisone. Data from SF-36 survey and Addi-QoL questionnaire demonstrated that subjective health outcomes were unaffected by either medication.

Discussion

Once-daily low-dose prednisolone causes weight loss and HbA1c improvement, without compromising wellbeing. This may be because hydrocortisone is associated with uncoupling from the normal physiological profile of cortisol, or multiple-daily doses causing increased steroid exposure.

Conclusion

This study supports the routine use of low dose prednisolone. Further studies should be completed using low-dose prednisolone, focussing on longer term outcomes such as bone-mineral density and real-world mortality.

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P9

Development of an LC-MS/MS assay for the measurement of urinary aldosterone and related metabolites to screen for primary aldosteronism

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Introduction

Primary Aldosteronism (PA) is the most common cause of secondary hypertension and is associated with increased risk of morbidity and mortality when compared to primary hypertension. We have developed a LC-MS/MS method for the measurement of aldosterone and related metabolites in early morning urine samples, to provide an alterative screening test for PA. This aims to streamline identification and subtyping of PA, particularly in patients with KCNJ5 mutations.

Method

Analysis of 18-hydroxycortisol, 18-oxocortisol, aldosterone, cortisol, 18-hydroxycortisosterone and tetrahydroaldosterone was performed in a single LC-MS/MS method on a Waters TQ-Absolute mass spectrometer. Steroids were deconjugated and extracted from early morning urine samples in a 96-well format. We assessed various deconjugation and extraction procedures.

Results

Liquid-liquid extraction (LLE) with ethyl acetate following an overnight enzyme deconjugation with aryl sulfatase/glucuronidase showed optimal recovery. The method demonstrated good recovery and minimal matrix effects.

Conclusion

We have developed an LC-MS/MS assay to measure aldosterone and related metabolites in early morning urine samples. This has clinical applications at providing an at-home screening test for PA, which could allow for early identification of PA subtypes. We hope to develop our in-house method further and aim to implement this approach in the future for the diagnostic work up of PA patients.

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P10

Salivary Steroids: profiling, quantification and validation using liquid chromatography triple quadrupole mass spectrometry

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Steroids play key roles in numerous biological processes, including blood pressure regulation, glucose metabolism, stress response, muscle development, and reproduction. Accurate, precise quantification in biological fluids is achieved using mass spectrometry. To date, most research has focused on serum or plasma requiring invasive sampling or on 24-hour urine, which is an inconvenient matrix to collect. Saliva provides a simple, non-invasive alternative, however current applications have been limited to single analytes or small steroid panels for targeted clinical use, such as diagnosing Cushing's syndrome. The broader salivary steroid profile remains less characterised, and its utility as a biofluid for steroid research is not well established. We therefore aimed to firstly comprehensively investigate the salivary steroid profile and secondly to develop a single liquid chromatography–triple quadrupole mass spectrometry (LC-MS/MS) method for their quantification. Using a top-down approach, saliva from six healthy volunteers (three males, three females) was screened across multiple LC-MS/MS and gas chromatography–mass spectrometry (GC–MS) assays for 68 candidate steroids. Of these, 44 were detectable, spanning androgens, 11-oxygenated androgens, glucocorticoids, mineralocorticoids, precursor steroids, and compounds usually observed in urine (e.g., THE, 20α/βDHE). A single LC-MS/MS extraction and analysis method for these steroids was then developed and validated according to EMA bioanalytical guidelines (2023). Its applicability was demonstrated in a cohort of healthy participants. These findings highlight saliva's potential as a practical, non-invasive bio-fluid with an extensive steroid profile. Future work will compare salivary, plasma, and urinary profiles, supporting saliva's use as a primary biofluid for endocrine research.

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P11

Long term medical control of ARMC5 related bilateral primary macronodular adrenal hyperplasia (BPMAH) with low-dose metyrapone

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Bilateral Primary Macro nodular Adrenal Hyperplasia (BPMAH) is a rare cause of endogenous Cushing's syndrome. The association with ARMC5 gene mutation was first described in 2013 and one recent series demonstrated 14% of BPMAH cases show germ-line pathological mutations in ARMC5 gene. The clinical phenotype of this condition is not fully described. There is a known association with meningioma.

Case 1

A 45-year-old woman with hypertension and diabetes was incidentally found to have bilateral adrenal masses on CT angiogram. Biochemistry showed Cushing's (post-overnight dexamethasone cortisol 687 nmol/l; 48-hour 575 nmol/l) with suppressed ACTH. Low-dose metyrapone 250 mg tds, later 500 mg bd, achieved mean cortisol 187 nmol/l, weight loss and diabetes remission. Germ-line testing revealed ARMC5 mutation (p.Y549*). Long-term therapy continues. A brain MRI showed a petrous ridge meningioma which is managed conservatively.

Case 2

A 53-year-old woman with type 2 diabetes, poorly controlled hypertension and osteoporosis had bilateral adrenal masses discovered during tuberculosis therapy. Biopsy confirmed cortical hyperplasia. Cushing's was demonstrated (9 am cortisol 500 nmol/l; post-1 mg dexamethasone 449 nmol/l; post-8 mg 607 nmol/l) with suppressed ACTH. Despite prior reported intolerance, low-dose metyrapone 250 mg tds produced excellent biochemical and clinical control, obviating adrenalectomy. Germline ARMC5 mutation (p.S458X) was confirmed; her brother had adrenal Cushing's. Brain CT was normal; MRI is pending.

Discussion

These two cases of BPMAH due to ARMC5 mutation show effective long term medical control with relatively low dose metyrapone. These cases suggest this form of BPMAH might be particularly responsive to metyrapone, avoiding the need for unilateral or bilateral adrenalectomy. The cases are also a reminder to assess for meningioma in patients with the ARMC5 mutation.

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P12

Validation of LC-MS–based post-saline infusion test aldosterone thresholds for the diagnosis of primary aldosteronism

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Background

Primary aldosteronism (PA), the most common cause of secondary hypertension, often goes under-diagnosed due to limitations in current screening and confirmatory tests. With laboratories shifting to liquid chromatography–mass spectrometry (LC-MS) over immunoassays for measuring aldosterone, the improved accuracy has initiated a re-evaluation of diagnostic criteria, particularly regarding the saline infusion test (SIT). Despite the shift, LC-MS-specific cut-offs have not been sufficiently defined. This study aimed to establish and validate LC-MS-derived SIT thresholds to enhance diagnostic accuracy for PA.

Methods

This was a retrospective study, analysing patients investigated for PA between January 2019 and March 2025. Patients completed SIT, captopril challenge test (CCT), and/or adrenal vein sampling (AVS). Receiver operating characteristic (ROC) curve analysis was used to identify the optimal SIT cut-off, with PA diagnosis established by AVS and/or CCT.

Results

Of the 46 patients initially screened, 41 completed the SIT and were included in the analysis. PA was confirmed in 36 patients, while 5 were excluded based on negative confirmatory testing with CCT or AVS. Mean age was 49.6 $\pm$ 9.6 years, with 58.5% male and 41.5% female. Average BMI was 31.6 $\pm$ 7.7 kg/m^2. Relevant comorbidities included cardiac disease (7.3%), stroke (2.4%), diabetes (14.6%), and chronic kidney disease (CKD; 12.2%). Post-SIT aldosterone measured by LC-MS showed excellent diagnostic performance, with an area under the curve of 0.978. The optimal diagnostic threshold was 165 pmol/l (Youden Index), yielding 91.2% sensitivity and 100% sensitivity (PPV = 100%; NPV = 57%). Interestingly, all patients with CKD ($n = 5$) were diagnosed with PA.

Conclusion

A post-SIT plasma aldosterone threshold of 165 pmol/l, measured via LC-MS, demonstrated strong diagnostic performance for PA and has practical relevance for clinical application.

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P13

Streamlining the management of adrenal incidentalomas: a retrospective audit and service improvement initiative

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Background

With the rising number of imaging investigations, incidental discovery of adrenal adenomas is becoming increasingly common. Strict adherence to the European Society of Endocrinology (ESE) guidelines for investigating these lesions poses logistical challenges, particularly in already overburdened endocrine clinics.

Objective

We developed a two-step strategy to address this issue. This abstract presents step one: a retrospective review of current practice to understand the nature and management of adrenal incidentalomas. The second step—implementation of a one-stop, nurse-led clinic supported by a multidisciplinary team (MDT)—is ongoing.

Methods and Results

We audited 150 patients over two years. Most lesions (86%) were unilateral; 80% were benign and non-functioning. Malignancy was identified in four patients, and 15 had functioning adenomas, out of these 14% measured < 2 cms. 5 underwent surgery and 6 patients died. ESE guidelines were generally followed; however, inconsistencies were noted in the evaluation of bilateral lesions. The number of clinic appointments varied widely (1–20), highlighting a lack of uniformity in clinical practice.

Conclusion

Our findings align with ESE, confirming that the majority of adrenal incidentalomas are benign and non-functioning. While adherence to guidelines was largely observed, variability in follow-up and appointment frequency revealed inefficiencies. In response, we have standardized care by educating healthcare professionals and launching a one-stop, nurse-led clinic followed by MDT review. A follow-up audit is planned to assess improvements in clinic capacity and cost-effectiveness.

Reference

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P14

"From collapse to control: pyridostigmine for postural hypotension in abiraterone-related adrenal insufficiency"

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Background

Abiraterone, a CYP17A1 inhibitor for metastatic prostate cancer, suppresses adrenal cortisol and androgen synthesis. Adrenal insufficiency may occur despite steroid supplementation, presenting with fatigue, dizziness, hypotension, particularly in those with pre-existing autonomic dysfunction.

Case

A 54-year-old man with metastatic prostate cancer, chronic postural hypotension and depression presented with generalized pain, dizziness and breathlessness three weeks after initiating Abiraterone with Prednisolone. Profound postural hypotension persisted despite Abiraterone discontinuation. Short Synacthen test off Prednisolone confirmed adrenal insufficiency (cortisol <28 nmol/l). Prednisolone was restarted and Fludrocortisone commenced, but despite dose escalation (Fludrocortisone 300 µg/day) and addition of Midodrine (10 mg three times a day) systolic blood pressure dropped >40 mmHg on standing. Ivabradine 5 mg BD was added to control symptomatic tachycardia. Historical asthma diagnosis was challenged and excluded following pulmonary function testing. Pyridostigmine was introduced, reducing postural drop and dramatically improving function, allowing the patient to tolerate 90 minutes sitting upright and walk indoors with a frame.

Blood Pressure Response Table:

Timepoint	Supine BP (mmHg)	Standing BP (mmHg)	Δ Systolic (mmHg)
Pre-Pyridostigmine	158/71	107/49	51
Post-Pyridostigmine	154/70	145/66	9

Discussion
Abiraterone may precipitate clinically significant adrenal insufficiency despite glucocorticoid supplementation, aggravating pre-existing autonomic dysfunction. Recognition is essential as conventional therapy with Fludrocortisone and Midodrine may be inadequate. Pyridostigmine, an acetylcholinesterase inhibitor that enhances ganglionic transmission without worsening supine hypertension, proved highly effective in this refractory case. This highlights the importance of considering adrenal insufficiency in Abiraterone-treated patients and suggests a potential adjunctive role for Pyridostigmine in severe postural hypotension unresponsive to standard measures. To our knowledge, no prior reports describe pyridostigmine for adrenal-insufficiency-related postural hypotension, making this a novel demonstration of its therapeutic potential.
Conclusion
Clinicians should recognise Abiraterone-induced adrenal insufficiency causing refractory postural hypotension. Pyridostigmine can achieve functional recovery when conventional therapy is insufficient, representing a novel adjunctive approach.

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P15

Beyond the 50 nmol/l cut-off: improving 1 mg-overnight dexamethasone suppression test accuracy with assay-specific thresholds

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Background
The 1 mg-overnight dexamethasone suppression test (1 mg-DST) is widely used to screen for autonomous cortisol secretion. Despite its simplicity, non-compliance and suboptimal dexamethasone exposure can affect its accuracy. Moreover, there is limited evidence on how different serum cortisol assays impact the commonly used 50 nmol/l cut-off.
Methods
All 1 mg-DST with immunoassay (IA; Abbott Alinity) serum cortisol >50 nmol/l measured at UHB NHS Foundation Trust between October 2018 and February 2025 had corresponding cortisol and dexamethasone levels assessed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). A dexamethasone cut-off ≥ 3.3 nmol/l defined adequate exposure. Linear regression, logistic regression, and Bland–Altman analyses compared IA and LC-MS/MS results.
Results
We analysed 521 1 mg-DST results from 437 patients; 46 (8.8%) had undetectable dexamethasone levels, suggesting non-compliance, and 45 (8.6%) had suboptimal levels. IA and LC-MS/MS cortisol measurements showed good agreement (R^2 0.867; $P < 0.001$), but IA had a mean bias of -10.4 nmol/l. Cortisol correlated negatively with dexamethasone levels (R^2 0.014; p 0.009), while dexamethasone correlated positively with age (R^2 0.027; $P < 0.001$) and negatively with estimated glomerular filtration rate (R^2 0.01; p 0.033). Multivariable logistic regression identified strong CYP3A4 inducer use as the only predictor of false-positive 1 mg-DST results (odds ratio 25.6, 95% confidence interval 9.3-77.6).
Conclusions
Routine dexamethasone measurement in abnormal 1 mg-DSTs identified a 17.4% false-positive rate. Careful drug history to exclude CYP3A4 inducers improves test accuracy. Despite good IA / LC-MS/MS agreement, IA shows negative bias; we propose a 40 nmol/l cut-off for IA Abbott Alinity to better detect autonomous cortisol secretion.

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P16

Failed surgery, failed theranostic, failing-functioning: any more evidenced-based therapeutic options in a 67year old man with multicentric locally aggressive familial sdhbparaganglioma

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SDHB mutations are associated with one of the most aggressive familial pheochromocytoma–paraganglioma syndromes (FPPS), characterized by a marked tendency for metastasis and poor prognosis. Emerging literature emphasizes that management strategies should be guided by molecular clusters of tumorigenesis, which define clinical, biochemical, radiological, and therapeutic behavior. We present the case of a 67-year-old man who initially reported long-standing, non-specific abdominal pain without red flag symptoms. With progressive worsening over several months, his general practitioner arranged an abdominal ultrasonography, which revealed multiple intra-abdominal masses involving both kidneys and the right para-aortic region. Subsequent PET-CT demonstrated moderate avidity in the right adrenal and left cervical regions. Biopsies confirmed a paraganglioma in the neck mass and bilateral renal oncocytomas. Plasma metanephrines were within normal limits. Genetic testing identified a heterozygous SDHB mutation. An attempted radical adrenalectomy was unsuccessful due to complex vascular anatomy, rendering the tumor inoperable. The patient subsequently received three sessions of 131I-MIBG therapy at a tertiary center, achieving borderline radiologic response without significant clinical improvement. He was later lost to follow-up and re-presented with worsening pain and functional decline. Repeat imaging demonstrated progressive disease with vascular invasion. Further MIBG therapy was recommended at the neuroendocrine tumor multidisciplinary team (NET MDT) meeting. However, as his main priority was pain relief and quality of life—and given the absence of meaningful clinical response to prior MIBG therapy—the appropriateness of this option was questioned, particularly in the context of his declining functional status. This case highlights the therapeutic challenges of managing locally aggressive, multicentric SDHB-related paragangliomas, particularly when first- and second-line therapies fail and functional status deteriorates. Although poor performance status can limit treatment options, evidence-based alternatives remain available that may reduce morbidity and improve quality of life.

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P17

Prolonged surgery and complex perioperative management in a patient with a large cerebellopontine angle paraganglioma

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Cerebellopontine angle (CPA) masses are relatively common; however, paragangliomas in this region are rare. Most reported CPA paragangliomas are diagnosed postoperatively, often non-secretory and identified only on histology. Vascular, secretory CPA paragangliomas are even rarer and pose significant surgical and anaesthetic challenges due to their location, vascularity, and hormonal activity. We report a case of a large, vascular, secretory right CPA paraganglioma managed with two-stage surgical approach in a 60-year-old retired engineer. He presented with worsening headaches following six months of hearing loss, voice changes, and gait unsteadiness. Imaging revealed a tumour likely originating from the right petrous bone. Plasma normetanephrine was markedly elevated at 18,500 pmol/l (normal <1180) and 3-methoxytyramine (3-MT) at 297 pmol/l (normal <180), confirming a secretory tumour. Preoperative alpha- and beta-blockade were optimised. A multidisciplinary team planned a two-stage intervention. On Day 1, the patient underwent 11 hours of interventional radiology embolisation and surgical exploration. On Day 2, a 10-hour definitive surgical debulking was performed. Both procedures were under general anaesthesia (rocuronium, propofol, alfentanil, remifentanil). Intraoperative haemodynamic management was complex, requiring sodium nitroprusside, nicardipine, magnesium sulphate, and clonidine to maintain mean arterial pressure between 70–86 mmHg and heart rate between 50–80 bpm. Blood

pressure and heart rate surges were proactively controlled. Postoperatively, rebound hypertension due to residual tumour was managed with gradual reintroduction of oral antihypertensives. Complications included mild hyponatraemia, transient ileus, and a pseudomeningocele treated with lumbar drainage. The patient was discharged on Day 20 on reduced antihypertensive therapy. Plasma normetanephrine three weeks post-surgery was 5090 pmol/l with negative 3-MT. This case highlights the perioperative complexity of secretory CPA paragangliomas and underscores the importance of tailored haemodynamic management and multidisciplinary care. It adds to the limited literature on these rare tumours and illustrates challenges from their vascularity and catecholamine secretion.

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P18

A retrospective evaluation of desmopressin prescribing for the management of AVP-D and AVP-R

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Introduction
Desmopressin is a synthetic analogue of anti-diuretic hormone (ADH) used in the management of arginine vasopressin deficiency (AVP-D) and arginine vasopressin resistance (AVP-R). Omission or delay of desmopressin in patients with AVP-D can result in life-threatening dehydration and hypernatremia, as highlighted in the 2016 NHS England Patient Safety Alert.
Objectives
To evaluate prescribing and monitoring practices for patients with AVP-D and AVP-R at a district general hospital in North West London.
Methods
This was a retrospective evaluation of all adult inpatients ($\geq$18 years) prescribed desmopressin for AVP-D or AVP-R between January and November 2024 across all LNWUH sites. Data were collected from Cerner electronic health records and analysed in Microsoft Excel. The following practices were evaluated: prevalence of daily fluid balance monitoring, daily sodium measurement daily weight measurement, and timely administration of desmopressin without omission [3].
Results
Eighteen patients met the inclusion criteria. Seventeen patients were established on desmopressin prior to admission; one was newly initiated. 65% ($n = 11$) of patients previously on desmopressin were prescribed on admission. Fluid balances were recorded daily in 22% ($n = 4$) of patients. Sodium levels were checked daily in 28% ($n = 5$) patients. At least one delayed dose was observed in 56% ($n = 10$) patients, and one or more omitted dose was observed in 44% ($n = 18$) patients.
Conclusion
This audit highlights significant gaps in desmopressin prescribing and monitoring. Despite 24-hour stock availability the criticality of desmopressin has potentially not been realised as demonstrated by the dose omissions in this evaluation. Lack of awareness of AVP disorders as life-threatening conditions may contribute to inadequate prioritisation. Key recommendations include improving multidisciplinary and patient awareness, reinforcing out-of-hours access processes, and ensuring desmopressin is available in high-use areas.

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P19

The Diagnostic puzzle of adrenal schwannomas- a rare case presentation

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Introduction
Adrenal schwannomas are benign tumours originating from schwann cells within the adrenal gland. They are extremely rare, representing only 0.2-0.5% of all adrenal tumours. Fewer than 50 cases have been reported in the literature to date
Case report
We present the case of a 45-year-old woman with the first histologically confirmed adrenal schwannoma from our endocrine unit. She initially presented with elevated liver enzymes on routine blood tests, and she had noticed unintentional weight loss and palpitations alongside a growing pressure on the right side of her ribs over the past 18 months. Abdominal ultrasonography revealed a large solid mass in her right upper quadrant and a subsequent CT scan showed a 76mm well defined heterogenous right suprarenal mass. Serum biochemistry tests including renin-aldosterone, cortisol and dehydroepiandrosterone were all normal. Urinary metanephrines and steroid profiling were also normal. A FDG-PET scan was then done which showed a FDG avid right adrenal mass with no active distant disease. At this point our MDT favoured a non-functioning phaeochromocytoma however her MIBG scan revealed the mass to be non-tracer avid. She later underwent a successful right adrenalectomy with no postoperative complications. Immunohistochemistry demonstrated strong positivity for S100 and was negative for SMA, CD34, desmin, STAT-6 and myogenin confirming a diagnosis of adrenal schwannoma. Her post operative CT scan showed no evidence of recurrence.
Conclusion
This case underscores the diagnostic difficulties of adrenal schwannomas due to limited collective experience to draw upon and its resemblance with other adrenal masses. Patients are often asymptomatic with vague symptoms allowing the tumour to reach considerable size before diagnosis. Currently, formal diagnosis relies solely on surgical excision and histological examination to distinguish it from other, more common adrenal tumours. Our case reports adds valuable insight to the limited literature on the diagnostic challenges of this elusive tumour.

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P20

Adrenal Venous Sampling at King's College Hospital, London - an audit of the current practice

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Introduction
Primary Aldosteronism (PA) is a leading cause of secondary hypertension. Adrenal venous sampling (AVS) remains the gold standard for differentiating unilateral from bilateral disease. However, AVS is technically challenging, with variable success rates. Our current recommendation is for all surgical candidates to undergo AVS. This audit aimed to evaluate technical success and post-adrenalectomy outcomes for patients undergoing AVS.
Methods
We conducted a retrospective audit of AVS procedures performed at King's College Hospital between October 2023 and May 2024. Successful adrenal cannulation was defined as adrenal/peripheral vein cortisol ratio $>$ 5:1 with synacthen infusion. Post-operative biochemical remission was defined by saline-suppression test (SST) demonstrating aldosterone $<$ 200 pmol/l (Diasorin Liaison XL). Follow-up data included management undertaken and outcomes post-adrenalectomy.
Results
Of the patients referred for AVS, 26/33 underwent the procedure. All patients had PA based on either aldosterone-renin ratio (19%) or SST (81%), with a mean aldosterone nadir of 756 pmol/l. Prior to AVS, 35% of patients were prescribed $\geq$3 antihypertensives and 85% had hypokalaemia. Bilateral adrenal vein cannulation was technically successful in 88% of procedures and 74% showed lateralisation of aldosterone secretion. Only 7 patients underwent adrenalectomy. Of these, 5/7 achieved complete biochemical remission, and 3/7 completely discontinued antihypertensives. Of the 2 patients with no biochemical remission, one had an AVS lateralisation ratio of $>$7, but bilateral secretion was noted. Histology showed micronodular disease. The other case had unsuccessful right-sided cannulation and elected for surgery based on a radiological left-sided nodule. These cases demonstrated some improvement in blood pressure control but remained on anti-hypertensives.
Discussion
This audit demonstrates a high success rate of bilateral adrenal vein cannulation. Some patients are still awaiting surgery, limiting the scope of analysis. A high proportion of patients demonstrate clinical benefit from surgery. This data will refine our multi-disciplinary decision-making and case selection.

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P21

Streamlining the Adrenal MDT Pathway: A Quality Improvement Project to Optimise Diagnostic Workflow and Resource Utilisation at Birmingham Heartlands Hospital

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Introduction
Quality Improvement Projects (QIPs) aim to enhance patient outcomes, safety, and efficiency through systematic process improvements. This QIP, conducted at a secondary care centre, evaluated the adrenal service by streamlining the patient pathway from multidisciplinary team (MDT) referral to clinic appointment or discharge.
Methods
A retrospective analysis was conducted on 144 patients referred to the adrenal MDT between January and July 2024. Data on demographics, comorbidities, lesion type, and investigation outcomes were collected. Key metrics included time from MDT referral to initial adrenal work-up, time to first specialist appointment, discharge rates, requirements for repeat work-up, and referrals to the tertiary adrenal MDT for further opinion or surgery.
Results
Of the 144 patients, 52% were female, with a mean age of 64.6 years (range 19–94). Adrenal work-up was completed within five months in 71.5% of cases, including 26% at the time of the MDT. The average time from MDT to clinic review was 6.6 months, although patients with large indeterminate lesions were prioritised. Over half (54%) were discharged following initial work-up without requiring a clinic visit; 40% were discharged after one follow-up, and 6% after two. The most common diagnosis was benign non-functioning adenoma (73.4%), followed by phaeochromocytoma (4%) and mild autonomous cortisol secretion (MACS) (6%). Repeat imaging was required in 33 cases (with additional plain CT, MIBG, or PET-CT), and 9% were referred to the tertiary MDT. Notably, 47% had both diabetes and hypertension, and 33 normotensive patients with radiologically benign lesions underwent renin/aldosterone testing—suggesting potential overuse of investigations.
Conclusions/recommendations
Recommendations included a pre-MDT checklist, registrar-led scan requests, template letters, and standardised post-MDT processes to create a virtual discharge pathway. These interventions aim to reduce waiting times, minimise unnecessary investigations, optimise resources, and ultimately improve patient outcomes.

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P22

Do variants in the AIRE (autoimmune regulator) gene contribute to regular autoimmune addison's disease susceptibility?

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Background
Despite a high heritability of Autoimmune Addison's Disease (AAD), genetic factors contributing to disease development are still not well defined. An association between the p.R471C variant of *AIRE* gene and AAD was suggested by a genome-wide association study performed by Eriksson *et al.* in 2021. However, variants within the *AIRE* gene are conventionally recognised as causing the rare monogenic Autoimmune Polyendocrine Syndrome Type 1 (APS-1), and not the much commoner sporadic AAD or the Autoimmune Polyendocrine Syndrome Type 2 (APS-2).
Methods
We performed allele-discrimination PCR genotyping of the p.R471C variant of *AIRE* gene (rs74203920) in DNA from 433 AAD patients, 535 patients with Graves' disease (GD) and 218 local healthy controls.
Results
There was a significant association between AAD and risk T allele of p.R471C variant of AIRE gene when compared to both healthy controls and GNOMAD Non-Finnish Europeans (Table 1)
Table 1

rs74203920	T allele, n (%)	C allele, n (%)	*P*-value
Controls (local)	4 (0.9%)	432 (99.1%)	-
Controls (GnomAD)	17084 (1.5%)	1167690 (98.5%)	-
AAD	35 (4.0%)	831 (96.0%)	*$P = 0.002$ †$P < 0.00001$
GD	17 (1.6%)	1053 (98.4%)	*$P = 0.3$

* Significance compared to local controls, chi-square test
† Significance compared to GnomAD Non-Finnish Europeans, chi-square test

To test whether the effect of rs74203920 was associated with different AAD phenotypes, we checked for difference in sporadic AAD, APS-2 (AAD with autoimmune thyroid disease and/or T1DM) and other autoimmune comorbidities like pernicious anaemia and premature ovarian insufficiency. There was no significant difference between isolated AAD and other autoimmune comorbidities, except T1DM (Table 2).

rs74203920	T allele, n (%)	C allele, n (%)	*P*-value, chi-square test
AAD without T1DM	31 (3.7%)	799 (96.3%)	$P = 0.028$
AAD with T1DM	4 (11.1%)	32 (88.9%)	

Conclusion
Our findings support the original suggestion by Eriksson *et al.* that SNP rs74203920 of *AIRE* gene is associated with AAD, but not with GD.

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P23

GTN-induced pheochromocytoma crisis: a rare but important clinical lesson

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Introduction
Pheochromocytoma is a rare catecholamine-secreting neuroendocrine tumour. A catecholamine crisis may be precipitated by certain drugs including β-blockers, steroids, anaesthetic agents, and nitrates. Reports of glyceryl trinitrate (GTN)-induced pheochromocytoma crisis are exceptionally rare, but recognition is critical to prevent catastrophic outcomes.
Case
A 50-year-old previously healthy male presented with a 4-year history of recurrent palpitations, tachycardia, sweating, anxiety, and episodic hypertension. Despite multiple attendances to the Emergency Department and outpatient cardiology assessments, no definitive diagnosis was made. During further evaluation, GTN spray was administered, precipitating a severe catecholamine crisis with haemodynamic collapse requiring intensive care. Urinary catecholamines were found to be elevated, with normetanephrines nine times the upper limit of normal MRI abdomen revealed a $49 \times 44 \times 47$ mm T2-hyperintense left adrenal mass. A 68Ga-DOTATATE PET/CT confirmed no extra-adrenal disease. The patient underwent laparoscopic left adrenalectomy in 2025. Postoperatively, his symptoms resolved, and plasma metanephrines and urinary catecholamine metabolites normalised. MEN screening (calcitonin, calcium, 5-HIAA, chromogranin A and B) was unremarkable.
Discussion
This case demonstrates both the diagnostic delay common in pheochromocytoma and the risk of pharmacologically induced crisis. GTN can provoke abrupt catecholamine release through vasodilatation and reflex sympathetic activation, precipitating life-threatening haemodynamic instability.
Conclusion
GTN should be avoided in suspected or confirmed pheochromocytoma due to the risk of precipitating crisis. Early recognition, appropriate biochemical testing, and awareness of drug triggers are vital in order to prevent a potentially avoidable crisis being provoked.
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P24

Loss of glucocorticoid receptor signalling causes a primary cilia defect in the fetal mouse kidney

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Primary cilia are microtubule-based organelles that protrude from cell membranes to mediate diverse developmental signalling pathways and senses extracellular stimuli to maintain tissue homeostasis. We show that glucocorticoid (GC) signalling via the glucocorticoid receptor (GR) regulates normal primary cilia formation in the renal tubule. RNA sequencing of E18.5 fetal kidney from GR-null mice compared to wild-type controls identified reduced mRNA levels of key ciliogenesis-associated genes. Real-time-qPCR analysis confirmed reduced mRNA levels for the cilia-associated proteins *Ccp110* (fold -2.18), *Cep97* (fold -1.78), *Cep290* (fold -2.91), *Kif3a* (fold -1.82) and *Rpgr* (fold -1.90). Confocal microscopy showed abnormal, stunted primary cilia in renal proximal tubules, collecting ducts and podocytes in GR-null or in renal tubule conditional GR-

deleted mice, created using the HoxB7 Cre-driver allele. Primary cilia length was decreased in kidney proximal tubule cells in GR-null mice (5.01 ± 0.11μm) compared with wildtype controls (6.20 ± 0.15μm). Scanning electron microscopy of E18.5 GR-null kidney showed aberrant primary cilia morphology in the proximal renal tubules. Activation of GR signalling with dexamethasone in cultured mouse IMCD3 and human HK2 kidney proximal tubule cells increased primary cilia length (IMCD3; 2.89 ± 0.04μm) compared to controls (2.46 ± 0.28μm), an effect blocked by the GR antagonist RU486 (vehicle + RU486: 2.06 ± 0.02μm, dexamethasone + RU486: 2.00 ± 0.02μm). Aurora kinase A (AURKA) is a known regulator of primary ciliogenesis in-part via the AKT cell signalling pathway. AURKA protein levels were downregulated in GR-null kidney and in DEX-treated IMCD3 cells which suggest the GR both positively and negatively regulates AURKA levels to control the assembly and disassembly of primary cilia. Together, these results demonstrate that GC signalling via the GR is required for normal primary ciliogenesis in the developing kidney and suggests that synthetic GR agonists may provide a novel therapy for human ciliopathies such as those observed in polycystic kidney disease.

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P25

Hypoglycaemia as a presentation of advanced adrenal cortical carcinoma, two case reports

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Hypoglycaemia is a rare presenting feature of ACC. We present two patients at our centre presenting with hypoglycaemia subsequently diagnosed with advanced ACC. Both patients were refractory to treatment and subsequently succumbed to their disease. Non islet cell tumour hypoglycaemia (NICTH) in ACC is a rare paraneoplastic phenomenon caused by tumour overproduction of IGF-2 and its precursor ("big-IGF-2"). This results in activation of insulin receptors and subsequent hypoglycaemia. A 59-year-old women with a short history of weight loss and hirsutism presented with malignant hypertension and hypoglycaemia. Imaging showed a 20 cm left suprarenal mass with liver metastases. Biochemistry and subsequent biopsy confirmed a diagnosis of ACC not amenable to surgery. Investigation of hypoglycaemia found low insulin, low beta-hydroxybutyrate, normal range c-peptide and cortisol. Both IGF-2 and IGF-2:IGF-1 were elevated diagnostic of NICTH. Initial treatment of hypoglycaemia was with dietary changes and glucagon, however hypoglycaemia remained refractory to treatment, and she was admitted for a continuous infusion of 10% dextrose and prednisolone. She showed no improvement with octreotide, or dexamethasone and required ongoing dextrose infusion. She died while awaiting a trial of pasireotide. A 24-year-old man presented following a collapse at a music festival and was admitted with a low GCS and refractory hypoglycaemia requiring a 10% dextrose infusion and NG feed. Investigations of hypoglycaemia showed low insulin, low c-peptide and low beta-hydroxybutrate and a normal cortisol. Subsequent IGF-2:IGF-1 found to be elevated in keeping with NICTH. CT showed a large adrenal mass. Biochemistry confirmed ACC and he underwent surgical debulking and subsequent chemotherapy treatment with improvement in hypoglycaemia. Unfortunately, hypoglycaemia recurred with tumour progression requiring inpatient treatment with glucagon and dextrose infusions, GH treatment and NG feed. Patient deteriorated and died in hospital. These cases highlight a rare cause of hypoglycaemia and the difficulties in managing NICTH in advanced ACC.

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P26

The role of cortisol and aldosterone in hypertensive nephropathy

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Introduction
This study investigated the independent and combined effects of baseline and longitudinal changes in serum cortisol and aldosterone levels on the risk and progression of hypertensive nephropathy in patients with essential hypertension.
Methodology
A prospective cohort study was conducted at Khyber Teaching Hospital, Peshawar, from January 2022 to December 2023, with 190 adults aged 30-70 years who had essential hypertension and preserved renal function at baseline without any secondary causes for CKD. Fasting blood samples for cortisol and Aldosterone levels were collected between 8:00 and 9:00 AM at baseline, 12 months, and 24 months (using immunoassays CLIA). Renal functions were monitored using serum creatinine, eGFR , and urine PCR, with hypertensive nephropathy defined per KDIGO criteria. Statistical analyses were performed using SPSS v26.0, employing Kaplan-Meier curves and Cox proportional hazards models adjusted for potential confounders. Hormonal interactions were evaluated using multiplicative and additive terms, and repeated-measures ANOVA and regression models assessed hormone trajectories over time.
Results
Over a median follow-up of 24 months, 43 patients (22.6%) developed hypertensive nephropathy. The absolute risk of nephropathy was substantially higher among those in the highest tertiles of both cortisol and aldosterone (34.4%) compared to those in the lowest tertiles (11.2%). Elevated baseline cortisol levels were independently associated with increased risk of nephropathy (hazard ratio [HR]: 2.31; 95% confidence interval [CI]: 1.29-4.13; $P = 0.005$). Similarly, elevated aldosterone levels were independently associated with risk (HR: 1.97; 95% CI: 1.11-3.50; $P = 0.021$). There was a significant interaction between cortisol and aldosterone levels ($P = 0.038$), indicating a synergistic effect on the risk of nephropathy.
Conclusion
Both elevated and increasing serum cortisol and aldosterone levels independently and synergistically predict the development of hypertensive nephropathy. It is suggested that incorporating hormonal profiling into early risk stratification models may enhance identification of hypertensive patients at risk for kidney damage.

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P27

Adrenal insufficiency in pregnant population: a diagnostic challenge

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Introduction
In pregnant women, diagnosis of adrenal insufficiency is particularly difficult as signs and symptoms of hypoadrenalism such as nausea and fatigue may mimic normal gestational changes. Investigations for adrenal insufficiency in pregnancy are also complicated due to effects of pregnancy on HPA axis. We therefore present a case report of adrenal insufficiency diagnosed during pregnancy.
Case
Endocrine consultation was requested for a 29-year-old Caucasian woman with 18 weeks gestation who had recurrent hospital admissions with hyperemesis and hyponatremia. The patient was readmitted to hospital two days after finishing a tapering course of prednisolone prescribed for hyperemesis. She was noted to have significant skin tanning, hyponatremia and previous history of Grave' disease. An urgent short synacthen test (SST) was performed, and she was prescribed replacement doses of hydrocortisone. Her SST showed baseline cortisol of 205nmol/l and 177nmol/l at 30 minutes, with ACTH level of 43ng/l. Her adrenal antibodies were subsequently recorded as elevated.
Conclusion
Pregnancy induces a rise in CBG and total cortisol, particularly in the third trimester, affecting SST interpretation. Standard cortisol cutoffs may not apply, and trimester-specific thresholds remain invalidated. Clinical judgment, supported by careful interpretation of the diagnostic tests remains essential. Early recognition and steroid replacement are key to preventing complications. Adrenal insufficiency should be considered in pregnant women with unexplained hyperemesis, hyponatraemia, or hyperpigmentation. SST can be used cautiously, but results must be interpreted in the context of pregnancy-related physiological changes. Timely diagnosis and management are critical for optimal maternal and fetal outcomes.

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P28

Mainstream genetic testing in the general adult endocrine clinic: pathogenic variants were detected in 21% of cases seen

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Since 2019 the nationally commissioned NHS Genomic Medicine Service (GMC) has provided the opportunity for endocrine doctors to directly request genetic testing, without the need to involve clinical genetics service, known as 'mainstreaming'. The tests are R coded and have specific eligibility criteria. At KCH we have developed a small endocrine genetics clinic. We conducted an audit/service review to see the range of tests that were being requested and the extent pathogenic variants were detected.
Methods
We reviewed the most recent 100 cases seen in our endocrine genetics clinic, from Feb 2023 to June 2025, and recorded the test completed and whether a pathogenic variant was detected. Patients with pathogenic variants were referred on to the local clinical genetics service for cascade testing where appropriate.
Results
The most common test requests are for Paraganglioma, MEN1, MEN2 and Li-Fraumeni testing, in the context of adrenal cancer. Pathogenic variants were detected in 21% of cases, these were predominantly paraganglioma cases (12/34), but also MEN1 (2/10), ARMC5 in the context bilateral adrenal nodularity (2/3) and Lynch syndrome in adrenal cancer (1/1). The rate of unexpected findings and variants of uncertain significance (VUS) was low at 2%. Examples include 2q microdeletion (on R26 test) and VUS of the AIP gene in R217 test.
Discussion
The range of tests requested reflects the clinical caseload of the department, with a large number of paragangliomas, adrenal cancer cases and pituitary tumours. Paediatric cases fall under a separate pathway. The highest rate of detection of pathogenic variants was in PGL at 35%, reflecting the high heritability of these tumours. The audit confirms the importance of genetic testing early in the pathway to inform care of affected individuals and to enable cascade testing in family members. The rate of unexpected genetic findings was low, and not clinically challenging.

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P29

Too much of a good thing: an interesting case of resistant hypokalaemia and hypertension due chronic liquorice ingestion mimicking apparent mineralocorticoid syndrome

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Background
Liquorice is commonly consumed across the world as a sweet treat or in traditional medicines. One of the key compounds in liquorice is Glycyrrhizin, which is metabolised to Glycyrrhetinic acid, a potent inhibitor of 11-ß-hydroxysteroid dehydrogenase 2 enzyme (11-ß-HSD 2). This enzyme is essential for deactivating cortisol. Blocking the 11-ß-HSD2 enzyme results in increased activity of cortisol, which increases the stimulation of mineralocorticoid receptors in the kidneys. This results in increased sodium retention, potassium loss and raised blood pressure. This can mimic apparent mineralocorticoid excess (AME), a rare autosomal recessive monogenic disease.
Clinical case
A 55-year-old woman with a history of hypertension for 20 years and hypothyroidism presented to hospital with dizziness and headaches. On admission, she was found to be profoundly hypertensive, with a systolic blood pressure of >230mmHg. Her regular medications were Ramipril 10 mg, Levothyroxine 50 micrograms and Omeprazole 10 mg. Her bloods revealed metabolic alkalosis with sodium of 147 mmol/l and potassium of 2.0 mmol/l. Renin was 0.5 nmol/l/hr and aldosterone was <50 pmol/l. 9-am cortisol was normal. Genetic testing for renal tubulopathies and apparent mineralocorticoid syndrome was negative. Her hypokalaemia required several rounds of IV replacement. Spironolactone 100 mg and Doxazocin 6 mg was added to control her blood pressure. Further history taking revealed that she had been consuming about 10 liquorice candies a day, which she was advised to stop. Within just a few weeks her potassium normalised, and blood pressure improved. Spironolactone and Doxazocin were stopped, leaving her on Ramipril alone.
Learning points
This case demonstrated the importance of asking questions regarding an individual's lifestyle and dietary intake. Awareness of liquorice consumption causing a clinical picture of mineralocorticoid excess will help clinicians to correctly identify the diagnosis and appropriately advise the patient.

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P30

Acute ACTH deficiency from high dose Quetiapine: a cautionary tale

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Introduction
Quetiapine has been found to reduce ACTH and cortisol secretion by blocking serotonergic receptors in clinical trials with healthy subjects and patients with depression, although a clinical presentation has not been reported. We present a patient who presented with acute ACTH deficiency from high dose Quetiapine.
Case report
We report a 21-year-old gentleman treated with high dose quetiapine for acute psychosis. Past medical history was fatigue, brain fog, and headache, following covid 19 infection four years ago. He subsequently had recurrent pulmonary emboli treated with edoxaban but made a full recovery. After being well for one year, he was diagnosed with acute psychosis and treated with 500 mg Quetiapine daily. His fatigue returned with new hypersomnolence, dizziness, and nausea. He had retained erections and pituitary profile showed low cortisol (35 nmol/l at 9AM, 133-537 nmol/l at 6-10AM), with other pituitary hormones like LH and Testosterone in range (LH 6.6 IU/l, 1.7-8.6, Total Testosterone 11.1 nmol/l, 7.6-31.4, SHBG 13 nmol/l, 16-55, calculated free Testosterone 0.336 nmol/l, > 0.225). He had a morning Cosyntropin stimulation test which showed low baseline but moderate adrenal response to Cosyntropin (cortisol 0 min: 16 nmol/l, 30 min: 358 nmol/l, 60 min: 400 nmol/l) and low ACTH (7.5 ng/l, 7.2-63.3) suggesting recent secondary hypoadrenalism. MRI pituitary was normal with preserved high T1 signal from posterior pituitary and unremarkable hypothalamus. Hydrocortisone supplement resulted in significant improvement in his symptoms. Fludrocortisone was added to treat dizziness from probable mineralocorticoid deficiency. His Quetiapine is currently being weaned down.
Conclusion
Our patient presented with acute ACTH deficiency from high dose Quetiapine. It is not certain whether this is reversible following discontinuation of Quetiapine. This demonstrates the need for caution in patients presenting with symptoms of hypoadrenalism following treatment with Quetiapine.

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P31

Modelling human adrenocortical tumours in a 3D organoid system

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Diseases and cancers of the adrenal gland disrupt key processes in the body such as stress and immune responses, sexual maturation, and salt balance and therefore have serious, potentially fatal consequences. Adrenocortical tumours include adrenocortical adenomas (ACAs) and adrenocortical carcinomas (ACCs). While ACAs are typically benign and often managed effectively, ACCs present significant clinical challenges due to limited treatment options and poor prognoses. The inherent rarity of these tumours makes development of novel therapies even more challenging. Development of new physiologically relevant *in vitro* models are critical in improving understanding of adrenocortical tumours and advancing therapeutic development. Here 3D organoid-like structures have been generated from patient-derived adrenocortical tumour tissue with a range of different pathologies and adjacent 'normal' adrenal tissue. Patient cells were seeded in suspension culture and allowed to grow for 2-3 weeks to generate organoids. Organoids were collected for embedding, sectioning, and immunohistochemistry staining for various antigens marking region specific adrenal populations. This histological analysis confirmed that patient-derived organoids retained not only the main cytoarchitecture but also key antigenic compositions characteristic of their tumours of origin, including expression of steroidogenic enzymes. Steroid analysis was also carried out on the organoid medium using ELISA and mass spectrometry to compare the steroid output of the organoids to the clinical analysis of patient serum, confirming that organoids were functional and steroidogenic. These findings support the potential of adrenal organoids as promising *in vitro* models that preserve the key histological and molecular characteristics of their tissues of origin. Further validation is required to optimise and fully establish their translational and research applications.

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P32

Systemic effects of targeted-release budesonide in patients with IgA nephropathy

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Background
Targeted-release formulation budesonide (TRf-budesonide) delivers budesonide to the distal ileum/ proximal colon where it acts on Peyer's patches to reduce the production of Gd-IgA1, improving proteinuria and preserving eGFR in patients with IgA nephropathy. Budesonide is a highly potent glucocorticoid; 16 mg is equivalent to oral prednisolone 213 mg. After extensive first pass metabolism (via CYP3A4), systemic bioavailability of budesonide is 10%, equating to a daily dose of prednisolone 20 mg. Concern remains over the side effects of systemic absorption of TRf-budesonide. We aimed to evaluate this in our patient cohort.
Methods
Retrospective study evaluating glucocorticoid-related adverse effects in patients treated with TRf-budesonide at a single glomerulonephritis clinic.
Results
To date, 16 patients remain on treatment; 13 patients have completed a >9-month course of treatment (full dose: $n = 9$; reduced dose: $n = 4$). Glucocorticoid-induced adverse effects were common. 14/29 (48.3%) patients experienced a median weight gain of 3.8 kg (1.5 – 8.6) on treatment. 8/29 (27.6%) patients developed acne, 6/29 (20.7%) patients developed an infection requiring antibiotics, two patients required inpatient treatment. 12/29 (41.3%) patients required a dose increase or new antihypertensive medication during the treatment period. All patients with pre-diabetes ($n = 3$) and T2D ($n = 1$) at the start of treatment had a mean increase in HbA1c of 4.75mmol/mol during the treatment period. A further two patients developed pre-diabetes. Morning serum cortisol was measured in 19 patients whilst on treatment. Levels were undetectable (<28nmol/l) in 9/19 (47.3%) of patients. Only five patients had a morning cortisol greater than 150nmol/l.
Conclusion
Nearly half of patients demonstrated systemic absorption with suppressed endogenous cortisol production. Glucocorticoid-induced adverse effects were frequent, as was an increased need for antihypertensive medication and an observed deterioration in glycaemia. Future work is required to evaluate the longer-term effects of TRf-budesonide, including its effect on the hypothalamic-pituitary-adrenal axis and burden of glucocorticoid associated morbidity.

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P33

Prolonged adrenal insufficiency after withdrawal of osilodrostat: a case report and literature review

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Osilodrostat is an oral inhibitor of steroidogenesis that blocks 11β-hydroxylase, a key enzyme in cortisol synthesis. Adrenal insufficiency (AI) is reported in around 40% of treated patients, usually considered an expected pharmacological effect. Recently, however, cases of prolonged AI persisting after drug withdrawal have been described. We report a 74-year-old woman with ectopic ACTH-dependent Cushing's syndrome who developed long-lasting AI after osilodrostat discontinuation. She presented with typical clinical features of hypercortisolism, including moon face, supraclavicular fat accumulation, buffalo hump, muscle wasting, easy bruising, arterial hypertension, and type 2 diabetes. Laboratory evaluation confirmed ACTH-dependent hypercortisolism, and Ga-68-DOTA-TATE PET-CT revealed a large neuroendocrine tumour in the anterior mediastinum. Histopathology showed a neuroendocrine tumour negative for ACTH staining. Because of technical difficulties with biopsy and resection, the patient underwent mediastinal radiotherapy (60 Gy/30 fr). Osilodrostat was started concurrently (titrated up to 4 mg/day). Four weeks later, prior to radiotherapy, AI developed and steroid replacement was required. Hydrocortisone and subsequently dexamethasone were administered, during which both morning cortisol and urinary free cortisol remained undetectable. After 10 months, dexamethasone was stopped and hydrocortisone resumed, but endogenous cortisol remained suppressed. Osilodrostat was tapered and discontinued after 15 months of treatment. Despite drug withdrawal, adrenal recovery was absent. A high-dose ACTH stimulation test four months later showed only minimal cortisol response (35.7 nmol/l). Even 11 months after stopping osilodrostat, the patient remained biochemically adrenally insufficient (morning cortisol 37.2 nmol/l; ACTH 108 pg/mL) and required hydrocortisone substitution. Retrospective CT analysis demonstrated a marked reduction in adrenal volume after therapy. This case demonstrates that osilodrostat-induced AI may persist long after treatment cessation. The mechanism is unclear but may involve persistent enzyme inhibition, interference with steroidogenesis, or even adrenolytic effects. Awareness of this potential complication is essential as more patients are treated with osilodrostat.

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P34

Overt Cushing's Disease in the ICU: Key Considerations and Challenges

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Background
Cyclical Cushing's syndrome can present with dramatic swings in cortisol, posing diagnostic and therapeutic challenges. Critically ill patients may develop severe metabolic, cardiovascular, and infectious complications. Rapid control of hypercortisolism is essential to stabilize patients and prepare for definitive therapy, yet oral medications may be poorly tolerated in unstable cases.
Case Presentation
We describe a 51-year-old woman presenting with seizure-like activity, behavioural changes, and refractory hypokalaemia (2.7 mmol/l). Biochemistry confirmed ACTH-dependent hypercortisolism (serum cortisol >1749 nmol/l, ACTH 182 pmol/l, urinary free cortisol >1900 nmol/24h), but imaging and inferior petrosal sinus sampling failed to localize a source. Her hospital course was complicated by colonic perforation requiring emergency surgery, post-operative diabetes, psychosis, and severe Klebsiella pneumoniae pneumonia leading to septic shock. Persistent cortisol excess contributed to profound metabolic instability despite oral therapy. She required ICU transfer for refractory hypercortisolaemia and hypokalaemia. Continuous intravenous etomidate (0.04 mg/kg/hr) was started, achieving rapid cortisol reduction within 24 hours. Serial serum and salivary cortisol guided titration, and hydrocortisone supplementation prevented adrenal insufficiency. While metabolic parameters improved, overwhelming infection ultimately proved fatal.
Discussion
Management of severe Cushing's in the ICU must balance haemodynamic stabilization, metabolic correction, infection control, and thromboprophylaxis. Etomidate is uniquely valuable for rapid parenteral cortisol suppression but demands vigilant monitoring due to its narrow therapeutic window. Its use is best viewed as a short-term bridge to oral steroidogenesis inhibitors or definitive surgery.
Conclusion
This case highlights the diagnostic complexity of cyclical Cushing's and underscores the importance of multidisciplinary ICU care. Etomidate can be life-saving for acute hypercortisolism, but careful titration, monitoring, and transition planning are essential for optimal outcomes.

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P35

Review of adrenal vein sampling in hypercortisolaemia and hyperandrogenaemia

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Background
Adrenal vein sampling (AVS) is well established for lateralising aldosterone excess in primary aldosteronism (PA) but its role in other steroid excess states such as hypercortisolaemia and hyperandrogenaemia remains less well defined. Diagnostic inconsistency arises from variation in stimulation protocols, reference hormone selection, and interpretative cut-offs across centres. In non-PA contexts, AVS is typically considered when imaging is inconclusive or when radiological findings, such as bilateral or unilateral adrenal abnormalities, raise uncertainty about the functional source.
Objective
To systematically review and assess application of use, consistency of AVS methodology and diagnostic cut-offs in the non-PA contexts of hypercortisolaemia and hyperandrogenaemia.
Methods
A systematic search of PubMed, Embase and Cochrane from 2015–2025 identified case reports, series, and cohort studies involving AVS in patients with hypercortisolaemia and hyperandrogenaemia. Data on stimulation/suppression protocols, reference hormones, selectivity index (SI), lateralisation index (LI), contralateral suppression, and clinical outcomes were captured.
Results
Forty-two studies were included, comprising variable protocols and thresholds. Cortisol was the most common reference hormone but proved unreliable in co-secreting states. Metadrenaline and adrenaline enabled a less confounded assessment of cannulation success, given their independence from cortisol production. SI thresholds ranged from 2.0–6.5 across both hypercortisolaemia and hyperandrogenaemia (reference hormone and stimulation protocol dependent). LI cut-offs for unilateral disease varied from ~ 2.0–4.0 in hypercortisolaemia and 2.0–2.3 in hyperandrogenaemia. Data on AVS in hyperandrogenaemia were limited and often lacked clear cut-offs. AVS has the potential to inform clinical management, for example decisions on adrenalectomy in bilateral disease.
Conclusion
AVS may have a meaningful role beyond PA, but methodological variation hinders reproducibility and clinical utility. These data highlight that further work on disease specific reference hormone selection, protocol adapted SI and LI thresholds, and a standardised reporting structure is required along with multicentre validation to improve clinical utility/outcomes.

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P36

Accessory renal artery stenosis: an incidental finding or a cause of hypertension?

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Background
Over 90% of hypertension cases are classed as primary, with no single identifiable cause. Of cases with a secondary cause, most are attributable to renal/renovascular disease. While the impact of renal arterial stenosis is well-established, it is less apparent whether a stenosed accessory renal artery contributes to systemic hypertension. An accessory renal artery is a common anatomical variant found in 20-30% of the population. Emerging literature has highlighted cases of resistant hypertension in the context of a stenosed accessory renal artery, which showed improvement post intervention.
Case report
A 38-year-old gentleman with a known small ventricular septal defect presented to hospital with a hypertensive crisis and flash pulmonary oedema, where he was commenced on IV duresis and a GTN infusion. An echocardiogram revealed a dilated LV with an EF of 19%, attributed to long-standing hypertension. The patient was offloaded and subsequently discharged on ramipril, hydralazine, alongside other cardiac modulators, with a blood pressure in the range of 140/85mmHg. As part of a secondary hypertension workup, Plasma Metanephrines were essentially normal, and an MIBG scan ruled out a Phaeochromocytoma. The initial aldosterone renin ratio was 3, and a 24hr urinary free cortisol was slightly raised however with no clinical features of Cushings syndrome. A renal MRA revealed normal right and left renal arteries, with a highly stenosed right inferior accessory renal artery. There was no evidence of adrenal pathology. In view of the patients' flash pulmonary oedema presentation and sub-optimal BP control, he was referred to the vascular team for consideration of arterial stenting.
Discussion
This case highlights the role of a stenosed accessory renal artery as a secondary cause of systemic hypertension. It also highlights the importance of a multidisciplinary approach in not only ruling out other secondary causes, but also in devising optimal pharmacological and interventional strategies.

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P37

Characterisation of MRAP and MC2R missense variants leading to familial glucocorticoid deficiency (FGD)

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Introduction
FGD is a rare autosomal recessive disorder associated with isolated glucocorticoid deficiency. Loss-of-function mutations in *MC2R* (ACTH receptor) and MC2R accessory protein *(MRAP)* cause FGD. Missense *MC2R* variants represent the commonest type of *MC2R* variant in our registry (78.5%) whereas missense *MRAP* variants represent the least common type of *MRAP* variant (14.3%).
Methods
Three variants, MC2R p.L225R(*c.674T>G*), MRAP p.L53P(*c.158T>C*) and MRAP p.E28K(*c.82G>A*) were studied. DNA variant constructs were created using site directed mutagenesis and confirmed by sequencing. HEK293T cells were transiently transfected with the constructs and cAMP bioluminescence assay performed to determine ACTH response. GraphPad Prism v.10.4.1 was used to generate dose response curves and two-way ANOVA analysis.
Results
All variants demonstrated significantly reduced or absent activity compared to WT MC2R and MRAP. When exposed to ACTH concentrations ($1x10^{-7}$ and $1x10^{-8}$ M), compared to WT, MRAP variants showed a much decreased cAMP response (p.L53P mounting a higher response than p.E28K) whereas the MC2R variant showed no response. When exposed to ACTH concentrations ($<1x10^{-9}$ M), there was minimal or no response from all variants.
Discussion
For MC2R p.L225R, residue 225 is located on the 6th transmembrane domain of MC2R, important for ACTH binding affinity and signalling, explaining why in the respective patient, symptom onset was in the neonatal period. For MRAP variants, residue 28 is located in the N terminus and residue 53 in the transmembrane domain. The N terminus is critical for the trafficking of MRAP/MC2R to the cell surface and interaction with MC2R, which could explain why there is a lower response to ACTH of MRAP p.E28K compared to the MRAP p.L53P variant.
Conclusion
We characterised one MC2R and two MRAP missense variants causing FGD. Such *in-vitro* analysis can improve understanding of genotype-phenotype correlations in FGD.

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P38

Does red hair lessen the frequency of pigmentation as a presenting feature of Addison's disease – implications for diagnosis

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Patients with Addison's disease classically show pigmentation of the skin before treatment which lessens on hydrocortisone therapy. There is a theoretical association between red hair and fair skin in patients who have fewer melanocytes who may not pigment so markedly or frequently as patients with brown hair when they present with Addison's. In the Addison's Disease Self Help Group we asked in a questionnaire, from which there were 1146 replies, what happened to pigmentation at presentation in patients who had red hair and fair skin when compared to a group of patients with brown or olive skin. In the red headed group, of which there were 83, 57% reported pigmentation as opposed to 42% who did not. In the non-redheaded group (1063) there were 13.8% who reported no pigmentation as opposed to 86% who did. For the experimental group, the frequency of pigmentation was 0.58 (95% confidence in interval 0.47-0.68). For the control group patients without red hair $n = 1063$, the frequency of pigmentation was 0.86 (95% confidence interval 0.84-0.88). These figures are different according to the two chi squared tests at 1 and 5%. This is the first time this observation has been made as far as we can ascertain. Further work needs to be done in a second cohort of patients to verify this and to ascertain whether red hair and a fair skin by being associated with lower rates of skin pigmentation delays diagnosis of Addison's disease.

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P39

ACTH stimulation testing is often unnecessary after appropriate patient preparation prior to cortisol screening

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Context
A low screening morning serum cortisol is used to select patients for ACTH stimulation testing (SST) to diagnose adrenal insufficiency (AI) but may be affected by pre-analytical factors. Careful preparation to hold potentially confounding medications beforehand may yield more reliable screening results and preclude the need for subsequent stimulation testing.
Objective
To compare the ability of a morning serum cortisol (ordered by clinicians in the real world setting) to an optimally collected basal zero-minute cortisol at the time of SST (after holding confounding medications) to predict the presence of AI with 100% sensitivity.
Methods
Retrospective chart review of 835 patients with ACTH stimulation testing from a tertiary endocrine testing clinic. Linear regression to compare Roche Cortisol II immunoassay screening cortisol vs optimally collected cortisol measurements after holding confounding medications. Receiver operating characteristic (ROC) curve analyses to identify 100% sensitivity threshold for AI.
Results
The majority of patients passed the SST ($n = 756$, 90.5%). There was a poor correlation between screening morning cortisol and optimally collected cortisol measurements, $r = 0.34$ (95% CI, 0.25-0.42). Real world screening morning cortisol measurements had moderate discrimination for the diagnosis of AI (AUC 0.80; 95% CI, 0.77-0.82; $P < 0.001$). A real world screening cortisol threshold of 262 nmol/l had 100% sensitivity for AI but only 15% specificity. Applying this threshold would save 112 (13.4%) SSTs. In contrast, an optimally collected cortisol had strong discrimination for AI (AUC 0.89; 95% CI, 0.87 – 0.91; $P < 0.0001$). A threshold of 245 nmol/l had 100% sensitivity and 43% specificity for the diagnosis. Applying this threshold would save 151(18.1%) tests.
Conclusion
A screening cortisol measured after careful attention to pre-test patient preparation variables may make a significant number of ACTH stimulation tests unnecessary without missing any cases of adrenal insufficiency.

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P40

Uncommon Presentation of Pheochromocytoma: Cortisol Co-secretion with Adrenal Cortical Hyperplasia

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Pheochromocytomas are rare adrenal tumors that produce catecholamines and may cause severe cardiovascular events. Even rarer are adrenal tumors that present with co-secretion of cortisol, which add metabolic, immunosuppressive, and psychiatric complications.
Case Presentation
A 34-year-old woman with a complex history—including long QT syndrome, ventricular fibrillation and cardiac arrest, Takotsubo cardiomyopathy, Graves' disease (in remission), and an implantable cardioverter-defibrillator—had a history of a left adrenal mass increasing from 2 cm to 3.8 cm. She experienced a cardiac arrest in April 2024, attributed to long QT. In March 2025, she presented with hypertensive crisis, mood changes, headache, and chest pain. Biochemical analysis showed non-suppression of cortisol post overnight 1 mg dexamethasone (>2500 nmol/l), elevated ACTH (130 pmol/l), markedly raised normetanephrine (>50,000 pmol/l), androgen excess, hypokalaemia (2.4 mmol/l), and a normal aldosterone-renin ratio. Imaging including MIBG scan confirmed a heterogeneous left adrenal lesion consistent with pheochromocytoma. Pituitary MRI was normal.
Treatment and Outcome
Pre-operative alpha-blockade was initiated, followed by robotic left adrenalectomy in April 2025. Post-operatively, Hydrocortisone replacement prevented adrenal insufficiency. Histology confirmed pheochromocytoma with adrenal cortical hyperplasia (30 × 15 × 34 mm, PASS 4/20, GAPP 3/10, Ki-67 <1%). Genetic testing was negative, suggesting an acquired type. By June 2025, biochemical markers normalized, including catecholamines, cortisol, ACTH, and androgens, with stable electrolytes and renal function. Patient reported significant improvement in her symptoms.
Conclusion
This case highlights the complex presentation of pheochromocytomas with hypercortisolism and hyperandrogenism with raised ACTH, a normal pituitary MRI, and normalization of ACTH post-surgery, suggesting paraneoplastic/ectopic pathophysiology of ACTH secretion from the tumor. It emphasizes the need for thorough endocrine evaluation in unexplained cardiac and psychiatric presentations. Multidisciplinary management ensured a favorable outcome.

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P41

The Impact of Acute Exercise on Arterial Stiffness and Blood Pressure Regulation in Polycystic Ovary Syndrome (PCOS)

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Polycystic Ovary Syndrome (PCOS) is associated with elevated cardiovascular risk, including increased arterial stiffness —independent predictor of hypertension and vascular dysfunction. Exercise acutely reduces arterial stiffness in healthy adults. However, acute vascular responses to exercise remain poorly characterised in women with PCOS. This study aimed to (a) assess whether resting arterial stiffness differs between women with PCOS and matched controls, and (b) evaluate whether acute exercise modulates arterial stiffness and haemodynamic responses differently in these cohorts. Data from the 'HIIT vs MISS in PCOS' study were analysed, involving women with confirmed PCOS ($n = 9$) and age- and BMI-matched controls ($n = 15$). Participants undertook high-intensity interval training (HIIT) and moderate-intensity steady-state exercise (MISS) on cycle ergometer. Vascular ultrasound of the common carotid artery was performed pre- and post-exercise, with post-processing via validated blood flow analysis software. Continuous peripheral blood pressure was recorded, and arterial stiffness quantified using the beta stiffness index (β1), Peterson's elastic modulus (Ep), and distensibility. Baseline carotid stiffness indices did not differ between PCOS ($n = 9$) and controls ($n = 15$). Mixed-model ANOVA showed greater improvements in distensibility ($P = 0.014$) and Ep ($P = 0.00045$), with a trend for β_1 ($P = 0.056$) following MISS vs HIIT. No group ($P = 0.52$) or interaction ($P = 0.47$) effects were observed. When HIIT and MISS were analysed separately no significant group differences were found—HIIT: ΔDistensibility ($P = 0.39$), $\Delta\beta_1$ ($P = 0.56$), ΔEp ($P = 0.36$); MISS: ΔDistensibility ($P = 0.74$), $\Delta\beta_1$ ($P = 0.90$), ΔEp ($P = 0.083$).In this exploratory study, PCOS did not affect changes in arterial stiffness indices after acute exercise, but MISS improved compliance more than HIIT. These findings suggest that PCOS does not impair vascular responses to acute exercise and may enhance long-term vascular function in this cohort.

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P42

Clinical spectrum and aetiological distribution of profound hyponatraemia (Na <120 mmol/l) in a tertiary UK centre

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Background
Hyponatraemia is the most frequent electrolyte disturbance with up to 30% inpatient prevalence; often associated with significant morbidity, prolonged admission and mortality. This review aimed to identify the main aetiologies of profound hyponatraemia (Na <120 mmol/l) among inpatients at University Hospitals of Leicester (UHL) over a 1-year period.
Methods
Consecutive profound hyponatraemia cases recorded between 1st January and 31st December 2022 were reviewed retrospectively. Patients were grouped into

hypovolaemic, euvolaemic and hypervolaemic categories after reviewing clinical assessment, investigations and discharge summaries at least 2 years after the initial profound hyponatraemia diagnosis; (UHL QIP No:11408).
Results
$n = 250$ cases. Hypovolaemic hyponatraemia 56%, Euvolaemic hyponatraemia (23%) and Hypervolaemic hyponatraemia (19%), with 2% remaining unclassified. Hypovolaemic hyponatraemia emerged as the predominant pattern & the contributing factors were dehydration, poor oral intake, infections (pneumonia, UTI etc), and diuretics (thiazide & indapamide). Smaller numbers were related to gastrointestinal losses, alcohol excess or postoperative fluid shifts. Euvolaemic hyponatraemia accounted for roughly 23% of cases, largely due to SIAD, secondary to malignancy (lung, prostate, breast and ovarian), medications including SSRIs/ TCAs (2.4%) and PPIs (4%), and endocrine disorders such as hypothyroidism (0.8%) and adrenal insufficiency (1.6%). Hypervolaemic hyponatraemia made up the remaining 19%, mainly in patients with heart failure, chronic liver disease or advanced renal impairment.
Discussion
• Hypovolaemic hyponatraemia remains the predominant presentation, reflecting the acute medical take population where infection, dehydration and diuretic use are common. The distribution is broadly similar to previous reports by Adrogué *et al* (NEJM, 2000) though our cohort showed a slightly higher rate of hypovolaemia: 56% vs 40%.
• Endocrine causes of profound hyponatraemia (2.4%) are in the minority, entirely reversible with hypoadrenalism being the main aetiology.
• Careful intravascular volume assessment and medication review continue to be key elements in profound hyponatraemia management

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P43

An uncommon presentation of Cushing's syndrome secondary to ectopic ACTH production in metastatic prostrate carcinoma

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Cushing's syndrome secondary to an ectopic ACTH producing tumour is relatively rare, accounting for approximately 10-20% of cases[1]. Usually, the primary tumour is bronchial carcinoid or pancreatic neuroendocrine neoplasia[2]. Prostrate carcinoma is emerging as rare cause of ectopic ACTH production, either as a small cell primary tumour or neuroendocrine differentiation into a small cell type at primary or metastatic sites, post hormonal treatment[4,5]. It is associated with lower PSA levels than are seen in pure adenocarcinoma and often runs an aggressive clinical course with a poor prognosis. In the literature, fewer than fifty cases of prostrate carcinoma associated with ectopic CS have been documented[3]. Here, we describe a case in which Cushing's syndrome was associated with advanced prostate cancer. A 62-year-old gentleman, with a background of prostate adenocarcinoma- pulmonary and hepatic metastases, treated with LHRH agonist + enzalutamide, presented with haematuria. During his admission, profound hypokalaemia (2.3mmol/l) was noted. In the absence of gastrointestinal losses, renal losses of potassium/phosphate was considered and confirmed. Given the atypical spread of his primary malignancy, the low PSA level and refractory hypokalaemia, a neuroendocrine cause was considered. Subsequent workup revealed ACTH-dependent hypercortisolism (cortisol 3182nmol/l; ACTH 262 ng/l). It was noteworthy that patient did not have typical cushingoid phenotype but on initiation of metyrapone, there was rapid resolution of the hypokalaemia. Liver biopsy confirmed neuroendocrine tumour of small-cell type with high Ki-67 index (70%).Although patient was scheduled to receive chemotherapy, he died within 2 weeks of this diagnosis. The case highlights an atypical presentation of Cushing's, secondary to ectopic ACTH production in the setting of neuroendocrine differentiation of advanced prostate cancer. Acute refractory hypokalaemia, low PSA levels and atypical metastatic spread (pulmonary), are important indicators to consider. The clinical course can be rapidly aggressive, with an associated poor prognosis.

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P44

A retrospective study to validate the utility of random cortisol screening to reduce the need for short Synacthen tests in secondary care

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Aim
The latest NICE Guidelines [NG243] on adrenal insufficiency recommends 9am cortisol >300nmol/l as a screening test to rule out adrenal insufficiency. The aim of our study was to assess the utility of using random cortisol in avoiding the need for short Synacthen tests (SST), and its impact on easing constraints on metabolic unit in a secondary care setting.
Methods
Clinical data on all patients who have undergone SST, at any time during the day, over a 12-month period was collected. Patients undergoing 6-week post-operative assessment after pituitary surgery were excluded ($n = 37$). Baseline cortisol, done as part of SST, was used as 'random' cortisol for analysis. A 30-min cortisol of $\geq$500nmol/l, usually with increment of $\geq$200nmol/l from baseline, was considered an adequate response in the SST.
Results
$n = 334$. 280 patients had an adequate response in the SST, with 259 having both 30-min cortisol $\geq$500nmol/l and increment of $\geq$200nmol/l from baseline. Baseline cortisol ranged between 85 and 1312nmol/l in this cohort. 181 of the 334 patients had baseline cortisol >300nmol/l, showing 54% of SST could be avoided by using NICE guidelines. Among the 54 patients with inadequate SST response, the baseline cortisol ranged between <50 to 288nmol/l. This conforms to the NICE cut-off of >300nmol/l to safely avoid conducting SST. 72% ($n = 39$) were secondary to glucocorticoid withdrawal, 15% ($n = 8$) related to pituitary issues and 6% ($n = 3$) for Addison's disease.
Conclusion
This study shows that random cortisol could help to predict an adequate response to SST in the low/moderate risk patients in secondary care. The 9am cortisol, as proposed by NICE, which would be more reliable than random cortisol, should be integrated into care pathways, with appropriate adjustment based on calibration for local assays. This initial screening is even more pertinent with increasing referrals and indications for assessing cortisol axis.

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P45

Adrenal Cushing's Syndrome in Twin Pregnancy: A Rare Presentation with Atraumatic Femoral Neck Fracture and Severe Fetal Growth Restriction

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Background
Cushing's syndrome during pregnancy is exceedingly rare and associated with significant maternal and fetal morbidity. Diagnosis is often delayed, as physiological adaptations in pregnancy can obscure the clinical and biochemical features of hypercortisolism. ACTH-independent Cushing's syndrome, most commonly due to an adrenal adenoma, is particularly uncommon in pregnancy.
Case
A 34-year-old woman, gravida 3 para 0, with a spontaneous monochorionic diamniotic twin pregnancy, presented at 20 weeks' gestation with an atraumatic right femoral neck fracture. She exhibited classic Cushingoid features, persistent hypertension, insulin-dependent diabetes, and recurrent hypokalaemia. Biochemical testing confirmed marked hypercortisolism with suppressed ACTH, and MRI identified a 4×3 cm left adrenal adenoma, consistent with ACTH-independent Cushing's syndrome. Due to maternal metabolic instability and twin gestation, adrenalectomy was deferred, and metyrapone therapy was initiated for medical control of hypercortisolism. Despite treatment, serial ultrasound scans demonstrated severe fetal growth restriction and reversed end-diastolic flow in one twin, necessitating emergency caesarean section at 27 + 4 weeks' gestation. Two liveborn female infants (610 g and 430 g) required neonatal intensive care for prematurity and transient adrenal suppression, successfully managed with hydrocortisone replacement. Postpartum, the mother's blood pressure and glycaemic control normalised. Definitive laparoscopic adrenalectomy performed three months later confirmed a benign cortisol-secreting adenoma.
Conclusion
This case illustrates an exceptionally rare presentation of ACTH-independent Cushing's syndrome in twin pregnancy, initially manifesting as an atraumatic fracture. Early recognition and coordinated multidisciplinary management were essential in achieving favourable maternal and neonatal outcomes despite significant metabolic and obstetric challenges.

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P46

Urine steroid profiles: to pee or not to pee?

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EURINE-ACT study (Bancos *et al*, Lancet 2020) proposed a 'triple test', incorporating Urine Steroid Profiles (USP) in adrenal cancer assessment in nodules over 4 cm and density above 20 Hounsfield Units (HU) on imaging. Without an agreed local protocol, USP testing was audited to evaluate its use, alongside other investigations of autonomous adrenal secretion. 44 patients had USP (41 spot urine, 3 x24hr collection) for investigation of adrenal nodules (from 467 referrals August 2022 to April 2025). 23 samples were completed for >4 cm and >20HU or unclassified on post-contrast images, 12 for <4 cm but >20HU or unclassified, 9 samples with <20HU. 32 had normal USP, 9 had elevated cortisol metabolites (deemed unsuitable for interpretation on random sampling), 3 had metabolites consistent with Adrenocortical Carcinoma (ACC). Of the positive USP, 1 patient had confirmed ACC on histology, with 2 unable to exclude ACC; diagnosed as myelolipoma and cortical adenoma (cortisol secreting). Of note, another patient had malignancy of unknown potential on histology with normal USP but abnormal cortisol dynamics on serum and salivary testing. The normal USP may allow a more favourable approach in follow-up post adrenalectomy. In this small cohort, USP aided differentiation between adrenal cancer and an isolated metastasis from previous cancer. Of those who underwent an adrenalectomy, the USP was not a differentiating factor in the decision to operate. Whilst EURINE-ACT proposed only testing >4 cm and >20HU, in this cohort a significant number of USP were performed without meeting these criteria. It may add value when differentiating from other retroperitoneal masses, or potential ovarian malignancies with raised testosterone, or for seemingly non-secretory lesions suspicious of ACC and as a marker for early recurrence in proven ACC. However, it is not currently going to replace other cortisol excess investigations and unlikely to directly influence surgical decisions in indeterminate adrenal incidentalomas.

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P47

Secondary Hypoaldosteronism – Post-Adrenalectomy Sequelae for Conn's Syndrome

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Background
Primary aldosteronism (PA), or Conn's syndrome, is a common cause of endocrine hypertension, typically due to aldosterone-producing adenomas. Unilateral adrenalectomy is the standard treatment, but secondary hypoaldosteronism post-surgery is a rare and clinically significant complication.
Case Presentation
We report a case involving a 76-year-old male diagnosed with Primary Aldosteronism in July 2019. His medical history included hypertension, hypokalaemia, chronic kidney disease, dyslipidaemia, and osteoarthritis. Investigations revealed an aldosterone-renin ratio >3400, confirmed by a saline infusion test. MRI identified a right adrenal adenoma (3×2 cm), which was functionally active on adrenal venous sampling. The patient underwent right adrenalectomy in July 2020. Postoperatively, he developed persistent hypoaldosteronism, presenting with hyperkalaemia (serum potassium above 5.4 mmol/l). Fludrocortisone replacement therapy was initiated, leading to normalization of potassium levels.
Discussion
Post-adrenalectomy hypoaldosteronism affects approximately 5% of patients treated for PA. Risk factors include advanced age, preoperative hypokalaemia, persistent hypertension, and impaired renal function. The condition may arise due to insufficient aldosterone production from the remaining adrenal gland, which may not respond adequately to renin-angiotensin feedback. This case highlights the importance of recognizing hypoaldosteronism as a potential sequelae, particularly in patients with predisposing factors.
Conclusion
Secondary hypoaldosteronism following adrenalectomy for Conn's syndrome, though uncommon, can lead to significant electrolyte disturbances and requires long-term monitoring. Awareness of risk factors and early intervention with mineralocorticoid replacement are essential to prevent complications. This case underscores the need for individualized postoperative care and vigilance in patients undergoing adrenalectomy for Primary Aldosteronism.

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P48

The HISTAR score: integrating CYP11B2 immunohistochemistry with clinical predictors to improve clinical cure prediction after adrenalectomy in primary aldosteronism - a pilot study

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Introduction
Predicting clinical cure post-adrenalectomy for primary aldosteronism (PA) remains challenging despite established tools like the Aldosteronoma Resolution Score (ARS). While ARS offers clinical simplicity, its accuracy is moderate. CYP11B2 (HISTALDO) staining identifies aldosterone-producing cells, with classical staining associated with better outcomes, but overlooks factors like vascular remodelling, which ARS can capture. To address this, we developed the HISTAR score by integrating HISTALDO with ARS to improve postoperative prognostication.
Methods
Thirty consecutive PA cases (2016–2025) post-unilateral adrenalectomy were reviewed. Clinical cure was defined according to PASO criteria (blood pressure $<140/90$mmHg without medication for ≥ 6 months). ARS (score:0–5, cutoff ≥ 4) includes BMI, sex, hypertension duration, and antihypertensive count. HISTAR added 1 point for classical HISTALDO, maintaining the cutoff ≥ 4 to improve sensitivity. In 15 patients with HISTALDO data, multivariable logistic regression and ROC analysis compared ARS and HISTAR models.
Results
Clinical cure rate was 33%. Classical HISTALDO showed higher cure rates than non-classical (67% vs 25%), but statistically non-significant ($p=0.24$). In HISTALDO-typed cases, higher ARS ($p=0.001$) and HISTAR ($p=0.002$) scores were significantly associated with cure. ARS achieved AUC 0.90 (95% CI: 0.76–1.00, $p<0.001$). At ARS ≥ 4, sensitivity was 80%, specificity 80%, NPV 89%, PPV 67%, and accuracy 80%, comparable to published data. HISTAR achieved AUC 0.91 (95% CI: 0.77–1.00, $p<0.001$). At HISTAR ≥ 4, sensitivity and NPV were 100%, specificity 80%, PPV 71%, and accuracy 87%, supporting its clinical applicability.
Conclusion
To our knowledge, this is the first clinical–immunohistochemical score for predicting clinical cure in PA. HISTAR demonstrated improved sensitivity and NPV, without specificity loss, a novel finding unmatched by previous scores. Although based on a small cohort, these proof-of-concept data suggest integrating HISTALDO with ARS may improve prognostic accuracy and guide early postoperative mineralocorticoid antagonist use and personalised follow-up in PA. However, further validation is needed.

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P49

Steroid metabolome profiling in chronic kidney disease

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Background
The kidneys are central to steroid hormone action, serving both as a target organ for steroid signalling and a key regulator of steroid metabolism. In chronic kidney disease (CKD), impaired enzymatic activity, dysregulated feedback loops, and reduced renal clearance disrupt these pathways, contributing to metabolic complications. While previous studies have identified specific disturbances in steroid metabolism in CKD, an integrated understanding of altered steroid profile is limited.
Aim
To characterise the adrenal steroid profile in chronic kidney disease in a comprehensive and integrated fashion.
Methods
A case-control study recruited 17 patients with CKD (pre-dialysis CKD stage 4-5) and 14 healthy volunteers, matched for age, sex and BMI. Liquid chromatography–mass spectrometry quantified progestogens, glucocorticoids, mineralocorticoids, androgens and their metabolites in 8am fasting serum (19 analytes) and 24-hour urine (29 analytes). Comparisons used Mann–Whitney U with Benjamini Hochberg correction (FDR 0.05). Exploratory analyses examined associations with skeletal muscle function (gait, chair-rise speed) and inflammation (CRP, TNFα).

Results
Mean participant age was 70.7 ± 5.1years, and 42% were female. CKD participants showed broad steroidogenic disruption. Serum levels in CKD were reduced for cortisone, 11-oxygenated androgens (11KT, 11OHT) and DHEA. Urine steroid amount in CKD was reduced for cortisone and its metabolites (THE, β-cortolone, β-cortolone), corticosterone metabolites (THA, 5αTHA, THB) and progestogen metabolites (5PT, PD, 5PD). Using urinary steroid ratios as surrogate markers, enzymatic activity appeared decreased for 11βHSD2 and increased for 3βHSD2. Better physical performance in CKD is associated with higher serum THF, 5αTHF and THE, and lower TNFα.
Conclusion
CKD is associated with multi-pathway disruption of steroid metabolism. Observations are consistent with previously reported alterations in 11β-HSD metabolism, but additionally reveal novel shifts suggesting increased 3β-HSD activity and other unexplained changes in adrenal steroid profiles. Further mechanistic and longitudinal studies are warranted to clarify underlying mechanisms and clinical implications.

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P50

An unusual cause of nocturnal hyperglycaemia

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Case Presentation
A 58-year-old man with type 2 diabetes mellitus (diagnosed five years earlier) on metformin, dapagliflozin, and amlodipine presented with progressive symptoms of nocturnal hyperglycaemia which started 0300hrs and lasted to 1100hrs on a daily basis. Continuous glucose monitoring confirmed glucose levels of 15–20 mmol/l between those hours followed by relative euglycaemia thereafter. Clinic review confirmed the concomitant presence of hypertension, palpitations, sweats with blood pressure surges up to 240 mmHg systolic. These likewise resolved by 11am each day. Plasma normetanephrines were elevated at 6,247 pmol/l (normal <1,180pmol/l). HbA1c was 56 mmol/mol, with MIBG scintigraphy demonstrating a 5 0× 4.1 cm right adrenal mass. Pituitary profile was unremarkable (ACTH 13 ng/l; random cortisol 246 nmol/l), and 24-hour salivary cortisol and cortisone were normal. He underwent right robotic adrenalectomy. Histopathology confirmed phaeochromocytoma with Ki-67 index 10% and PASS score 6. SDH staining was negative for SDH mutation. Postoperatively, his HbA1c improved to 52 mmol/mol, and all antihyperglycemic medications were discontinued.
Discussion
This case describes an unusual pattern of hyperglycaemia limited to the hours of 0300-1100hrs which has not been previously described. The pattern raises the hypothesis of ACTH or CRH receptor expression within the tumour contributing to nocturnal activation and hyperglycaemia. Further histopathological and molecular studies, including RNA analysis for ACTH and CRH receptors, are underway.
Conclusion
This is a unique presentation of phaeochromocytoma characterised by nocturnal hypertensive and hyperglycaemic episodes, highlighting the need to consider atypical circadian behaviour in catecholamine-secreting tumours.

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P51

The screening yield for phaeochromocytomas and paragangliomas from hypertension clinic is low with a significant false positive rate

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Introduction
Phaeochromocytomas and paragangliomas (PPGL) are rare but important causes of hypertension requiring a different treatment paradigm to essential hypertension. Despite this, national guidelines on PPGL screening in hypertension are vague. We evaluated the yield of PPGL screening in a regional hypertension service.
Methods
All patients who had undergone a 24-hour urine collection for metanephrines from the Hypertension Clinic at Sheffield Teaching Hospitals NHS Foundation Trust between 1/1/23 and 31/12/24 inclusive were identified. Biochemical and clinical data were extracted from the electronic patient record. Metanephrine and normetanephrine were analysed by high-performance liquid chromatography with the use of in house derived reference intervals.
Results
222 patients (126 male, median age 37 years) were included in the analysis. Indications for testing were young-onset hypertension ($n = 173$, 78.0%), resistant hypertension ($n = 31$, 14.0%), or both ($n = 18$, 8.1%). 21 results (9.5%) were above the above the upper limit of the reference interval (metanephrine 1, normetanephrine 20); 7 (3.2%) of which were also above the 'borderline' reference interval (metanephrine 1, normetanephrine 6). No patients were ultimately diagnosed with a PPGL. Of the 21 abnormal results, 17 were attributable to medications and/or obstructive sleep apnoea, with no clear cause being identified in 4 individuals. Abnormal results were associated with increased weight (median 108.2 kg v. 87.9 kg, $p<0.001$), higher 24-hour urine volume (median 2705 ml v. 2039 ml, $p<0.01$) and the presence of obstructive sleep apnoea (OSA, 23.8% v. 6.9%, $p<0.01$)
Conclusion
No patients in this at-risk cohort were diagnosed with a PPGL. There was a significant false positive rate which was largely attributable to medications and/or OSA. Increased weight and larger 24-hour urine volumes were potentially implicated. These data question the utility and cost effectiveness of blanket PPGL screening from hypertension clinic. Weight-adjusted reference intervals may be useful to reduce the number of false positive results.

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P52

Case Series of Three Distinct Clinical Paths for Recurrent Pheochromocytoma / Paraganglioma (PPGLs) Managed at University Hospitals Derby & Burton NHS Trust in Collaboration with Regional Neuroendocrine Tumour (NET) MDTs

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Background
Pheochromocytomas and paragangliomas (PPGLs) are rare, often catecholamine-secreting tumours with unpredictable malignant potential and risk of late recurrence. We hereby highlight three cases with variable progression under ongoing care at University Hospitals Derby & Burton NHS Trust.
Case Series
Case 1: A 32-year-old man with Von Hippel–Lindau (VHL) syndrome who developed bilateral adrenal pheochromocytomas requiring adrenalectomy in 2012, over the next decade went blind due to ocular hemangioblastomas, had treatment for renal cell carcinoma, and resection of a spermatic cord paraganglioma. Surveillance imaging in 2024 highlighted a new retrohilar paraganglioma, with elevated plasma normetadrenaline (1,600 pmol/l). Surgical resection at Derby is planned, but it prompted discussion about belzutifan therapy with Sheffield NET MDT. **Case 2:** A 72-year-old man presented with collapse with a 12 cm adrenal pheochromocytoma. Following resection, metanephrines remained markedly raised (8,620 pmol/l) and histology was suggestive of malignancy (PASS= 7). Within a year, MIBG scintigraphy surveillance demonstrated residual adrenal bed disease and new skeletal metastases. Following discussion with Birmingham NET MDT, therapeutic MIBG in Sheffield (Aug 2023–Feb 2024) led to radiological stability and continued under regular imaging surveillance at Derby. **Case 3:** A 72-year-old man post adrenalectomy in 2015 showed rising Normetanephrines from 2019 that prompted SPECT/CT MIBG, Octreotide scan that were all negative until Ga-68 DOTATATE PET identified multifocal nodal disease. A conservative approach with potential radiotherapy at Derby was decided via Birmingham NET MDT.
Learning Points
PPGLs may recur years after curative surgery, even with "low-risk" histology. Persistent biochemical–radiological discordance warrants Ga-68 DOTATATE PET. VHL-associated disease highlights multisystem burden and the promise of HIF-2α inhibitors (belzutifan). Access to regional facilities i.e. Ga-68 DOTATATE PET & MIBG therapy and collaborative MDT's is crucial for enabling high quality local patient care without clogging up tertiary services with routine investigations and appointments.

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P53

Variation in serum cortisol thresholds and use of salivary cortisol/cortisone in the biochemical diagnosis of adrenal insufficiency (AI) in the UK: Results from the Society for Endocrinology survey

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Introduction
Since the introduction of modern cortisol immunoassays, many clinical teams have changed cortisol thresholds in the biochemical diagnosis of AI. The aim of this survey was to evaluate the current practice among UK endocrinologists.
Methods
An online anonymous cross-sectional survey, comprising of 27 multiple-choice questions was developed and disseminated to members of the Society for Endocrinology in July and October 2024.
Results
Forty-three responses from 35 NHS Trusts were received. Respondents worked in both university ($n = 12$; 34.3%) and district general ($n = 23$; 65.7%) hospitals. Several cortisol immunoassays platforms are in use with the Roche assay the most common (54.3%). In 90.5% of respondents, 9am or random cortisol threshold was used prior to selecting patients for a Short Synacthen test (SST). However, there were considerable variations in threshold above which cortisol level was considered sufficient to exclude AI (200-400nmol/l), and that indicative of adrenal insufficiency (between <50 and 150nmol/l). Thirty-minute SST responses were used by 57% of Trusts, with 40% using 30- and 60-minute values. Thirty- and 60-minute cut-offs ranged between 380 to 450nmol/l and 375 to 500nmol/l, respectively. The term "subnormal response" was employed by 64% of clinicians with wide threshold range. Insulin tolerance tests are used by 44% of respondents, predominantly for pituitary patients. An adequate response varied between 415 to 500nmol/l, with 25% classifying "subnormal responses" Currently, 20% of Trusts use *salivary* cortisol/cortisone in current clinical practice analysing the sample by LC-MS/MS.
Conclusions
There are marked variations in current clinical practice in the UK regarding serum cortisol thresholds in the biochemical diagnosis of AI, even using measurement of cortisol by the same immunoassay. However, some Trusts have already started to use salivary cortisol/cortisone, measured by LC-MS/MS. Consensus to establish cortisol thresholds for different modern immunoassays in the biochemical diagnosis of AI is essential.

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P54

Shallow Whole-Genome Sequencing of Cell-Free DNA for Copy Number Analysis in Adrenocortical Carcinoma Monitoring

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Introduction
Circulating tumour DNA (ctDNA)–based monitoring in adrenocortical carcinoma (ACC) remains sparsely characterised relative to breast, colorectal, and lung cancers. We evaluated whether copy-number alteration (CNA) profiling of cell-free DNA (cfDNA) using shallow whole-genome sequencing (sWGS) could serve as a minimally invasive biomarker in ACC.
Methods
Serial plasma samples ($n = 7$) were collected from two patients with adrenocortical carcinoma (ACC) during periods of stable disease, tumour progression, and following surgical intervention. Total cfDNA was isolated from 4 mL plasma using the MagMAX™ Cell-Free DNA Isolation Kit on a KingFisher™ Flex Magnetic Particle Processor. Quantity and fragment-size distributions were assessed on Agilent 4200 TapeStation. Libraries were prepared for sWGS with the ReproSeq PGS kit and sequenced at low coverage. CNA profiling and tumour-fraction estimation were performed with ichorCNA pipeline under default parameters.
Results
Total cfDNA yields across the two patients were a median of 424 pg/μL (range 206-633); within normal limits, and fragment analyses demonstrated typical cfDNA profiles with a predominant mononucleosomal peak and a secondary dinucleosomal peak, supporting suitability for downstream analysis. Unfortunately, sWGS generated uniformly flat copy-number profiles across all 7 samples; hence no CNAs were detected by ichorCNA,and no ctDNA was detected by this method.
Discussion
In these 2 patients with ACC, sWGS did not reveal evidence of ctDNA, consistent with either (i) absence of CNA-bearing ctDNA in circulation or (ii) ctDNA levels below the detection threshold of sWGS/ichorCNA at times of active disease in ACC. To improve analytical sensitivity in ACC, future studies should focus on detection of ctDNA using more sensitive approaches such as next generation sequencing with either cancer mutation assays, or tumour-informed approaches.
Learning points
Reference
1. sWGS-based CNA profiling of cfDNA may lack sensitivity for ACC.
2. Negative CNA results should prompt complementary assays (tumour agnostic and/or tumour-informed approaches).

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Bone and Calcium

P55

A case of McCune-Albright Syndrome – the importance of a multidisciplinary approach and symptom-focused management

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Introduction
McCune-Albright Syndrome (MAS) is a rare genetic disorder that often affects bones and causes polyostotic fibrous dysplasia (FD). Craniofacial FD is rare and may present as facial asymmetry, orbital pain, or vision loss due to compressive optic neuropathy (ON), which can significantly impact quality of life (QOL). We present a case of orbital FD.
Case
A 15-year-old boy presented with a one-year history of fluctuating swelling above his left eye and temple, limiting eye opening. MRI revealed a 4 x 3.3 x 3.3 cm mass at the left orbit, displacing the globe and indenting the basal frontal lobe, suggestive of FD. Further skeletal survey showed no additional bone involvement. Genetic studies confirmed McCune-Albright syndrome, with normal endocrine investigations including LH/FSH, IGF-1, testosterone, thyroid function, and bone profile. He attained puberty at the same age as his peers. He later developed severe pain over his left orbit, due to soft tissue compression and expansion of fibrous bone. Zoledronate infusions were started due to persistent, painful swelling unresponsive to simple analgesia, initially at a paediatric dose of 0.025-0.05 mg/kg. This resulted in marked improvement in symptoms and QOL. ALP also reduced from 134U/l to 86U/l.
Discussion
MAS is caused by sporadic mutations in the GNAS gene and is characterised by fibrous dysplasia, café-au-lait spots, and endocrine disruptions. Orbital FD, particularly fluctuating in size, is less well-recognised and led to a delay in diagnosis in this case. Management of MAS is primarily symptom-targeted and a multidisciplinary approach is imperative due to the diverse spectrum of presentations. Although bisphosphonate therapy can effectively help in managing bone pain, it has a limited impact on bone disease progression. Therefore, long-term, continuous bisphosphonate therapy is not recommended. Instead, intermittent use with regular assessment is preferred, particularly in the paediatric population where bone mass has not peaked.

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P56

When calcium tells a deeper story: a case of atypical parathyroid adenoma with malignant features

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Introduction
Parathyroid carcinoma represents a rare malignant etiology of primary hyperparathyroidism, with an incidence of 0.36 per 10 million individuals annually, accounting for 0.4% to 5% of all hyper parathyroid cases. Clinical suspicion arises in patients presenting with severe hypercalcemia, markedly

elevated parathyroid hormone levels, palpable neck masses, and evidence of end-organ damage affecting bone and renal systems. Preoperative diagnosis remains challenging, necessitating multimodal imaging and histopathological confirmation. Long-term surveillance through serial biochemical monitoring and imaging is essential given the propensity for local recurrence and distant metastases.
Case Presentation
We report a case of a 24-year-old woman with ulcerative colitis who presented with neuropsychiatric symptoms including depression, irritability, and dysphagia. Laboratory investigations revealed severe hypercalcemia (adjusted calcium 3.24 mmol/l), elevated parathyroid hormone (42.2 pmol/l), hypophosphatemia, and hypercalciuria (16.91 mmol/day). Bone densitometry demonstrated osteopenia (lumbar spine Z-score -1.5, left hip Z-score -1.7, femoral neck T-score -1.6). Four-dimensional computed tomography identified a 16×15×54 mm hyper vascular lesion inferior to the right thyroid lobe with arterial enhancement and prominent vascular supply from the right inferior thyroid artery, consistent with parathyroid adenoma. Right inferior parathyroidectomy was performed successfully. Histopathological examination revealed a hypercellular parathyroid lesion composed predominantly of chief cells with mild to moderate nuclear atypia, low mitotic activity (1-2/10 high-power fields), and positive margins. Immunohistochemistry demonstrated retained parafibromin expression and Ki-67 proliferation index of 4-5%. While features Features were fall short of parathyroid carcinoma but atypical parathyroid is a consideration. Postoperative biochemical parameters normalized and whole body imaging negative for metastatic lesions.
Conclusion
This case highlights the diagnostic complexity of atypical parathyroid lesions that exhibit concerning histological features without meeting definitive criteria for malignancy. Such cases require prolonged surveillance protocols to monitor for potential recurrence and ensure optimal patient outcomes.

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Long-Term Efficacy and Safety of Palopegteriparatide Treatment in Adults With Chronic Hypoparathyroidism: 4-Year Results From the Phase 2 PaTH Forward Trial

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Background
Palopegteriparatide is a prodrug of PTH (1-34), administered once daily, designed to provide active PTH within the physiological range for 24 hours/day. It is approved in the US, EU, UK and several other countries.
Methods
This analysis investigated the efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of PaTH Forward, a phase 2 trial with a 4-week randomized, double-blind, placebo-controlled period, followed by open-label extension through week 266.
Results
At week 214, 95% (56/59) of participants remained in the trial; of those, 93% were independent from conventional therapy (no active vitamin D and ≤600 mg/day elemental calcium) and 98% had normocalcemia (2.07-2.64 mmol/l). Mean bone turnover markers C-terminal telopeptide of type 1 collagen (CTx) and procollagen type 1 N-terminal propeptide (P1NP) increased from low end of normal at baseline, peaked by week 26, and declined thereafter, remaining stable above baseline. Elevated baseline mean BMD Z-scores trended towards age- and sex-matched norms at lumbar spine, femoral neck, and total hip, largely stabilized after week 26 and remained above zero. At week 214, mean (SD) eGFR was 86.0 (21.7) mL/min/1.73 m^2, reflecting a mean (SD) increase of 7.6 (13.7) mL/min/1.73 m^2 from baseline. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide and were maintained (≤6.2 mmol/day). TEAEs were mostly mild/moderate; no new safety signals were identified.
Conclusion
These results demonstrate sustained efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of PaTH Forward, suggesting continued benefits in skeletal dynamics and renal function.

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Primary hyperparathyroidism in pregnancy: two case reports

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Background
As primary hyperparathyroidism during pregnancy can pose serious maternal (hypercalcaemic crisis, acute pancreatitis, preeclampsia) and foetal (miscarriage, preterm labour, neonatal tetany) complications, early diagnosis and management are essential. We report two patients with primary hyperparathyroidism during pregnancy.
Case reports
Case 1: A 30-year-old woman was diagnosed with primary hyperparathyroidism during investigations for subfertility in 2020. She underwent right superior parathyroidectomy (histology: parathyroid adenoma) and right inferior parathyroidectomy (histology: normal parathyroid tissue) in 2022. She remained hypercalcaemic postoperatively and conceived while awaiting genetic testing and further surgery. Despite receiving intravenous hydration throughout early pregnancy, her albumin-adjusted calcium levels remained consistently above 2.9mmol/l and she underwent a left superior parathyroidectomy (histology: parathyroid hyperplasia) during the second trimester. Her genetic testing confirmed the diagnosis of multiple endocrine neoplasia type 1. Case 2: A 32-year-old woman was referred for symptomatic hypercalcaemia at eight weeks gestation. Investigations confirmed primary hyperparathyroidism with an albumin-adjusted calcium of 2.71mmol/l subsequently increasing to 3mmol/l despite intravenous hydration. Ultrasound parathyroid confirmed right parathyroid adenoma and she underwent right en-bloc parathyroidectomy (histology: parathyroid adenoma) and hemithyroidectomy. The genetic screening was negative and she remained eucalcaemic post-operatively.
Discussion
Management of primary hyperparathyroidism in pregnancy depends on severity of hypercalcaemia, gestational age, and maternal and foetal status. Parathyroidectomy during second trimester as definitive treatment is advised if the patient has moderate to severe hypercalcaemia. If primary hyperparathyroidism is diagnosed prior to pregnancy, preconception counselling, genetic screening, and parathyroid surgery before conception is advised.
Conclusion
These cases underpin the complexities associated with managing primary hyperparathyroidism during pregnancy. Proactive management can optimise both maternal and foetal outcomes.

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FGF-23–driven hypophosphatemia: a rare puzzle in clinical practice

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Background
Fibroblast growth factor-23 (FGF-23) mediated chronic hypophosphataemia is rare, usually caused by genetic or acquired renal phosphate-wasting disorders. Due to their rarity, they are often under-recognised and suboptimally managed, leading to poor bone health.
Case
A 61-year-old man with hypophosphataemia, initially identified in 2014, was reviewed by renal specialists in 2016. A 24-hour urine collection demonstrated

inappropriately high phosphate excretion. CT of the chest, abdomen, and pelvis was unremarkable; therefore he was discharged on oral phosphate supplementation. Seven years later, he was referred to endocrinology for further evaluation. Although he was asymptomatic and had no fracture history, his serum phosphate levels persistently fluctuated, requiring a high dose of oral phosphate (4g/day). He had osteopenia in the hip and family history was unremarkable, aside from osteoporosis. Oral phosphate was suspended for repeat assessment. Biochemistry showed low phosphate of 0.55 (N-0.80-1.50mmol/l), normal adjusted calcium, 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D. Parathyroid hormone and alkaline phosphatase were elevated, 9.7pmol/l (N-1.6-6.9pmol/l) and 131U/l (N-30-130U/l), respectively. 24-hour urine showed increased phosphate excretion of 57.1mmol/24h (N-11-33mmol/24h) and a low TmP/GFR, confirming renal phosphate wasting. FGF-23 was elevated at 165.5 (N-33-100pg/mL). Tektrotyd scintigraphy was normal; whole-body FDG-PET is pending, and genetic testing is being considered.

Discussion

FGF-23 secreted by osteocytes, is a key regulator of phosphate homeostasis. Excess FGF-23 reduces renal phosphate reabsorption, causing renal phosphate wasting. Measurement of FGF-23 and TmP/GFR is central to the diagnostic evaluation of unexplained hypophosphataemia. FGF-23–mediated hypophosphataemia is associated with genetic conditions such as X-linked hypophosphataemia (XLH) or acquired causes like tumour-induced osteomalacia (TIO). Differentiating between these is crucial, as XLH is treated with oral phosphate, activated vitamin D, or burosumab, an anti-FGF-23 monoclonal antibody, while TIO requires tumour localisation and removal. This case highlights the importance of a structured evaluation of chronic hypophosphataemia to guide appropriate management.

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A rare case of hypocalcaemia – diagnosis and therapeutic delima

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Background

Hypocalcaemia is a common biochemical disorder; accurate distinction between inherited and acquired aetiologies is essential, as it directly influences treatment and long-term prognosis. This case highlights the diagnostic and therapeutic complexities inherent in hypocalcaemia in the presence of underlying genetic predisposition.

Case

A 57-year-old previously healthy gentleman presented with lethargy and non-specific paraesthesia. Routine blood tests indicated marked hypocalcaemia, adjusted calcium of 1.62mmol/l (Ref-2.2-2.6). He was admitted for intravenous calcium infusions, followed by oral alfacalcidol and calcium supplementation. However, hypocalcaemia persisted, necessitating further biochemical and clinical assessments. Investigations revealed suppressed parathyroid hormone (PTH), hyperphosphataemia, and hypercalciuria, raising suspicion of inherited calcium disorders, a calcium-sensing receptor (CASR)-related disorder. Family history uncovered his son had presented similarly in childhood, with persistent hypocalcaemia and suppressed PTH. Subsequent genetic evaluation confirmed autosomal dominant hypocalcaemia (ADH), a rare condition caused by activating mutations in CASR (ADH1). His alfacalcidol and calcium have been stopped, and he is managed with simple observation only, he remains well despite calcium of 1.6mmol/l. ADH is characterised biochemically by low serum calcium, inappropriately low or suppressed parathyroid hormone, hyperphosphataemia, and hypercalciuria. While approximately half of patients are asymptomatic or mildly symptomatic, others may present with paraesthesia, tetany, seizures, nephrocalcinosis, or basal ganglia calcifications. Notably, treatment with conventional calcium and vitamin D analogues can exacerbate hypercalciuria, predisposing to renal complications. This case highlights the significance of measuring urine calcium in the assessment of unexplained hypocalcaemia and considering genetic predisposition. The management of ADH should be symptom-driven, with maintaining serum calcium within the low-normal range while minimising the risk of renal impairment.

Conclusion

Not all cases of hypocalcaemia warrant aggressive treatment. The identification of ADH is paramount, as indiscriminate therapy could potentially result in greater harm than benefit. A personalised approach, incorporating genetic diagnosis and symptom evaluation, ensures optimal patient outcomes.

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Clinical utility of urinary calcium-creatinine clearance ratio (UCCCR) and calcium excretion index (CEI) in the diagnosis and management of primary hyperparathyroidism (PHPT): a single-centre audit

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Background

The urinary calcium–creatinine clearance ratio (UCCCR) and Calcium excretion index (CEI) are commonly used to differentiate PHPT from familial hypocalciuric hypercalcemia (FHH) and to support surgical decision-making. However, its diagnostic accuracy and predictive value for postoperative outcomes remain uncertain.

Aim

To assess the clinical utility of UCCCR and CaE in managing PHPT and its impact on surgical outcomes in a single-centre cohort.

Methods

A retrospective audit of 28 patients who underwent parathyroid surgery for primary hyperparathyroidism (PHPT) between April 2024 and March 2025 was conducted. Patient demographics, imaging findings, UCCCR & CEI values were correlated with histopathological diagnosis and postoperative biochemical outcomes.

Results

Among 28 patients (median age 70 years; 86% female), 26 (92.9%) had parathyroid adenomas and 2 (7.1%) had hyperplasia. UCCCR values were high in 6 (21.4%), borderline in 12 (42.9%), and low in 10 (35.7%) patients. 17 patients (60.7%) had CEI $\geq$ 30, while 11 patients (39.3%) had CEI $<$ 30. Patients with adenomas generally demonstrated higher UCCCR & CEI values compared to those without adenomas, clustering above the clinical cutoffs (~0.01) & 30 respectively. Normocalcemia was achieved postoperatively in 25 patients (89.3%), with 1 case of hypocalcemia (3.6%) and 2 cases of persistent hypercalcemia (7.1%). There was no statistically significant difference in median UCCCR & CEI between those achieving normocalcemia and those who did not ($P > 0.05$). The contingency coefficient between UCCCR and normocalcemia status was 0.103, indicating a very weak association, while CEI showed no association in achieving normocalcemic status.

Conclusion

While UCCCR and CEI demonstrate some association with underlying pathology (parathyroid adenoma vs. others), they are not a reliable standalone predictor of postoperative normocalcemia. Interpretation should be contextualized in conjunction with clinical and imaging data. Larger studies are warranted to refine diagnostic thresholds and assess prognostic utility.

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Referral accuracy of romosozumab candidates: lessons from an expedited fracture liaison service pathway

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Introduction

Romosozumab is approved for the treatment of post-menopausal osteoporosis with very high fracture risk and recent fragility fracture (1). Timely assessment and treatment prevent morbidity. The National Osteoporosis Guideline Group (NOGG) recommends a Fracture Liaison Service (FLS) to identify potential candidates (2). This study evaluates identification of Romosozumab candidates via an expedited FLS referral pathway at a UK teaching hospital.

Methods

All post-menopausal female referrals between December 2023 and April 2024 were reviewed. Standardised data were collected including demographics, fracture site, treatment, cardiovascular history, NOGG and fracture risks. Eligibility for Romosozumab was assessed against local criteria, based on NICE and NOGG guidelines. Classification data analysis assessed alignment of referrals with local criteria.

Results

257 patients were included, mean age 80.1years (range 50-97). 87% were not on osteoporosis treatment at referral. 68% had a very high-risk FRAX score. 56% of referrals were accurate. 43% were referred as eligible for Romosozumab but 8% were actually eligible. The main reasons for non-eligibility were cardiovascular

risk and clinical frailty. 20 patients from the cohort were true Romosozumab candidates, of whom 45% were correctly identified at referral.
Conclusions
Most patients referred via FLS were classed as very high risk and deemed potential candidates for Romosozumab. However, only a minority were eligible based on NICE/NOGG criteria. Over half of suitable patients were not appropriately identified. These inaccuracies may result in under-identification of eligible patients and impede the expedited pathway. Targeted clinician education and improved referral processes may enhance identification of women at very high fracture risk and enable timely intervention.
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A case report of symptomatic hypercalcemia in familial hypocalciuric hypercalcemia

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Background
Familial hypocalciuric hypercalcemia (FHH) is a rare disorder inherited as an autosomal dominant trait, characterized by an inactivating mutation in the calcium-sensing receptor (CASR) gene. This most often presents clinically as a mild, persistent, and asymptomatic hypercalcemia with normal to mildly elevated serum parathyroid hormone, which rarely requires management with pharmacologic agents[1].
Case Presentation
We present a case of a 36 years old female who presented with 3 months history of polyuria and polydipsia along with worsening joint pains on the background of Ehlers Danlos syndrome. She was found to have moderate hypercalcemia of 3.24 mmol/l (normal range: 2.20-2.60 mmol/l) with borderline raised parathyroid hormone of 7.5 pmol/l (normal range:1.3–7.3 pmol/l) and adequate Vitamin D of 71.1 nmol/l. Her urinary calcium creatinine excretion ratio was low, in keeping with FHH. She had genetic testing which was consistent with Familial hypocalciuric hypercalcemia type 1. Over the course of few months, her symptoms and hypercalcemia did not improve despite adequate fluid resuscitation and IV Zolendronic acid. She had ultrasound neck and Sestimibi parathyroid scan to pick up any coexisting parathyroid adenoma, which came back negative. Her ultrasound renal and bone densitometry did not show any evidence of end organ damage. Eventually she was commenced on cinacalcet 30 mg twice daily which led to normalisation of hypercalcemia and the symptoms over the next few weeks.
Conclusion
This case highlights the diagnostic and management challenges posed by such presentation which is usually not expected in patients with Familial hypocalciuric hypercalcemia. This shows that FHH can present with moderate symptomatic hypercalcemia which require pharmacological intervention.
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GCM2 Activation association with hyperparathyroidism and oncogenic potential

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Introduction
Primary Hyperparathyroidism (PHPT) has a prevalence of 0.2% to 1.3% worldwide. 10% of all PHPT cases are hereditary. These include multiple endocrine neoplasia (MEN) 1, MEN2A, familial hypocalciuric hypercalcemia (FHH), familial isolated hyperparathyroidism (FIHP), neonatal severe hyperparathyroidism and hyperparathyroidism jaw tumour syndrome (HPT-JT). GCM2 variant gain-of-function heterozygous mutations have been reported in FHIP (which can mimic FHH) and sporadic PHPT in 1.5%-26.9% cases, seen more often in the Ashkenazi Jewish population [1]. There is often multiglandular involvement. A loss of function mutation in GCM2 is associated with *hypoparathyroidism*. There are no reported cases of GCM2 mutations and non-parathyroid cancers.
Case presentation
We present the case of a 49-yr old woman of Ashkenazi Jewish descent who had mild hyperparathyroidism, renal cell carcinoma, basal cell carcinoma along with a family history of hyperparathyroidism, breast cancer and kidney cancer. Her BRCA1 gene test was negative. She had borderline hypercalcemia (2.59 mmol/l), normal PTH (5.4 pmol/l), low urine calcium excretion (CCCR 0.83%), suggestive of FHH; an R151 gene panel test was sent which revealed a heterozygous variant GCM2 c.1181A>C p.(Tyr394Ser). She was osteopenic and a possible parathyroid adenoma was identified on ultrasound. Upon repeat testing, she had normal serum calcium levels and was asymptomatic. No further localising scans were performed as she was not for surgery.
Conclusion
This case highlights GCM2 gene activation and a possible link with non-parathyroid cancers. It is essential to take an in-depth family history and consider familial genetic screening for GCM2 mutations to identify FHIP and other possibly associated cancers; further studies on this mutation and other cancers are warranted to deduce whether there is an actual association.
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Incomplete bone density normalisation following long-term reproductive hormone treatment in male hypogonadotropic hypogonadism: a systematic review and meta-analysis

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Background
Men with hypogonadotropic hypogonadism (HH) are predisposed to reduced bone mineral density (BMD) and fracture risk. While reproductive-hormone therapy improves bone parameters, the degree of skeletal recovery and normalisation remains uncertain, and the long-term trajectory of bone health in this population is not well defined. We aimed to synthesise evidence on BMD in men with HH, compare values with healthy eugonadal men, and evaluate whether reproductive-hormone therapy achieves normalisation of BMD.
Methods
We systematically searched OVID Medline, Embase, CINAHL, Scopus, Web of Science, and the Cochrane Library from inception to July 2024 for studies reporting BMD or fracture outcomes in men with HH. Study selection and data extraction were performed using COVIDENCE and a pre-specified data extraction tool. Meta-analysis compared lumbar-spine (LS) BMD between HH and controls, and meta-regression assessed relationships of LS and femoral-neck (FN) Z-scores with treatment duration and HH subtype.
Results
Twenty-five studies meeting inclusion criteria reported 625 men with HH. LS BMD was significantly lower in HH than healthy controls (standardised mean difference -5.98; 95% CI -11.5 to -0.47; $P = 0.03$). Pooled mean Z-scores were -0.87 (LS) and -0.70 (FN). Meta-regression showed lower Z-scores in congenital vs acquired HH at LS (coefficient -2.28; $P = 0.027$) and FN (coefficient -1.31; $P = 0.0049$), with a non-significant trend toward higher LS Z-scores with longer treatment duration ($+0.07$ per year; $P = 0.094$). Younger age at treatment initiation, partial HH, and higher sex hormone concentrations were associated with better BMD. Among studies that reported fracture outcomes, prevalence ranged from 17–23%.
Conclusion
Reproductive-hormone therapy improves BMD in men with HH but does not fully restore skeletal health, particularly in congenital cases. Persistent bone

deficits highlight the importance of early diagnosis, optimised long-term hormone replacement, and prospective studies to clarify fracture risk and define bone-recovery potential.

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Our experience with intraoperative PTH measurement (IOPTH) during the initial surgery for primary hyperparathyroidism (PHPT): data on 250 patients

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Background
Since 2017, we have used IOPTH during surgery for all patients with PHPT and collected pre-incision (S1), pre-excision (S2), and 20 minutes post-excision (S3) samples. >50% drop in S3 from S1 or S2 predicts cure. We use second-generation PTH (intact) measurement by the Abbott immunoassay analyzer.
Patients and methods
We reviewed biochemical, histological, surgical, and imaging details of patients who had IOPTH from 2017-2024. We analysed the impact of IOPTH on surgical outcomes and its positive and negative predictive values. We mathematically estimated 10- and 15-minute post-excision PTH and correlated the presumed outcomes with our findings. We audited 40 patients for the time taken for the availability of results.
Results
$n = 251$; mean age 65years, 75% females; mean calcium 2.9mmol/l, PTH 25pmol/l. 236 (94%) patients were cured and 15 (6%) were not. 221 (88%) patients had >50% IOPTH drop, of which 217 were cured (true positive) and 4 were not (false positive). 30 (12%) patients had a PTH drop of <50% of which 1 was cured (false negative) and 29/30 were not (true negative). 18/29 patients were cured after further surgery, attributable to IOPTH use, while 1 had unnecessary dissection. The overall PPV was 98% and NPV 96.7%. With the use of a 10-minute sample, 28 and with a 15-minute sample 7 more false negative results would have been achieved. The per-patient cost is £10 as compared to around £400 with point-of-care testing. Mean availability time for IOPTH result was 35 minutes.
Conclusions
Although NICE does not recommend routine IOPTH for initial surgery, our experience shows it predicts surgical outcomes, improves cure rates, and limits dissection. Collecting samples at 20-minutes (rather than using Miami criteria) and using laboratory-based analyzer has replicated the best-reported success rates, keeping the expense at a negligible level at the cost of delayed results (35 minutes).

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Comparative analysis of ultrasound, SPECT-MIBI, and co-registered CT concordance with surgical outcomes in parathyroid adenomas

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Introduction
Surgery is the definitive treatment for primary hyperparathyroidism. Accurate preoperative localisation of parathyroid adenomas is paramount for minimally invasive parathyroidectomy. Common imaging modalities include 99mTc-SPECT-MIBI, co-registered CT, and ultrasound (US), though adding CT increases radiation dose, cost, and time. This retrospective study evaluated concordance among SPECT, CT, and US in lesion detection and surgical outcomes.
Methods
Patients with suspected primary hyperparathyroidism who underwent imaging and successful surgery between September 2023 and August 2025 were included. Out of 348 records screened, 47 met inclusion criteria, as most others were either waitlisted for surgery or managed medically.
Results
Out of 47 patients, 77% were female ($n = 36$), aged 28–85 years (median 52, IQR 20). Ten were <40 yrs, 10 aged 41–50 yrs, 21 aged 51–65yrs, and 6 were >65 yrs. FECa-based genetic testing ($n = 8$) showed two positives. Mean serum calcium was 2.92 mmol/l (median 2.82, IQR 0.23). Forty-six patients underwent all three imaging modalities; one had US only. US detected 31 lesions (4 inconclusive, 12 negative); 99mTc-SPECT-MIBI detected 30 (2 inconclusive, 15 negative); and co-registered SPECT/CT identified 29 (5 inconclusive, 13 negative). Twenty-two showed concordant SPECT/CT and US findings—20 of them (91%) matched surgical localisation, with 2 differing only by superior/inferior position. Seven lesions were diagnosed on CT-only, nine on US-only, and nine were undetected on imaging but underwent surgery due to severe hypercalcemia. Post-operative normocalcemia was achieved in all patients indicating excellent surgical outcomes.
Conclusion
This study demonstrated 91% accuracy for concordant preoperative parathyroid adenoma localisation, indicating that only two modalities are necessary—either 99mTc-SPECT-MIBI+ co-registered CT or 99mTc-SPECT-MIBI + US (when co-registered CT is unavailable). The choice depends on equipment and expertise. Simplifying from three to two modalities may reduce patient burden, streamline workflow, and lower costs without compromising diagnostic accuracy.

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A tanned clue: severe hypercalcaemia and multisystem involvement unmasking underlying diagnosis

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Introduction
Hypercalcaemic crisis (adjusted calcium>3.5 mmol/l) is a medical emergency requiring urgent treatment. This is usually associated with malignancy, but here, we present a case of a young woman admitted with hypercalcaemic crisis and multisystem involvement.
Case Presentation
A 28-year-old Caucasian woman with no medical history presented to emergency department with a 4-month history of weight loss (7 kg), abdominal pain, anorexia, recurrent vomiting, and amenorrhoea. On initial investigations, she was found to have severe hypercalcaemia (adjusted calcium 4.06 mmol/l) and severe acute kidney injury (serum creatinine 197 µmol/l, eGFR 29ml/min/1.73m2), with profound microcytic anaemia (Hb 56 g/l). An urgent computerized tomography (CT) scan demonstrated massive splenomegaly, hepatomegaly with multiple para-aortic, portal and peri-splenic lymph nodes. Further investigations revealed low parathyroid hormone (PTH) levels (0.7 pmol/l), and an oesophago-gastro-duodenoscopy (OGD) was normal except a small anterior stomach wall lesion, which was biopsied with normal pathology. On examination, she appeared very tanned, and further questioning revealed that her symptoms began after two back-to-back holidays along the Mediterranean coast with substantial sun exposure. Serum cortisol levels were 528 nmol/l ruling out adrenal insufficiency, and 1,25(OH) vitamin D levels were very high (261pmol/l; normal=43-144), suggesting extra-renal vitamin D conversion. Serum angiotensin converting enzyme (ACE) levels were markedly elevated (>150 IU/l; normal=20-70). Hypercalcaemia was conservatively managed with intravenous fluids initially, with partial success. Supraclavicular lymph node biopsy revealed non-caseating granulomatous lymphadenitis, confirming sarcoidosis. The patient was subsequently started on glucocorticoids with rapid normalization of symptoms and calcium levels.
Conclusions
1. Detailed history in this case established the link between sun exposure and onset of symptoms.
2. Sun exposure in granulomatous disorders results in extra-renal conversion of 25(OH) vitamin D to activated 1,25(OH) vitamin D via 1-alpha-hydroxylase enzyme in the macrophages, resulting in hypercalcaemia.

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Metachronous presentation of hypercalcaemia with Graves' hyperthyroidism followed by primary hyperparathyroidism: random occurrence or is there an association?

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Background
Hyperthyroidism can cause mild-to-moderate hypercalcemia due to parathyroid (PTH)-independent increase in bone turnover. Whether people predisposed to primary hyperparathyroidism are more likely to manifest hyperthyroidism-induced hypercalcaemia is unknown. We report a case of primary hyperparathyroidism diagnosed a decade after an initial presentation with Graves' disease associated with transient PTH-independent hypercalcaemia.
Case presentation
A 50-year-old woman was admitted to the hospital with a 10-week history of weight loss, lethargy, palpitation and polydipsia. TSH was undetectable, freeT4 >100.0 pmol/l and corrected calcium 3.03 mmol/l. Further investigations showed low PTH at 12 ng/l (≈1.27 pmol/l); thyroid peroxidase and TSH receptor antibody titres were raised. After initial rehydration and commencement of antithyroid therapy with Carbimazole, the acute hypercalcaemia resolved. She eventually underwent total thyroidectomy for recurrent Graves' hyperthyroidism 5 years after the initial presentation and was treated with lifelong levothyroxine therapy. Eleven years after the initial presentation, she re-presented with hypercalcaemia (levels ranging from 2.62 to 2.89 mmol/l). PTH was raised (ranging from 10.1 to 12.5 pmol/l). The urinary calcium excretion index was raised to 0.072 mmol/l. Subsequent investigations identified an enlarged right inferior parathyroid adenoma in the postoperative thyroid bed and osteoporosis. She underwent unilateral right inferior parathyroidectomy with a successful biochemical cure of primary hyperparathyroidism.
Discussion
This case demonstrates the uncommon presentation of PTH-independent hypercalcemia due to Graves' hyperthyroidism, followed years later by PTH-dependent hypercalcemia due to primary hyperparathyroidism. The metachronous presentations of these hypercalcaemic pathologies may reflect a random occurrence or yet unrecognised shared predispositions.

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P70

Longitudinal biochemical trends following parathyroidectomy for primary hyperparathyroidism: a single-centre experience from University Hospitals Birmingham

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Background
Primary hyperparathyroidism (PHPT) is a prevalent endocrine disorder, curable in most cases by parathyroidectomy. The *PARAT Consensus Statement* (Eur J Endocrinol 2022) and the *Fifth International Workshop* highlight limited real-world data describing long-term biochemical trajectories post-surgery, including the natural history of calcium homeostasis, renal function, and bone turnover. Understanding these dynamics is essential to refine post-operative monitoring and prevent chronic hypoparathyroidism (HypoPT)
Objective(s)
To define longitudinal biochemical trends following parathyroidectomy for PHPT and assess their implications for follow-up and risk stratification
Methods
Retrospective single-centre study of adults undergoing parathyroidectomy at Queen Elizabeth Hospital Birmingham (2011–2022). Demographic and biochemical data were extracted from electronic records. Longitudinal analyses used mixed-effects modelling (REML) to accommodate incomplete repeated measures.
Results
351 patients met inclusion criteria (mean age 58.1 ± 13.1 years; 76.1% female; 68.7% White British). 73.8% underwent single-gland excision, but increases, e.g.in CKD and MEN, correlated with reduced survival ($P < 0.001$). Mean calcium fell from 2.82 ± 0.18 mmol/l (<6 months pre-op) to 2.44 ± 0.16 mmol/l (0–1 month post-op), stabilising at 2.34 mmol/l ≥ 5 years. Phosphate rose from 0.84 ± 0.17 to 1.11 ± 0.22 mmol/l early post-op. Mean PTH decreased from 17.2 ± 15 to 3.97 ± 4.91 pmol/l early post-op, and median urine calcium:creatinine ratio from 0.73 to 0.38 ($P = 0.0463$). ALP declined from 106 ± 50 to ~86 U/l within 12 months. eGFR fell modestly (77 → 72 mL/min/1.73 m^2 at 5 years). Early hypocalcaemia (<2.10 mmol/l) occurred in 8%, but persistent HypoPT was uncommon.
Conclusions
This real-world cohort provides a detailed 10-year longitudinal biochemical dataset for PHPT in UK practice. Findings define expected post-operative trajectories and confirm low rates of sustained HypoPT. These data operationalise *PARAT* and international taskforce recommendations, supporting targeted monitoring and renal surveillance. They provide a benchmark for developing risk-stratified, resource-efficient follow-up pathways post-parathyroidectomy

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P71

Identifying an androgen-bone axis across reproductive-endocrine states

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Background
Reproductive-endocrine disorders influence bone homeostasis through complex, not fully understood hormonal mechanisms. Here, we compared bone turnover markers (BTMs) across distinct reproductive-endocrine states to investigate hormonal determinants of bone metabolism.
Methods
Fasting BTMs (P1NP, CTx) were assessed in women aged 20-36yrs, not receiving hormonal therapy: eugonadal controls ($n = 26$), hypothalamic amenorrhoea (HA;$n = 29$), congenital hypogonadotrophic hypogonadism (CHH;$n = 9$), and polycystic ovary syndrome (PCOS;$n = 56$). Groups were compared using Kruskal-Wallis test. Hormone-BTM correlations were assessed using Spearman-r.
Results
BTMs were highest in CHH: CTx - 0.61ng/ml vs controls (0.38ng/ml; $P = 0.01$), HA (0.39ng/ml; $P = 0.02$), and PCOS (0.34ng/m $P = 0.002$); P1NP - 86.7ng/ml vs controls (57.3ng/ml; $P = 0.01$), HA (58.1ng/ml; $P = 0.02$), and PCOS (53.1ng/ml; $P = 0.005$). Notably, bone turnover was higher in CHH than HA despite comparable oestradiol (HA:86pmol/l; CHH:85pmol/l), indicating additional modulators. Indeed, in HA, P1NP correlated with hypogonadism severity-indices (LH:$r = 0.51$, $P = 0.01$; oestradiol:$r = 0.53$, $P = 0.008$), and hormones of other endocrine axes characteristically disrupted in HA (IGF-1:$r = 0.44$, $P = 0.03$; fT3:$r = 0.49$, $P = 0.02$). Androgens consistently and positively correlated with bone turnover across groups: CTx correlated with androstenedione in controls ($r = 0.44$, $P = 0.04$) and HA ($r = 0.46$, $P = 0.03$), dihydrotestosterone in controls ($r = 0.44$, $P = 0.04$), and DHEAS in PCOS ($r = 0.29$, $P = 0.04$). P1NP correlated with dihydrotestosterone and androstenedione in controls ($r = 0.53$, $P = 0.01$;$r = 0.45$, $P = 0.03$) and HA ($r = 0.49$, $P = 0.02$;$r = 0.46$, $P = 0.03$), and testosterone in PCOS ($r = 0.36$, $P = 0.01$). P1NP also correlated with DHEAS in CHH ($r = 0.82$, $P = 0.03$) and PCOS ($r = 0.32$, $P = 0.02$). Finally, CTx correlated inversely with BMI in PCOS (r=-0.31, $P = 0.02$).
Discussion
Androgens emerged as consistent positive correlates of bone turnover across reproductive-endocrine states, underscoring potential mechanistic roles for androgens in female bone metabolism beyond oestrogen. Additionally, the strong DHEAS-bone association in CHH suggests adrenal androgen compensation for hypoestrogenism. In HA, our data identify multi-hormonal impacts on bone turnover, while in PCOS we identified BMI-dependent suppression of resorption. Together, these findings offer novel insights into the hormonal influences on bone metabolism across diverse reproductive-endocrine states.

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P72

Parathyroid bone disease in the medical management of primary hyperparathyroidism

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Background
The natural history of bone disease in primary hyperparathyroidism (PHPT) is uncertain when managed without parathyroidectomy. 25-hydroxyvitamin D

deficiency can further raise parathyroid hormone and potentially worsen bone disease. This study aimed to assess the prevalence of reduced bone mineral density (BMD) in a cohort with medically managed PHPT and to establish efficacy and tolerability of vitamin D supplementation, BMD-targeted therapy and cinacalcet.
Methods
A retrospective review of 90 individuals with PHPT attending a single centre. Parameters included biochemistry, radiology and prescription history. Data are described in mean +/- SD and percentages and frequencies (Graphpad v10.4.2).
Results
The mean age was 66.3 $\pm$ 11.7 years, adjusted calcium 2.77 $\pm$ 0.1mmol/l, PTH 10.7 $\pm$ 4.4mmol/l and vitamin D 64 $\pm$ 36nmol/l. 83 (92%) had a DEXA scan. Osteoporosis and osteopenia were identified in 30 (36%) and 37 (45%) respectively. Single site reduced forearm BMD was identified in seven cases (14%). There was no difference in age, gender, adjusted calcium, PTH and vitamin D in those with reduced and preserved BMD (all $P > 0.05$). 36 individuals (40%) commenced vitamin D at daily dose of 855 $\pm$ 237units with no significant change in adjusted calcium (2.68 $\pm$ 0.06 vs 2.69 $\pm$ 0.06 mmol/l, $P = 0.39$), serum phosphate (0.85 $\pm$ 0.13 vs 0.88 $\pm$ 0.16 mmol/l, $P = 0.26$) or PTH (11.7 $\pm$ 4.5 vs 11.0 $\pm$ 4.3 pmol/l, $P = 0.17$). BMD-targeted therapy and cinacalcet were prescribed to 32 (36%) and 23 patients (26%) respectively. 23 patients (26%) commenced cinacalcet.
Conclusion
Parathyroid bone disease is common in medically managed PHPT. Biochemical parameters are a poor predictor of the severity of bone disease. These findings suggest that maintenance dose vitamin D in PHPT does not significantly alter adjusted calcium, phosphate or PTH over the observed treatment period.

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P73

Somatostatin analogue induced-recalcitrant hypocalcaemia in post-surgical hypoparathyroidism

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Background
Somatostatin analogues are widely used in neuroendocrine tumours (NETs). While their metabolic and gastrointestinal (GI) side-effects are recognised, its clinical implications in calcium homeostasis are rarely reported. We describe a case of recalcitrant hypocalcaemia precipitated by somatostatin analogue in a patient with post-surgical hypoparathyroidism,
Case presentation
A 65-year-old woman with post-surgical hypoparathyroidism maintained a stable serum calcium concentration with a total daily dose of 2.25 mg alfacalcidol for years. Somatostatin analogue was commenced following the diagnosis of metastatic gastric NET. She developed loose stool and abdominal bloatedness after commencing on Octreotide LAR. Following the fourth monthly dose of Octreotide LAR 30 mg, she was admitted with a serum adjusted calcium of 1.46 mmol/l. She experienced severe symptomatic hypocalcaemia with perioral and extremities paraesthesia, along with carpopedal spasm. She required intravenous calcium infusion. Oral alfacalcidol dose was increased to 3 mg daily and regular calcium supplementation was started. She had two further admissions within two weeks for recurrent recalcitrant hypocalcaemia, with the lowest serum adjusted calcium of 1.55 mmol/l. Her adjusted calcium concentration eventually maintained at 2.00-2.20mmo/l, with a total daily dose of 4 mg alfacalcidol, along with 3g of calcium tablets. Octreotide LAR was discontinued and her diarrhoea and abdominal bloatedness resolved. Four months after cessation of Octreotide LAR, her adjusted calcium increased to 2.40mmol/l, alfacalcidol was gradually titrated down and she eventually returned to 2.25 mg alfacalcidol daily without calcium supplement.
Learning points
Somatostatin analogue therapy could exacerbates hypocalcaemia in patients previously established on active vitamin D analogue and calcium supplement. Pancreatic exocrine insufficiency could be induced by somatostatin analogue within 3 months, resulting in significant reduction in vitamin D absorption. Reduced gastrin and gastric acid secretion would also reduce intestinal calcium absorption, especially for calcium carbonate. Calcium citrate would be preferred in patients with achlorhydria and proton pump inhibitor use.

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P74

Missed opportunities in hypercalcaemic stone formers: detecting primary hyperparathyroidism

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Background
Primary hyperparathyroidism (PHPT) is an underdiagnosed metabolic cause of renal calculi, accounting for 3–5% of cases. This may lead to recurrent stone formation, pain, and repeated invasive interventions. Early detection and curative parathyroidectomy can prevent recurrence and reduce morbidity.
Methods
A single centre retrospective cohort study was performed including all patients presenting with renal calculi during 2023. Patients were stratified by serum calcium: hypercalcaemic (>2.6 mmol/l), high-normal (2.5–2.6 mmol/l), or normal (<2.5 mmol/l). Those with adjusted calcium >2.50 mmol/l were assessed for possible PHPT after exclusions including known alternative causes of hypercalcaemia and death. Eligible patients underwent testing for serum calcium, parathyroid hormone (PTH), 25-hydroxyvitamin D, and renal function. Patients with findings suggestive of PHPT were referred for endocrine surgical review and 24-hour urinary calcium analysis.
Results
Of 643 patients, 544 (84.6%) had serum calcium measured; 21% underwent lithotripsy or stenting. Elevated or high-normal calcium was found in 77 patients (14%; mean age 59 $\pm$ 17 years; 54% male). Following exclusions, 35 of 55 eligible patients (69%) completed further biochemical testing. Mean initial calcium was 2.57 mmol/l (SD 0.08; median 2.54, IQR 2.53–2.60). Mean PTH was 92.7 U/l (SD 57; median 83, IQR 53–118). 68% ($n = 21$) had elevated PTH (>68 U/l) of whom 76% ($n = 16$) had normal-range calcium on repeat testing. Vitamin D deficiency (<50 nmol/l) occurred in 31% ($n = 11$). Following endocrine surgical review; four underwent parathyroidectomy, and ten remain under evaluation for PHPT or normocalcaemic PHPT (nPHPT).
Conclusion
Targeted biochemical screening in renal stone patients enables early detection of PHPT, facilitating curative intervention and reducing recurrent stones disease. PTH and vitamin D testing should be considered in recurrent stone formers. nPHPT remains challenging to diagnose.

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P75

What's the highest calcium you have ever seen? A case of profound hypercalcaemia causing irreversible end stage renal disease

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Introduction
Worsening of hypercalcaemia is common during intercurrent illnesses in patients with primary hyperparathyroidism. Here, we present a patient with primary hyperparathyroidism developing an acute, severe exacerbation with the highest calcium level we have seen.
Case
A 66-year-old female was referred to the Endocrinology clinic by her GP with an incidental finding of hypercalcaemia on routine blood tests (adjusted calcium 2.61nmol/l (NR 2.12-2.51), phosphate 0.92nmol/l (NR 0.8-1.5), PTH 12.82pmol/l (NR 1.95-8.49), creatinine 73umol/l (NR 60-120)). She was asymptomatic with no evidence of end organ damage at the time so conservative management was pursued with a request for DEXA (showed osteoporosis) and urinary calcium:creatinine ratio (0.15mmol/mmol creatinine (NR0-0.59)). There was no family history of calcium disorders. Whilst awaiting follow-up, she had an acute admission with nausea, vomiting, drowsiness, polydipsia and constipation and serum calcium was profoundly elevated at 5.66mmol/l, phosphate 1.32nmol/l, creatinine 239umol/l, PTH 187.98pmol/l. This hypercalcaemia was consistent on repeat testing making a lab error unlikely. She was treated with IV fluids cautiously due to a history of heart failure. With this, the calcium gradually fell to 2.32nmol/l and has remained stable at 2.55-2.8nmol/l since, but creatinine did not improve and she has now developed CKD5. Ultrasound and SPECT both revealed a culprit parathyroid lesion but her journey has been complicated by calculus cholecystitis and exacerbations of heart failure and she has been deemed high risk for an anaesthetic. She is being prepared for dialysis.
Learning points
• Adjusted calcium level higher than 5.66mmol/l in primary hyperparathyroidism could not be found in the literature.

• Parathyroid malignancy must be a concern in sudden and profound hypercalcaemia but is difficult to diagnose without evidence of metastatic disease.
• Irreversible renal impairment can occur with profound hypercalcaemia in primary hyperparathyroidism, especially with coinciding risk factors such as hypertension, diabetes and diuretic therapy.

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P76

Successful treatment of tumour-induced osteomalacia with CT guided radiofrequency ablation

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A 71-year-old female with no significant past medical history was referred to endocrinology for persistently low serum phosphate and raised alkaline phosphate levels despite adequate replacement of vitamin D. She reported 10 years history of generalised body aches and muscle weakness. X ray imaging picked up multiple healed rib fractures. No history of childhood rickets, nor family history of hypophosphatemic rickets. She had significant proximal myopathy. Her laboratory workup in the clinic showed serum phosphate of 0.64 (0.8 to 1.5) nmol/l, adjusted calcium of 2.18 (2.2 to 2.6) nmol/l, 25 hydroxyvitamin D of 76 (>50) nmol/l, Parathyroid hormone of 15 (1.6 to 6.9) pmol/l, serum alkaline phosphatase of 390 (30-130) unit/l, serum creatinine of 77 (48-84) umol/l. Initially, a differential diagnosis of partial vitamin D resistance was considered and was commenced on calcitriol 1.5 mg once daily. DXA scan confirmed osteoporosis with T score of -3.6 at femoral neck and -2.3 at lumber spine. Calcitriol replacement normalised her calcium and PTH levels, but serum Phosphate remained low with inappropriately normal 24-hour urine phosphate at 12.6mmols. FGF-23 was elevated at 126 (reference range< 100) RU/ml. Ga 68 DOTATAE whole body PET CT showed avid lesion within the left anterolateral T7 vertebral body and 15 mm lesion was confirmed on MRI whole spine. She was treated with CT guided radiofrequency ablation. Day 4 post procedure, her phosphate levels were within normal range at 0.93nmol/l. Although, the histology was not convincing of phosphaturic mesenchymal tumour, her phosphate levels have remained within normal range off calcitriol for 5 months. Her muscle aches and bony pain have resolved. Repeat FGF-23 has dropped to 57 RU/ml and repeat DXA scan showed significant improvement in bone density with T score of -2.3 at femoral neck and -0.3 at lumber spine

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P77

Optimising referral for FHH: the role of CCCR thresholds and clinical confounders

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Background
Familial Hypocalciuric Hypercalcaemia (FHH) is a rare, benign cause of hypercalcaemia that closely mimics primary hyperparathyroidism (PHPT). Distinguishing FHH from PHPT is essential, as PHPT is often managed with parathyroidectomy. Surgery offers no benefit in FHH and carries unnecessary risk. FHH is characterised by elevated serum calcium, normal/mildly raised parathyroid hormone (PTH), and low urinary calcium excretion. The calcium–creatinine clearance ratio (CCCR) is a key discriminator: values <0.01 strongly suggest FHH, >0.02 usually exclude it, and 0.01–0.02 are considered indeterminate and may prompt genetic testing. CCCR results may be artificially lowered by vitamin D deficiency, renal impairment and medications, potentially leading to unnecessary genetic testing. Genetic testing is definitive but costly and inappropriate referrals burden NHS resources.
Methods
We retrospectively reviewed 35 patients referred for FHH genetic testing over a 4-year period. Data included serum calcium, PTH, CCCR, vitamin D, renal function, medication, family history, and genetic testing outcomes.
Results
CCCR values were available for 32 patients: <0.01 ($n = 16$), 0.01–0.02 ($n = 10$), >0.02 ($n = 6$). All 3 confirmed FHH cases had CCCR <0.01. All patients with CCCR ≥0.01 tested negative, giving an NPV of 100%. The PPV of CCCR <0.01 was 19% (3/16). Within the <0.01 group, 8/16 (50%) had vitamin D deficiency or confounding medication. Within the 0.01–0.02 group, 6/10 (60%) had confounders; all tested negative. 6 patients with CCCR >0.02 were inappropriately referred.
Conclusion
All FHH cases were identified by CCCR <0.01, while no positives were seen in higher ranges, supporting its use as a reliable rule-out test. Addressing confounders before referral could have reduced genetic testing by at least 54% (19/35 patients) without missing any true cases, with further reductions possible if <0.01 patients with confounders were re-evaluated. This would improve appropriateness of testing, deliver cost savings, and maintain safe investigation of hypercalcaemia.

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P78

Efficacy of Recombinant Human Parathyroid Hormone (rhPTH 1-84, Natpar) in Patients with Treatment-Resistant Chronic Hypoparathyroidism

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Background
Conventional treatment for chronic hypoparathyroidism (HypoPT) is activated vitamin D analogues and calcium supplementation. Recombinant parathormone (rhPTH 1-84, Natpar) provides physiological replacement and has demonstrated better biochemical control & QoL in REPLACE & BALANCE trials.
Aims
To assess the impact of Natpar on biochemical parameters and QoL in HypoPT.
Methods
Retrospective electronic records review of 128 consecutive Hypoparathyroid patients with at least 12-months treatment between 1987 & 2025, focusing on pre-/post Natpar arms, comparing conventional treatment (non-Natpar); audit No 9217.
Results
$n = 128$ (Natpar 5, Non-Natpar 123), mean age 53yrs, Mean duration of follow up 16.5yrs. $n = 5$ Natpar patients with mean follow-up 4.6yrs. Pre-Natpar Mean calcium 2.31 mmol/l (1.72–3.70); post-Natpar Mean Calcium 2.18 mmol/l (1.90–2.56). Mean eGFR improved from 77 to 92 mL/min. 1 hospital admission for hypocalcaemia; 1 patient had osteopenia (likely pre-existent); others had normal bone density. HPQ-28 scores (QoL questionnaire): pre-Natpar (24, 45, 15, 19) vs post-Natpar (8, 3, 2.5, 6.6), with the greatest gains in mood and energy. Patients describe Natpar as 'a game changer'.

Parameter	Pre-Natpar	Post-Natpar	Non-Natpar
Number of patients	$n = 5$	$n = 5$	$n = 123$
Mean follow up (years)	9.6 yrs	4.6 yrs	16.5 yrs
Male:Female ratio	3:2	3:2	34:89
Mean age	50	51.75	53 yrs
Mean Adj' Calcium	2.31	2.18	2.2
Range of Adj' Calcium	1.72-3.20	1.90-2.56	1.87- 2.84
Hypo/-hypercalcaemia admissions	13 & 3	1	423 & 99
Mean e-GFR	77	92	72
Calciuria	5/5	0/5	Not collected
Mean HPQ-28 score	24	5	Not collected

Discussion
1. Natpar improves biochemical control, renal function and QoL in HypoPT, & is an option in patients inadequately controlled on conventional treatment.
2. Natpar is withdrawn from the market in December 2025 due to production issues; PTH analogues such as Palopegteriparatide & Eneboparatide bear similar beneficial outcomes & could potentially be considered as alternatives.

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P79

Hypophosphatasia: the hidden diagnosis behind persistently low alkaline phosphatase: case report

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Background
Hypophosphatasia (HPP) is a rare autosomal recessive metabolic bone disease caused by mutations in the ALPL gene, which encodes tissue non-specific

alkaline phosphatase (TNSALP). Reduced TNSALP activity disrupts mineral homeostasis, impairing bone and teeth mineralization. Heterozygous mutations may produce asymptomatic carriers or mild disease through a dominant negative effect. Clinical severity depends on the mutation type and whether it is mono- or biallelic. Perinatal and infantile forms are severe and often fatal. Childhood and adult forms are milder, with bone pain, fractures, bowed legs, premature loss of deciduous teeth, dental caries, muscle weakness, and fatigue. These forms respond to enzyme replacement therapy -Asfotase alfa. Mildest cases, as this case, features are limited to early tooth loss and severe dental caries. Diagnosis is challenging due to HPP's rarity, non-specific symptoms, and limited clinician awareness.

Case

A 16-year-old female was referred for persistently low ALP noted over several years. Reported a three-year h/o knee, knuckle, lower back pain, and fatigue. Due to extensive dental caries and fillings unusual for her age, dentist suggested medical evaluation. No family history or fractures. Biochemistry showed consistently low ALP (24–26 U/l; ref 60–425) and elevated urinary phosphoethanolamine, with normal calcium, phosphate, vitamin D, and copper studies (excluding Wilson's disease). Genetics revealed a heterozygous pathogenic ALPL variant (p.Q76R), confirming hypophosphatasia. Management involved multidisciplinary care with regular dental follow-up, optimal oral hygiene, pain control, and ongoing bone health surveillance with imaging as indicated.

Conclusion

HPP should be suspected in young individuals with low ALP, joint pain, and dental complications. Early recognition and multidisciplinary medical-dental care are essential for better long-term outcomes. **Bisphosphonates** and other antiresorptives **should be avoided** as these can further impair bone mineralization. Prompt diagnosis prevents misdiagnosis as osteoporosis later in life and avoids further harm to bone and dental health.

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P80

A rare case of hypocalcemia due to a genetic form of isolated hypoparathyroidism

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A 60 years old male patient was referred due to persistent asymptomatic hypocalcaemia with an adjusted calcium ranging between 1.9 to 2.08 mmol/l. He has always had normal Kidney functions, Magnesium, Phosphate and Vitamin D and normal PTH (ranging between 2.6-3.2 pmol/l) when checked. To investigate the hypo-parathyroidism, Genetic testing was done and he was found to be heterozygous for a pathogenic CASR variant consistent with Autosomal dominant hypocalcaemia type 1 (ADH1). He was started on Vitamin D replacement (Calci D 1000 mg/1000 units once daily) and he was also investigated for the possible complications by having an Ultrasound (KUB) which didn't show any stones. ADH1 is a rare form of hypoparathyroidism due to activating variants of the calcium-sensing receptor gene (*CASR*) altering the set point for extracellular calcium, resulting in inadequate parathyroid hormone (PTH) secretion and inappropriate renal calcium excretion leading to hypocalcemia and hypercalciuria Despite our patient being asymptomatic, ADH1 is often associated with severe symptomatology at presentation with an increase in the risk of renal complications after initiation of conventional therapy. Conventional treatment consists of active vitamin D analogues and/or calcium supplements. Thiazides and a low sodium diet may be considered. Raising serum calcium may induce or exacerbate pre-existing hypercalciuria, increasing the risk for long-term renal complications, therefore, treatment aims to achieve serum calcium levels within or just below the lower normal reference range for calcium. Distinct from postsurgical hypoparathyroidism, ADH1 is often associated with more pronounced hypercalciuria, especially after the initiation of treatment. Assessment for complications includes nephrocalcinosis, nephrolithiasis, renal impairment. Regular 6 monthly follow-up includes monitoring adjusted calcium, magnesium, phosphate ,Vitamin D , 24-hours urinalysis of calcium and creatinine. Renal ultrasonography (RUS) or CT should be performed at the initial assessment. Serum calcium should be re-measured within days after adjustments in treatment.

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P81

From longstanding hypercalcaemia to spontaneous normocalcaemia: parathyroid auto-infarction or alternative mechanisms?

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Introduction

Primary hyperparathyroidism (PHPT) is a common endocrine disorder. It is most often caused by one or more autonomously functioning parathyroid adenomas (up to 85%), less commonly by parathyroid hyperplasia (<15%), and rarely (1–2%) by parathyroid carcinoma. Spontaneous remission due to necrosis, haemorrhage, or infarction of a parathyroid adenoma—referred to as "parathyroid auto-infarction" or "parathyroid apoplexy" is rare. We present a case of suspected parathyroid auto-infarction managed conservatively with clinical and biochemical surveillance.

Case Presentation

A 72-year-old woman was diagnosed with PHPT in 2013, based on persistent hypercalcaemia (2.70–3.09 mmol/l), elevated PTH levels (7.2–13.1 pmol/l). Conservative management was initially recommended. She was lost to follow-up. Re-referred in 2021 after sustaining a left wrist fragility fracture. DEXA scan showed progression from osteopenia (2013) to osteoporosis (T-score -2.5). Kidney ultrasound revealed stones. Surgical management was considered. However, initial localisation studies (ultrasound and MIBI scans) were inconclusive. PET-CT performed for a lung nodule incidentally identified a 9mm parathyroid adenoma anteroinferior to left thyroid and a second 9mm ectopic adenoma in anterior mediastinum. She was referred for surgery, but a review in February 2023—prior to further intervention—revealed unexpected normalisation of calcium (2.47 mmol/l), PTH (4.3 pmol/l), and low fractional calcium excretion (0.07%), with optimal vitamin D levels (84.6 nmol/l) (eGFR 78). Her biochemistry has remained normal since. She reported no symptoms of neck pain or dysphagia.Most plausible explanation for this spontaneous resolution is auto-infarction of a parathyroid adenoma. She remains under close follow-up with biochemical monitoring every 3–4 months.

Conclusion

Parathyroid auto-infarction should be considered in cases of spontaneous PHPT resolution. Though rare, recurrence is well-documented, making long-term clinical and biochemical surveillance crucial. While surgery is often recommended following auto-infarction, selected patients—like this case -may be managed conservatively with close monitoring.

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P82

An audit of management of Vertebral Fractures detected and reported from lateral CXR using AI technology in a tertiary Oncology centre

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Vertebral Fractures (VF) are common (10-15% on routine imaging), associated with significant morbidity, and strongly predict further fractures. Up to 70% of VF don't come to medical attention. Of VFs reported there are low levels of subsequent action to improve bone health. AI techniques to detect VF on imaging (lateral CXR, CT) are available and undergoing evaluation by NICE. A project using AI technology to detect VF on lateral CXR is underway in our institution. This audit aimed to review the impact of reporting VF detected by AI on lateral CXR. Patients with a VF (n = 173) detected by Al on CXR within a 3 month period (Oct-Dec2024) were identified (audit registered with local QICA committee). Data from n = 80 were analysed (n = 35/80 new VF) using local EPR system. Demographic data, CXR indication, oncology history (known metastatic disease), ECOG performance score and fracture management were collected into a pseudo-anonymised EXCEL spreadsheet. Mean(+/-SD) age 67(+/-10)yrs (43Female), Cancer diagnoses: Lung(n = 21), haematological (n = 16), breast(n = 11), oropharyngeal(n = 9) gynaecological(n = 8), other (n = 15). 18/80 died subsequent to CXR, 51/80 were on curative treatment pathway(29 palliative/end of life). 50/80 had CXR for infection, 8/80 chest pain, 7/80 disease specific follow-up, 6/80 pretreatment imaging. 27/35 of the new VF were classified as osteoporotic (8 metastatic). 23/35 had further imaging with only

9/23 mentioning VF, 8/35 had a referral for a DXA scan, 27/35 were taking calcium/vitD, 7/35 were prescribed bisphosphonates/denosumab and 0/35 were referred to a metabolic bone clinic. VFs were commonly found on CXR in this population. 77% of new fractures were osteoporotic, 63% on a curative pathway, but only 22% referred for DXA and 22% on bisphosphonates/denosumab with no patients referred to metabolic bone clinic. This highlights a significant opportunity for development of defined VF pathways.

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Endocrine Cancer and Late Effects

P83

Audit of adrenal biopsies at a large tertiary referral centre: a decade of improving outcomes

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Background
Adrenal biopsies are used sparingly in the diagnosis of adrenal tumours and should only be undertaken when stringent criteria are met. A 2014 audit at Queen Elizabeth Hospital Birmingham (QEHB) showed only 17% of biopsies performed over a 10-year period were undertaken in accordance with guideline recommendations. This formed the basis for the implementation of a specific local pathway, including the recommendation that adrenal biopsies should only be undertaken after adrenal Multidisciplinary Team (MDT) review.
Aim
To re-audit indications and outcomes of adrenal biopsies (2015-2024) at QEHB against 2014 standards.
Methods
Electronic databases were searched for entries associated with the term 'adrenal biopsy' (01/01/2015 – 30/09/2024). Two independent researchers reviewed each biopsy against criteria: i) exclusion of phaeochromocytoma, ii) prior discussion in adrenal MDT, iii) clinical indication according to ESE-ENSAT guidelines, and iv) biopsy completion within two weeks.
Secondary analyses
- Sensitivity and specificity for diagnosis of malignancy.
- Rate of non-diagnostic and abandoned biopsy attempts.

Results
48 adrenal biopsies were reviewed, of which 15 (31%) m*et a*ll criteria. Biochemical exclusion of a phaeochromocytoma had been secured in 43 cases (90%, vs 21% in 2014). 46 requests were clinically indicated (96%, vs 47% in 2014), while 37 had been discussed in adrenal MDT. Median wait was 15 days, with 23 (48%) biopsies completed within 2 weeks. The rate of biopsies not resulting in diagnosis was 12.5% (4/6 non-diagnostic, 2/6 insufficient), abandoned attempts 2.1%, complications 0%. Of 30 biopsies assessed for diagnostic performance for malignancy, sensitivity and specificity were 95% (CI: 75.1-99.9%) and 100% (CI: 69.1-100%), respectively. Biopsy results changed management in 29 (60%) cases.
Conclusions
This audit showed improved standards of care for patients undergoing adrenal biopsy QEHB including appropriate use and prior exclusion of catecholamine excess for most patients. Referral to procedure time was highlighted as an area for improvement.

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Epigenetic characterisation of canine insulinoma: a comparative model for human disease

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Background
Pancreatic neuroendocrine tumours (PNETs), including insulinomas, are rare but clinically important neoplasms for which surgery remains the only curative treatment. Development of effective non-surgical therapies is hindered by the lack of representative pre-clinical models, particularly of complex biological pathways including epigenetic gene regulation. Dogs spontaneously develop insulinomas that closely mimic human insulinomas, providing a unique opportunity for comparative studies.
Aim
Compare the epigenetic landscape and response to epigenetic-targeting drugs, of canine insulinoma cell line canINS with existing models to assess its translational relevance to human insulinomas.
Methods
We performed single-cell RNA-sequencing (scRNA-seq) of canINS and MIN6 (mouse) and examined the expression of known human PNET driver genes in canINS, BON1 (human) and MIN6 using quantitative real-time PCR (qPCR) and western blotting. The efficacy of various epigenetic-targeting drugs was tested using CellTiter-Blue assays.
Results
scRNA-seq analysis demonstrated high *ATRX* and *YY1*, intermediate *DAXX* and low *MEN1* expression in canINS and MIN6. qPCR confirmed canINS expressed high *ATRX* and *YY1*, however showed low *DAXX* and intermediate *MEN1* expression. Compared with BON1 and MIN6, canINS showed the highest relative *YY1* (>5-fold) and *ATRX* (>12-fold) expression. *DAXX* expression was similar across all cell lines. *MEN1* expression was highest in MIN6 (>21-fold) and intermediate in canINS, confirmed by western blotting. Five-day treatments with 1μM DNA methyltransferase (DNMT), histone deacetylase (HDAC) and histone methyltransferase (KDM) inhibitors all significantly ($P<0.05$) reduced canINS and MIN6 viability. In BON1 only HDAC and bromodomain and extra-terminal inhibitors significantly reduced viability.
Conclusion
High expression of *MEN1* and *ATRX* observed in canINS indicated it may represent an improved epigenetic insulinoma model compared to BON1 and MIN6, as *DAXX/ATRX* and *MEN1* mutations are not typically observed in insulinoma patients. Multispecies drug screening revealed conserved sensitivity to epigenetic-targeting drugs in insulinoma cell lines, particularly HDAC inhibitors, supporting their potential therapeutic utility.

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P85

Mapping the endocrine impact of immunotherapy: a retrospective audit and future service implications

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Background
Immune checkpoint inhibitors (ICIs) targeting PD-1, PD-L1 or CTLA-4 have transformed cancer therapy across multiple malignancies. However, they can induce immune-related adverse events (irAEs), with thyroid dysfunction being the most common endocrine toxicity. This audit assessed the incidence, timing and management of thyroid dysfunction in patients receiving ICIs, and evaluated projected implications for endocrine service provision.
Methods
A retrospective review was conducted of patients who received ICIs at St. James's Hospital, Dublin, between July and December 2022. Data collected included cancer type, immunotherapy regimen, thyroid function test (TFT) abnormalities, dates of onset and resolution, and whether levothyroxine was initiated. Management was assessed against European Society of Endocrinology guidelines. Q4 2024 prescribing data was then used to more accurately estimate future impact, given the exponential growth of ICI use since 2022.
Results
Of 96 patients, 10.4% developed thyroiditis (median onset 31 days; resolution 35 days), 9.4% developed hypothyroidism without preceding thyroiditis (median onset 105 days), and 47.9% had other TFT derangements. Among 11 patients initiated on levothyroxine, 9 were treated in accordance with guideline recommendations. There was no significant association between cancer type and thyroid irAE ($P = 0.138$), but a trend toward significance with ICI type was noted ($P = 0.07$). Based on prescribing trends, approximately 412 patients may receive ICIs between July and December 2025, with an estimated 43 developing thyroiditis, 39 hypothyroidism, and 197 with TFT derangements requiring clinical interpretation.
Conclusions
Thyroid dysfunction is a frequent IRAE following ICIs, with early onset in most cases. These findings highlight the need for proactive TFT monitoring and structured endocrine-oncology collaboration to support the growing immunotherapy patient population.

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Oesophageal neuroendocrine tumour masquerading as small cell oesophageal carcinoma: a case series of conundrums

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Oesophageal neuroendocrine tumours (NETs) are much rarer than other GI NETs, the majority showing aggressive behaviour. Amongst these, well-differentiated neuroendocrine tumours, poorly differentiated neuroendocrine carcinomas (NECs), and mixed neuroendocrine-non-neuroendocrine neoplasms can be recognized. A 66-year-old male with no past medical history presented with progressive dysphagia. Upper gastrointestinal endoscopy revealed circumferential narrowing at 33-37 cm with superficial ulceration. Biopsy was suggestive of poorly differentiated squamous cell carcinoma (SCC). Despite seven cycles of neoadjuvant chemotherapy (docetaxel, cisplatin, fluorouracil), a suboptimal response was noted, and tumour progression was seen on repeat endoscopy. Repeat oesophageal biopsy immunohistochemical (IHC) staining revealed cytokeratin, CD56 and chromogranin, and synaptophysin were positive, and p63 was negative. 54-year-old male presented with 3 months of dysphagia. Upper gastrointestinal endoscopy revealed ulcero-proliferative growth at the mid-thoracic oesophagus. On biopsy, a diagnosis of possible poorly differentiated SCC was given. On IHC, CD56 and chromogranin were positive. 63-year-old female being followed up in NET clinic, initial histology suggestive of well-differentiated gastrin-positive oesophageal NET. Noted marked tumour aggressiveness and poor response to chemotherapy. Repeat endoscopy was suggestive of oesophageal SCC. Accurate pathological diagnosis of NETs is challenging due to difficulties in distinguishing NETs/NECs from other poorly differentiated oesophageal neoplasms. NECs have often been misdiagnosed as SCCs due to the co-existence of squamous cell carcinoma and/or adenocarcinoma. Generally, neuroendocrine biomarkers, such as Synaptophysin and Chromogranin, are essential for the diagnosis of NETs. IHC is very useful for identifying typical NET histology and cell differentiation. Immunohistochemistry may prevent confounders with small cell carcinoma and mixed histology. Recognising possible co-existence of neuroendocrine tumours or carcinomas with parent organ malignancy is essential. Variability in tumour behaviour may be an indicator of a dual nature that needs close liaison of endocrine, oncology, and histopathology.

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P87

RAD-PIT: Novel PPIE-driven protocol co-design for the use of Macimorelin as a diagnostic test of pituitary function for patients undergoing proton and photon radiotherapy

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Growing evidence suggests that co-designing research protocols with patient and public involvement and engagement (PPIE) members, industry partners and other relevant stakeholders enhances acceptability, feasibility, and engagement. There are no recognised UK protocol co-design recommendations. This project aimed to explore best practice for co-design by developing a research protocol for the use of Macimorelin to diagnose Growth Hormone Deficiency in adults and teenagers and young adults (TYAs), with brain, head, and neck cancer experience. Macimorelin is a NICE-approved diagnostic test, with reduced side effects, currently untested in this cranial radiotherapy population. Validation of its effectiveness may be too burdensome for these vulnerable patients; it is, therefore, imperative that we investigate patient/clinician acceptability. Co-design took place through in-person and online exploratory stakeholder events across three work packages (WPs) to understand (1) the barriers of working together, (2) the acceptability of the diagnostic test, and (3) the creation of the research protocol. Stakeholders included PPIE members, project leads, pharmaceutical representative, clinicians, statistician, and PPIE expert host (Vocal). We captured feedback about the process from all involved. Eight working together principles were identified during WP1: trust, honesty, communication, unity, respect, inclusivity, learning, and support. These formed our 'Working Together Guidelines', ensuring open, respectful and supportive communication throughout the project. In WP2, events for TYAs and adults were held, increasing engagement and allowing tailored age-appropriate sessions. Contributors shared protocol preferences and reservations, resulting in a potential protocol to take forward to WP3. WP3 was held online (5 sessions) and involved clinicians, scientists and public advisors ($n = 2$) to create a fully informed and co-designed research protocol. The process was well-received by all stakeholders. Collaborative research protocol co-design for endocrine studies using working together principles is inclusive, generates novel and diverse perspectives and enhances equality and satisfaction for all stakeholders. *(Stakeholder quotes available for presentation)*

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A metastatic pulmonary neuroendocrine tumour presenting as wisdom tooth pain

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Neuroendocrine tumours (NETs) are rare malignancies often presenting with non-specific symptoms, delaying diagnosis[1]. Most are detected at advanced stages, commonly metastasising to the liver, bone, and lymph nodes[2]. Metastasis to the head and neck, particularly the mandible, is exceedingly uncommon[3]. We present a rare case of metastatic pulmonary NET initially manifesting as dental pain, highlighting the diagnostic challenges and importance of multidisciplinary evaluation in such atypical presentations. A 71-year-old man with a previous history of thyroid and prostate cancer presented with persistent left lower third molar pain. Dental radiography revealed a radiolucent lesion surrounding the tooth and involving the inferior alveolar nerve. During extraction, the mandibular bone appeared moth-eaten, raising suspicion of malignancy. Histopathology demonstrated malignant cells positive for CK7, CK20, CK19 (~35%), synaptophysin, and CD56, consistent with a neuroendocrine phenotype, and negative for markers including Melan-A, TTF-1, PAX8, and PSA, suggesting a third primary malignancy. CT and DOTATATE PET imaging revealed widespread metastases in the lungs, liver, and bone. Biopsy of a liver lesion confirmed a large-cell neuroendocrine carcinoma (Ki-67 40%) with focal TTF-1 positivity, indicating a pulmonary origin[4]. The patient commenced carboplatin–etoposide chemotherapy and received palliative radiotherapy to the bone lesions. This case demonstrates a rare presentation of metastatic pulmonary NET with mandibular involvement, mimicking odontogenic pathology[3,5]. Such cases emphasise the need for early biopsy when clinical or radiographic features are atypical. Multidisciplinary input was crucial in diagnosis and management. In patients with known malignancy or unexplained oral symptoms, metastasis should be considered early. Mandibular metastasis from a pulmonary NET is extremely rare and can mimic benign dental disease. Prompt recognition, histological confirmation, and coordinated MDT care are essential for optimal management of such atypical cases.

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Adrenocortical Carcinoma in Lynch Syndrome – an oft-forgotten marriage

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Background
Lynch Syndrome (LS) is a genetic syndrome that increases the risk of various forms of cancers, including ovarian, pancreatic and bowel cancers. A rare but oft-forgotten association is with adrenocortical carcinoma (ACC). A previous study revealed that LS has a prevalence of 3.2% in patients presenting with ACC. Failure to consider this association and arrange the appropriate genetic testing may result in disastrous consequences for patients diagnosed with ACC. Our case demonstrates the positive patient outcomes that can be achieved when this association is kept in mind.

Case Presentation
A 31-year-old male patient presented to the emergency department at Frimley Park Hospital with a multiple week history of vague right-sided abdominal pain associated with weight loss. Abdominal imaging revealed a 14 cm right-sided adrenal tumour which appeared to be causing a mass effect in the region. Subsequent biochemical testing revealed that this tumour was consistent with ACC, with failure to suppress on overnight dexamethasone testing and the presence of androgens detected in a 24-hour urinary collection. This patient was referred for urgent adrenalectomy and was started on mitotane in the post-operative phase, along with appropriate hormone replacement therapy. Genetic testing was positive for Lynch Syndrome, thus appropriate post-operative monitoring was arranged. Post-operative imaging has thus far revealed no evidence of metastatic spread. Furthermore, both post-operative upper GI endoscopy and colonoscopy have excluded the presence of any gastrointestinal carcinomas, and the patient has been placed in the appropriate screening programme.
Conclusion
This case reinforces the importance of screening for Lynch Syndrome in those with confirmed adrenocortical carcinoma to facilitate early identification and treatment of any associated malignancies. Referral to the NHS Bowel Cancer Screening Programme, with bowel surveillance every two years, is especially essential.

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P90

Selective internal radiation therapy (SIRT) for stage IV adrenal cortical cancer: a case report and review of the literature

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Case presentation
We present a case of a 32-year-old male who presented with Cushing's syndrome. Investigations confirmed a diagnosis of metastatic adrenal cortical carcinoma (ACC) with bilobar liver and multiple lung metastases. He underwent primary tumour resection (histology confirmed 21 cm ACC, T2N0M1, ENSAT stage IV, ki-67 22%), and he commenced mitotane and etoposide, doxorubicin and cisplatin (EDP) chemotherapy. There was a good partial response (PR) with reduction in the size of liver lesions and complete resolution of all lung metastases. Liver only disease was targeted by left segment liver resection, followed by selective internal radiation therapy (SIRT). This was well tolerated and resulted in initial complete response (CR). On subsequent imaging there were two small areas in segment 7 and 8 with viability, and a new right upper lobe lung nodule. He underwent VATS lobectomy for the lung lesion (histologically confirmed metastasis) and repeat SIRT to the segment 7 lesion and irreversible electroporation (IRE) for the segment 8 lesion. Post-treatment imaging revealed a good response, but showed an ablation-related segmental portal vein thrombus. Clinically he is well and is on therapeutic dose anticoagulation. A 6-month restaging scan post repeat SIRT/IRE demonstrated no measurable viable disease.
Discussion
Metastatic ACC has a poor prognosis with limited treatment options. This case highlights the successful use of a multimodality strategy for disseminated metastatic ACC, with combination systemic and locoregional therapies including SIRT to achieve complete treatment response. To our knowledge there are only five published case reports of SIRT in patients with ACC. Two patients had CR and 3 had PR. The reported progression-free survival (PFS) ranged 1-3 years, with minimal adverse events reported.
Conclusion
SIRT has been used effectively to manage metastatic ACC with liver only disease. Prospective studies are warranted to investigate its role in treatment of metastatic ACC.

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Androgen steroidogenesis and functional effect in mucinous ovarian cancer cells, organoids and patient tumours

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Background
Ovarian cancer (OC) is the sixth most prevalent cancer and the deadliest gynaecological malignancy among UK females. Epithelial ovarian carcinoma (EOC) accounts for 90% of OC; mucinous ovarian carcinoma (MOC) is a rare EOC subtype, representing 3–5%, with advanced/ recurrent MOC carrying poor clinical outcomes. Previous work from our laboratory suggests steroidal metabolism in MOC patients is distinct from other EOC subtypes and healthy controls. Here, we investigate androgen metabolism and its consequences on MOC cell lines, organoids, and primary tumour tissue.
Methods
Steroidogenesis enzymes and receptor expression in MOC cells were assessed utilising two publicly available datasets and through RT-qPCR. Metabolism of androgenic steroids were investigated using LC-MS/MS in EOC cell lines, MOC organoid models and in human tumour tissue. Functional consequences of androgens on proliferation and migration in MOC cell lines were also investigated.
Results
The androgen metabolism enzymes SRD5A1/3 and HSD17B2/4 show similar RNA levels across cell lines. AKR1C3 expression is higher in MOC (2–10 TPM) than HGSOC (1–6 TPM). Androgen receptor (AR) and KLK4, an AR-response gene, RNA levels alter following androgen treatment. After 24-hours of testosterone treatment, synthesis of the less biologically active androstenedione was >6 times higher in MOC cell lines than HGSOC. Androstenedione was also the predominant metabolite of T conversion across MOC organoids (24nM after 6hrs, 40nM after 24hrs) and matched fresh patient tumour tissue (36nM after 24hrs). Androgens were also shown to negatively impact MOC proliferation compared to HGSOC.
Conclusion
Androgen metabolism is different between MOC and HGSOC cell lines. MOC cells demonstrated a preference towards synthesis of inactive androgens, which is consistent across 2D cells, organoids, and primary models. Furthermore, androgens may have a different functional effect in MOC compared to HGSOC.

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RNA-seq analysis of transcriptional co-regulators of NIS in a murine model of triple negative breast cancer

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Introduction
The sodium iodide symporter (NIS; *SLC5A5*) is the sole transporter of iodide, exploited in radioiodide treatment of differentiated thyroid cancer. NIS is expressed in breast cancer (BrCa), but its intracellular retention prevents sufficient radioiodide uptake for tumoural ablation. Pre-clinical studies suggest that upregulation of *SLC5A5* is promoted by retinoic acid receptor alpha (RARα), and that this mechanism is epigenetically corrupted in BrCa via upregulation of the RARα co-repressor PRAME. We recently reported that the histone deacetylase (HDAC) inhibitor SAHA - combined with the disulfiram metabolite $Cu(DDC)_2$ - significantly increased NIS function in MDA-MB-231 orthotopic tumours. Here, we employed RNA-seq analysis of these tumours to determine whether transcriptional co-regulators impact NIS expression in BrCa.

Methods
Global changes in gene expression in response to SAHA and $Cu(DDC)_2$ were appraised by RNA-seq analysis. Differentially expressed genes (DEGs) were identified and analysed using DSeq2 and DAVID.
Results
PRAME-overexpressing MDA-MB-231 cells demonstrated significantly lower anti-proliferative responses to ATRA (pan RAR ligand) and AM580 (RARa ligand). PRAME overexpression led to trans-repression of RARα canonical target genes and *SLC5A5* in response to ATRA. We therefore established a panel of BrCa cell lines (MDA-MB-231, SUM52, AU565, SKBR3) stably transfected with either CRISPR-VP64 (activator) or CRISPR-KRAB (repressor), measuring the expression of *SLC5A5* and the ability to transport radioiodide. Gene ontology enrichment analysis and pathway mapping of *in vivo* BrCa tumours treated with SAHA and $Cu(DDC)_2$ highlighted transcriptional regulation as the most significantly altered biological process (474/1230; $q=9.05x10^{-15}$) and chromatin remodelling linked to HDAC4 ($q=2.5x10^{-7}$). Interestingly, 1081 genes regulated by RARα were significantly dysregulated due to drug treatment ($q=3.21x10^{-84}$).
Discussion
These studies reveal that our drug strategies to enhance NIS function in orthotopic breast tumours are accompanied by unexpectedly potent transcriptional activation, yielding further insight into the mechanisms that control SLC5A5 expression in breast cancer.

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ccfDNA concentrations in adrenal pheochromocytoma and other adrenal tumours

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Background
Circulating cell-free DNA (ccfDNA) is a promising biomarker in adrenal neoplasms. Previous studies showed elevated ccfDNA levels in adrenocortical carcinoma (ACC) compared with endocrine inactive adenomas (EIA) and healthy subjects (HS), but data in pheochromocytoma (Pheo) are limited.
Objectives
To assess total ccfDNA concentrations in Pheo compared with other adrenal tumour types and HS, and to explore potential correlations with plasma metanephrine (MN) and normetanephrine (NMN) levels.
Methods
We analysed a cohort of 37 patients with adrenal tumours: Pheo ($n = 6$; 1 female; median age 64.5 years), EIA ($n = 13$; 8 females; 56 years), or ACC ($n = 18$; 13 females; 50 years). Fifteen healthy subjects (HS; 8 females; 34 years) served as controls. Peripheral blood samples were collected at baseline. ccfDNA was isolated using a commercial extraction kit and quantified by fluorimetry, with integrity verified via Tapestation analysis. Plasma MN and NMN levels were quantified using liquid chromatography–tandem mass spectrometry following our institutional diagnostic protocol. Statistical tests were performed to compare ccfDNA concentrations among tumour groups and to evaluate associations with clinical and biochemical parameters.
Results
Median ccfDNA concentrations were 0.069 ng/μl in Pheo (range 0.001–0.320), 0.091 ng/μl in EIA (0.042–0.253), 0.263 ng/μl in ACC (0.049–1.680), and 0.025 ng/μl in HS (0–0.186). Overall group differences were significant ($P = 0.047$, Kruskal–Wallis test). ACC had higher ccfDNA levels than EIA ($P = 0.024$) and HS ($P = 0.001$), while Pheo values were comparable to EIA and HS. No significant correlations were observed between ccfDNA and age, tumour size, or plasma MN/NMN levels.
Conclusions
ccfDNA concentrations in Pheo resemble those in benign adenomas and healthy controls but are lower than in ACC. These findings support the potential of ccfDNA as a minimally invasive biomarker to aid in distinguishing adrenal tumour types.

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From audit to action: standardising care for the immune-related endocrinopathies of immune checkpoint inhibitor therapy

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Background
Immune checkpoint inhibitors (ICIs) have revolutionised cancer treatment, but are associated with a range of immune-related adverse events (irAEs). Endocrinopathies are particularly common, ranging from thyroid dysfunction to life-threatening adrenal insufficiency due to hypophysitis.
Objective
We performed a retrospective audit to evaluate the incidence, management, and monitoring of endocrine irAEs in a real-world cohort, assessing current practice against guideline recommendations to create a robust standard operating procedure (SOP).
Methods
A 12-month retrospective audit was conducted on 45 patients receiving ICI therapy (monotherapy, combination immunotherapy, or chemo-immunotherapy). Patient demographics, treatment regimens, and longitudinal biochemical results were analysed to identify the incidence of irAEs and evaluate adherence to screening protocols.
Results
Endocrine irAEs occurred in 28.8% of patients ($n = 13$). Thyroid dysfunction was the most frequent event, with 10 patients (22%) developing primary hypothyroidism. Severe irAEs included two cases of adrenal insufficiency and one of panhypophysitis requiring hospitalisation. The Endocrinology team was consulted in all cases. Overall, 20 patients received combined ICI therapy. Out of 6 patients receiving combination immunotherapy, 3 patients (50%) developed irAEs. Out of 14 patients who received chemo-immunotherapy, 4 (28.5%) developed irAEs.
Conclusion
This audit demonstrated the significant burden of irAEs, particularly when combination therapy is used, the risk significantly increases. It highlights the need for clinicians to be aware of irAEs, particularly as their use is increasing, and it is likely that the true prevalence is even greater. Collaboration between Oncology and Endocrinology teams is essential to create SOPs to ensure early intervention to avoid life-threatening complications such as adrenal crises and diabetic ketoacidosis. As a result of this audit, we created SOPs for thyroid dysfunction, adrenal insufficiency, hypophysitis and new diabetes, and summarised these into infographs with clear pathways for any clinician to utilise.

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Metabolism, Obesity and Diabetes

P95

Anti-diabetic activity of ethanolic fractions of *Cocos nucifera* (coconut) husk in streptozotocin-induced gestational diabetes: an *in vivo* study

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Gestational diabetes mellitus (GDM) is a metabolic disorder characterized by glucose intolerance with onset during pregnancy and poses significant health risks to both the mother and fetus. *Cocos nucifera* (coconut) husk, an underutilized agricultural by-product and waste with reported therapeutic properties. This study aimed to evaluate the antidiabetic, hormonal, and fetal-protective effects of ethanolic fractions of *Cocos nucifera* husk in Streptozotocin-induced gestational diabetic in female rat model. Thirty-two female Wistar rats were randomized into eight groups ($n = 4$). Group 1 and 2 as the control group, group 3 to 8 as experimental groups. The female rats were mated ratio 2:1 with male and the presence of semen in the vaginal as seen on the otoscope indicate gestation day 0. GDM was induced in groups 3–8 via intraperitoneal injection of Streptozotocin (50 mg/kg) and high-fat diet feeding. The rats were treated with either metformin (8.19 mg/kg) or 25 mg/kg of one of three ethanolic fractions of coconut husk (EEFAcc, EEFBcc, EEFCcc), administered via oro-gastric tube. *in vivo*, **EEFBcc significantly decreased fasting blood glucose** compared to metformin-treated GDM rats ($p<0.05$). **EEFCcc significantly** ($p<0.05$) **decreased body weight** compared to metformin-treated group. **EEFBcc significantly** ($p<0.05$) **increased insulin levels,** indicating improved β-cell function. **EEFAcc significantly** ($p<0.05$) **increased estradiol,** while **EEFCcc elevated progesterone,** suggesting hormonal support in diabetic pregnancy. The EEFBcc and EEFCcc demonstrated glycemic control and hormone-modulating effects compared to metformin. These findings support the therapeutic potential of

Cocos nucifera husk as a herbal intervention for GDM, especially in low-resource settings, subject to further investigations.

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P96

Benefits of Wegovy independent of weight loss in a patient with hypertrophic cardiomyopathy and obesity

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Background
The demand for GLP-1 receptor agonists is placing huge strain on under-resourced NHS services. There is increasing evidence of health benefits independent of weight loss, with Semaglutide (Wegovy 2.4 mg) now also licensed for patients with BMI $\geq$ 27 kg/m^2 and previous cardiovascular disease, with NICE recommendations expected soon.
Case
We present a 31-year-old male with hypertrophic cardiomyopathy (HCM) diagnosed in 2018 and obesity (weight 155 kg, BMI 45 kg/m^2). The patient experienced severe symptoms such as shortness of breath, fatigue and decreased exercise tolerance, particularly postprandially. This can be common in HCM due to an abnormal haemodynamic response to eating, which is exacerbated by exertion. Consequently, the patient only ate one meal daily, triggering periods of extreme exhaustion, negatively impacting his quality of life. His symptoms were unmanaged with available medical therapy, with plans for a myomectomy and the newly approved Mavacamten when available. In June 2024, he was started on Semaglutide, along with diet and lifestyle advice, to support weight loss prior to potential surgery. The dose was titrated up to 2.4 mg over five months. Within a month, the patient noticed his post-prandial symptoms disappeared and his exercise tolerance improved significantly. He established regular meals and weight loss at 1 year was around 9% (weight 140 kg). A repeat echocardiogram showed a reduction in the peak left ventricular outflow tract gradient from 66 mmHg to 29 mmHg at rest, and from 69 mmHg to 41 mmHg following valsalva. This case demonstrates unexpected effects of Wegovy, which are likely independent of weight loss given how quickly the symptoms improved on commencing treatment and the modest fall in weight observed. There was significant improvement in cardiac function and symptoms related to HCM, allowing the patient to avoid surgical intervention.

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P97

Pickwickian Syndrome: Semaglutide, Weight Loss, and Resolution

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Obesity hypoventilation syndrome (OHS) occurs in the setting of excessive weight gain and is characterized by chronic hypercapnia. Most subjects have associated obstructive sleep apnea and daytime somnolence. It's a condition which is amenable to weight loss in the range of 25-30 % of body weight. 67-year-old lady presented to the endocrine clinic 8 months ago, with a longstanding history of obesity, hypertension, type 2 diabetes mellitus, hypertensive heart disease, low-back pain, bilateral knee osteoarthritis and left shoulder arthritis. She was followed up in the last five years by the cardiologist for hypertensive heart disease and recurrent heart failure. Also, by the pulmonologist for chronic obstructive airway disease and OHS: was on domiciliary oxygen therapy, in addition to a CPAP device. She was admitted for respiratory failure at the intensive care unit in March 2025. Findings at presentation include: respiratory distress, difficulties walking and a BMI of 49.1 kg/m2. Her FBS was 140 mg/dl and HbA1c was 7.5%. On a subsequent follow up visit a month later, her respiratory symptoms and signs predominate, and was counselled on the need for weight loss. She was started on S/C Ozempic 0.25 mg weekly for four weeks; and increased to 0.5 mg weekly for another four weeks. Ozempic was thereafter continued at 1 mg weekly. After 2 months on Ozempic, she lost 7 kg with improvement in respiratory symptoms. At 4 months, she lost a total of 9 kg. And lost a total of 22.5 kg at 6 months. Her current BMI is 39.5 kg/m2, with resolution of respiratory distress and obstructive sleep apnea. She now sleeps well at night without a CPAP machine and no longer needs domiciliary oxygen. Weight loss is the definitive treatment for obesity hypoventilation syndrome. GLP-1RAs, such as semaglutide, is a useful therapeutic option for treatment.

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P98

The possibilities of using flash glucose monitoring in a hospital

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Glucose flash monitoring, which continuously records the glucose level in the interstitial fluid, is increasingly used to assess glycemia.The aim of the study was to evaluate the effectiveness of flash glucose monitoring in patients with diabetes hospitalized in intensive care units, surgical profile (purulent surgery) and endocrinology. The variability of glycemia, the time spent in the target range, above and below the target range, the frequency and duration of hypo- and hyperglycemic episodes, the effect on the effectiveness of inpatient treatment, and the frequency of repeated hospitalizations were evaluated. The study included 140 patients divided into 3 groups who were hospitalized in intensive care units, endocrinology and purulent surgery. Flash monitoring of glycemia compared with the laboratory test method and glucose measurement allowed to reduce the time spent in a state of hypo- and hyperglycemia, achieve lower variability, and also contributed to a longer maintenance of the target glucose level. After discharge from the medical facility, patients using flash glucose monitoring did not need to be readmitted to the hospital. As a result of the study, patients with type 1 and type 2 diabetes who were hospitalized in the departments of endocrinology, purulent surgery and intensive care, and who used flash monitoring of glycemia, had a more significant improvement in metabolic control compared with laboratory determination and glucometry. In the intensive care unit, the number of blood samples and the time for determining blood glucose were reduced tenfold. Although in real clinical practice it was not possible to fully achieve the recommended time targets in the target ranges and glycemic variability, better values were obtained in patients with flash glucose monitoring; thus, it was possible to avoid the development of acute complications of diabetes mellitus, repeated hospitalizations and reduce hospital stays.

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P99

Macrophage glucocorticoid metabolism as a therapeutic target to improve muscle regeneration

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Background
Macrophages are key regulators of skeletal muscle regeneration, orchestrating both inflammatory and reparative processes. Glucocorticoids, including cortisone(E) and cortisol(F), critically influence muscle anabolic and catabolic pathways. Previous work has demonstrated that inflammation dynamically regulates glucocorticoid metabolism in macrophages, yet the consequences for muscle cell function and regeneration remain poorly understood. This study aimed to investigate how macrophage-mediated glucocorticoid metabolism affects muscle cell proliferation, differentiation, and metabolic function.
Methods
Primary human macrophages were polarized with TNFα/IFNγ or left unpolarized and treated with cortisone(E;100 nmol/l). Treated macrophages or their conditioned media(CM) were co-cultured with human myotubes and myoblasts. Cortisol synthesis was quantified via LC-MS/MS. Muscle cell responses (myotube thickness, proliferation, protein synthesis, migration, and metabolic gene expression) were assessed using microscopy, BrdU incorporation, fluorescent synthesis assays, scratch assays, and qRT-PCR. Mitochondrial function was evaluated by measuring respiration and glycolysis, and the 11β-HSD1 inhibitor LJ1 was used to block cortisone-to-cortisol activation in macrophages.

Results
Inflammatory macrophages exhibited enhanced cortisol activation from cortisone. CM or co-culture with activated macrophages reduced myotube fibre size without altering metabolic gene expression. Cortisone CM significantly decreased myoblast proliferation ($P = 0.0009$) and promoted a catabolic gene expression profile(↑Foxo1, ↑Fbox32, ↓Igf-1). Direct cortisol treatment further suppressed proliferation($P < 0.0001$) without increasing protein synthesis. While macrophage CM stimulated baseline myoblast migration and proliferation, these effects were blunted by cortisone exposure. Cortisone CM also impaired mitochondrial function, reducing maximal respiration, basal proton efflux rate($P < 0.01$), and spare respiratory capacity, while inducing glycolysis($P < 0.05$); the inhibitor reversed these deficits.
Conclusions
Inflammatory macrophages dynamically regulate glucocorticoid metabolism, enhancing cortisol activation and promoting catabolic responses in muscle cells. Dysregulated macrophage glucocorticoid metabolism during inflammation may impair muscle regeneration and contribute to muscle wasting in chronic disease. Pharmacological inhibition of 11β-HSD1 represents a potential strategy to preserve muscle function.

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P100

Developing a fluorescent reporter system for scalable detection of PYY production from enteroendocrine cells in real time with single-event resolution

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Peptide YY (PYY) is secreted by enteroendocrine L-cells in response to nutrient and microbiota-derived stimuli. Acting through neuropeptide Y (NPY) receptors, PYY regulates central appetite pathways, modulates gastrointestinal motility, and exerts **growth factor–like trophic effects** on epithelial and endocrine tissues. NPY receptor agonism via PYY analogs (e.g PYY1875, BI 1820237, NNC0165-1273) and multi-receptor agonists (e.g GEP44, bGLP/PYY-19) is in early stages of investigation for weight loss and glucose-lowering efficacy, exhibiting promising preclinical and clinical outcomes. However, *in-vitro* screening of PYY secretagogues is limited by a lack of scalable human models: immortalised lines express PYY poorly, while intestinal organoids, though physiologically relevant, require complex differentiation protocols yielding low and variable proportions of enteroendocrine cells. We present a fluorescent PYY biosensor, super-ecliptic phluorin (SEP)-tagged PYY (SEP-PYY), for functional high-throughput and cost-effective readout of PYY synthesis and secretion in real-time, in human enteroendocrine NCI-H716 cells. Iterative construct design of SEP-PYY by computational methods ensured faithful pro-hormone processing of SEP-PYY and targeting to secretory vesicles in NCI-H716 cells which we validated by super-resolution confocal microscopy. SEP-PYY failed to form secretory granules in non-enteroendocrine cells, confirming dependence on endogenous enteroendocrine machinery. We developed protocols for detection of SEP-PYY production by flow cytometry and secretion by spectrofluorometric plate readout. SEP-PYY responded robustly to acute and chronic nutrient stimulation, mirroring endogenous PYY release. Notably, butyrate upregulated SEP-PYY production and secretion in a dose- and time-dependent manner. Finally, we leveraged the pH sensitivity of SEP to capture single-event exocytosis events of SEP-PYY at the plasma membrane in live NCI-H716 cells by total internal reflection microscopy (TIRF). Fusion of acidic granules with the extracellular milieu produced ~1000 ms fluorescence flashes, which were significantly upregulated by butyrate treatment. In summary, our study provides a scalable, real-time platform for investigating nutritional and pharmacological regulation of gut hormone secretion.

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P101

Flavonoids from *Hunteria umbellata* Seeds Mitigate Diabetic Nephropathy in Streptozotocin-Induced Rats

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Diabetic nephropathy is a major complication of diabetes, characterized by programmed cell death and oxidative stress. This study investigates the therapeutic potential of flavonoids extracted from *Hunteria umbellata* seeds in ameliorating nephrotoxicity. Flavonoids were extracted from *H. umbellata* seeds and evaluated for antioxidant activity. Rats were randomly separated into 6 groups each containing six rats. The induction of diabetes in rats was by a single intraperitoneal injection of STZ (45 mg/kg body weight) followed by oral administration of flavonoid extract at 12.5, 25 and 50 200 mg/kg body weight for 28 days. Metformin (50 mg/kg body weight) served as positive control. Biochemical parameters (apoptotic markers, lipid peroxidation indices, kidney function tests, lipid profiles) and histopathological examinations of renal tissues were analyzed. The flavonoid extract demonstrated concentration-dependent antioxidant activity and improved biochemical parameters, including reduced apoptotic markers, improved kidney functions and lipid peroxidation indices. Histopathological examination revealed preserved renal tissue structure. Flavonoid from *H. umbellata* seeds show promise in mitigating diabetic nephropathy by reducing oxidative stress and apoptosis, suggesting potential therapeutic applications.

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P102

Trajectory of weight regain after cessation of glucagon-like-peptide-1 receptor agonists: a systematic review and nonlinear meta-regression

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Background
Glucagon-like peptide 1 receptor agonists (GLP-1RAs) have emerged as breakthrough weight loss agents[1, 2]. However, discontinuation is common[3], and clinical trials have demonstrated significant weight regain following cessation[4,5]. In this systematic review, we aimed to characterise the trajectory of weight regain after GLP-1RA cessation.
Methods
This systematic review and meta-regression analysis followed Cochrane and PRISMA guidelines. We searched MEDLINE, Embase, Cochrane Library, Scopus and Web of Science from inception to 26/12/2024 for randomised controlled trials and observational studies reporting weight outcomes after cessation of GLP-1RAs in overweight/obese adults. Weight regain was the primary outcome and was modelled using nonlinear regression. Secondary outcomes included HbA1c and systolic blood pressure. The study protocol is registered with PROSPERO (CRD420250631751).
Findings
We identified 44 relevant studies. Weight, HbA1c and systolic blood pressure consistently rebounded after GLP-1RA cessation. 6 trials with 3,236 participants were included in the exponential recovery model. Weight regain was estimated to plateau at 75.6% (95% CI 68.5-82.7) of the weight lost on GLP-1RA treatment. The rate constant was 0.0302 per week (95% CI 0.0204-0.0399), corresponding to a half-life of 23.0 weeks. At 1 year post-cessation, an estimated 40.2% of the on-treatment weight loss remained. Most studies were assessed to have moderate risk of bias.
Interpretation
GLP-1RA cessation is associated with a predictable and decelerating pattern of weight regain, which appears to plateau below pre-treatment levels, suggesting partial weight-loss benefit persists long-term but is substantially attenuated.
Funding
None
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P103

Consistency of basal insulin prescription and rate of insulin reduction during DKA therapy to prevent rebound ketosis and hypoglycemia during therapy- a retrospective audit of the management of diabetes ketoacidosis against JBDS standards

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Background
Diabetic ketoacidosis (DKA) is a life-threatening complication of diabetes. Treatment associated morbidity is commonly due to omission of basal insulin and hypoglycemia which can prolong hospital stay. We audited the management of DKA against Joint British Diabetes Societies (JBDS) guidelines, assessing the consistency of basal insulin prescribing and insulin rate reduction to < 0.05 U/kg/h when blood glucose fell below 14 mmol/l. Process-of-care measures audited included documentation of secondary-care follow-up, HbA1c and ACR measurement in the preceding year.
Methods
A retrospective observational study was conducted on 25 acute medical admissions with DKA. Data were extracted from electronic patient records and diabetes-clinic correspondence. Variables included demographics, precipitating causes, insulin management, biochemical parameters, and process-of-care measures.
Results
Mean age was 45 years (52% male) The predominant precipitating cause was non-compliance with insulin therapy. Mean admission glucose was 20 mmol/l and mean pH was 7.24. Basal insulin was prescribed in 84% of cases, and 64% had insulin-rate reduction to < 0.05 U/kg/h once glucose fell < 14 mmol/l.The incidence of hypoglycaemia was low in this cohort ($n = 2/25$; 8%). However, the rate of hypoglycaemia doubled when the insulin infusion rate was not reduced (12.5% vs 5.9%). SGLT-2 inhibitor–induced DKA occurred in 2/25 patients (8%). Psychosocial factors as a precipitant were identified in 40% of patients. Only 56% of patients had documented secondary-care follow-up; those without follow-up averaged 3.1 admissions in the preceding year vs 2.0 among those under regular review. Median length of hospital stay was 2 days and DKA resolved within 24 hours in 76 % of patients.
Conclusion
While DKA management broadly aligns with guidelines, gaps persist in basal-insulin use, insulin-rate titration, and follow-up. Improved staff and patient education and structured secondary-care reviews will help reduce recurrences of DKA and improve long term health outcomes for patients with diabetes.

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P104

Severe hypertriglyceridemia in pregnancy: diagnostic delay, therapeutic challenges, and unanswered questions

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Background
Physiological rise in lipids is expected in pregnancy, but pathological hypertriglyceridemia carries potential feto-maternal complications. Evidence to guide management is sparse and decision-making is often based on case reports. This case illustrates the diagnostic and therapeutic challenges of severe hypertriglyceridemia in pregnancy.
Case
A 32-year-old woman at 32 + 3 weeks gestation, with gestational diabetes on metformin, initially presented with proximal leg DVT and was treated with enoxaparin. Three weeks later, she re-presented with chest tightness, abdominal discomfort, and persistent tachycardia. Despite raised CRP and ongoing abdominal pain, clinical attention was focused on excluding cardiopulmonary causes. The initial lipemic sample showing hypertriglyceridemia (TG-57.6 mmol/l) and raised lipase of 500 U/l (8-78 U/l) consistent with acute pancreatitis secondary to hypertriglyceridemia, was only acknowledged retrospectively 10 days later. By then, TG had spontaneously fallen (21 mmol/l), possibly due to reduced intake or partial saponification. Intravenous insulin and omega-3 fatty acids were initiated, with dietary restrictions. However, intolerance to IV insulin necessitated transition to subcutaneous insulin. Despite adherence, TGs fluctuated between 17–33 mmol/l. Chylomicrons were positive. Lipoprotein electrophoresis was inconclusive. She was closely monitored in the joint antenatal-endocrine clinic.
Outcome
After multidisciplinary consensus, early delivery was performed at 37 weeks. TG normalised rapidly post-delivery, without needing ongoing treatment.
Learning points
- Lipaemic samples should trigger urgent review; overlooking them risks significant feto-maternal morbidity.
- Increased plasma viscosity poses the risk of thrombotic events as in this case, DVT. However, prolonged enoxaparin may paradoxically worsen TGs via lipoprotein lipase depletion.
- Spontaneous TG reduction without therapy raised suspicion of saponification at the pancreatic bed, although dietary restriction likely contributed more significantly.
- Fenofibrate remains a therapeutic dilemma in pregnancy due to limited safety data.
- Complete postpartum resolution highlights uncertainty over the relative contribution of gestational physiology, diet, enoxaparin exposure, and possible genetic predisposition.

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P105

Latent autoimmune diabetes in a young male – a case report

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Background
Latent autoimmune diabetes (LAD) is a slow progressive autoimmune destruction of pancreatic beta cells leading to reduced insulin production. When it occurs in a young people, it is called as latent autoimmune diabetes of young (LADY)[1].
Case Presentation
We present a case of a 36 years old male who presented at the age of 26 years with new diagnosis of diabetes. He was initially treated as type 2 diabetes given minimal osmotic symptoms, high basal mass index (BMI) of 31 kg/m2 and good response to metformin and gliclazide bringing the HbA1c from 90 to 48 mmol/mol in 3 months. His C-peptide was detected however Anti GAD (Glutamic Acid Decarboxylase) antibodies was slightly raised with negative rest of the diabetes autoantibodies. He remained insulin independent for approximately 3 years when his diabetes control started to deteriorate with HbA1c rising to 79 mmol/mol. He was then started on basal insulin glargine and continued with metformin to improve insulin resistance given high BMI. This resulted in improvement in HbA1c. His C-peptide was again checked which showed only slight reduction as compared to the diagnosis C-peptide however it was still detectable. His insulin requirement remained low at 0.2 Units/kg. 10 years post diabetes diagnosis, his diabetes remained excellent on low dose of insulin glargine and metformin 2g/day and C-peptide still remained detectable confirming the diagnosis of LADY.
Conclusion
This case highlights the need for better knowledge to prevent misdiagnosis of LAD as type 2 diabetes, the importance of regular follow-up, and a low threshold for starting insulin therapy to prevent diabetic ketoacidosis and long-term complications[1].
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P106

Proof of concept audit looking at the potential for opportunistic intervention to improve glycaemic control and process of care measures in acute hospital admissions in patients with diabetes

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Introduction
Diabetes Mellitus affects 14 in 100 adults aged 18 or over. In the acute setting, 18 in 100 people occupying a bed have diabetes. As poor glycaemic control is linked

to adverse health outcomes, our aim was to identify the proportion of patients admitted to acute medicine with a most-recent HbA1c > 60mmol/mol as a marker of sub-optimal glycaemic control that might benefit from point-of-contact diabetes specialist nurse (DSN) intervention. Secondary areas of interest were to check if serum creatinine, albumin creatinine ratio (ACR), HbA1c and lipids were checked in the preceding 12 months.
Methods
Data on 48 patients with diabetes admitted to acute medicine was collected prospectively at point of presentation.
Results
Recent median HbA1c was 52.5mmol/mol. 31% of patients had recent HbA1c > 60mmol/mol, with a median age of 73.5 yrs. 38% of patients were on oral hypoglycaemic agents, 29% were taking insulin only, and 6% were taking both insulin and OHA. In the 12 months before presentation, 54%, 92% and 81% had their ACR, HbA1c and lipids investigated respectively. Inpatient DSN activity for a calendar month showed that 173 patients (362 total episodes) were reviewed in acute medicine. Intervention by the DSN team resulted in expedited discharges / admissions avoidance in 33.5 % of patients.
Conclusion
Advancing age is associated with sub-optimal glycaemic control. Whilst glycaemic control in this age group is not expected to be tight, controlling hyperglycaemia is important to reduce diabetes hyperosmolar symptoms to reduce polyuria, nocturia and the risk of falls. Community monitoring of HbA1c and lipids were satisfactory for the majority but ACR checks were suboptimal. The inpatient DSN team play a vital role in optimising glycaemic control in acute medical admissions and their role could potentially be extended to opportunistic intervention for non-glycaemic process of care measures to improve health outcomes.

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P107

Vamorolone attenuates 11β-HSD1 induction and catabolic signalling in human skeletal muscle under inflammatory conditions

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Introduction
Duchenne Muscular Dystrophy (DMD) is a lethal genetic disease characterised by chronic inflammation and progressive muscle wasting. Potent anti-inflammatory glucocorticoids (GCs) are highly effective in the management of DMD, but their application is limited by severe metabolic side effects. The enzyme 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) potently activates and amplifies the actions of GCs and is synergistically upregulated with inflammation, exacerbating GC-induced metabolic side effects. Vamorolone is a novel dissociated anti-inflammatory steroid developed for the treatment of DMD while exhibiting reduced side effects relative to traditional glucocorticoids. We hypothesised that Vamorolone possesses a reduced synergistic capacity to upregulate 11β-HSD1 in DMD inflammation, limiting GC amplification and off-target GC induced side effects.
Methods
LHCN-M2 human skeletal muscle cells were cultured and differentiated for 10 days into multinucleated myotubes. LHCN-M2 myotubes were treated with either TNFα (10 mg/mL), Prednisolone (100nM), Vamorolone (200nM) or at a combination for 4 hours for gene expression (qRT-PCR) or 48 hours for 11β-HSD1 activity (TLC).
Results
While Prednisolone (100nM) and Vamorolone (200nM) did not alter 11β-HSD1 expression or activity alone, both compounds showed a significant synergistic induction of 11β-HSD1 expression and activity when combined with TNFα (10 ng/ml) relative to TNFα alone, with Vamorolone showing a modestly lower response than Prednisolone. In contrast, classic GC induced genes (such as GILZ) that were induced by both Prednisolone and Vamorolone were abrogated following TNFα exposure. Whilst synergy responses were preserved following Vamorolone treatment, skeletal muscle catabolic genes FOXO1 and Trim63 showed a marked reduction in response relative to Prednisolone, both alone and in combination with TNFα.
Conclusions
Vamorolone demonstrates anti-inflammatory activity while limiting 11β-HSD1 activation and downstream muscle catabolic signalling, supporting its potential as a dissociated steroid that limits GCs amplification and associated muscle wasting in DMD.

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P108

Utilising untargeted metabolomics as a tool to dissect dysfunctional skeletal muscle lipid metabolism in men with hypogonadism: results from a metabolic phenotyping study

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Hypogonadism in men is linked to an adverse metabolic phenotype that improves with testosterone replacement therapy (TRT), however tissue-specific molecular mechanisms remain incompletely defined. Skeletal muscle (SkM) is the principal site of peripheral glucose uptake and fatty acid oxidation and is therefore a potential site of androgen-mediated metabolic remodelling. Here we performed clinical phenotyping and untargeted metabolomic profiling in two independent clinical cohorts before and after pharmacological intervention. Men with prostate cancer ($n = 15$) underwent blood sampling, anthropometric assessment, bioimpedance analysis and SkM biopsies at baseline and after three months of androgen deprivation therapy (ADT). The protocol was replicated in men with hypogonadism ($n = 15$) before and after six months of TRT. Plasma and SkM metabolomic profiling was performed using ultra-high performance liquid chromatography–mass spectrometry. ADT significantly increased total body fat ($P = 0.01$) and trunk fat % ($P = 0.0003$), with reductions in total muscle mass ($P = 0.02$). Conversely, TRT induced non-significant reductions in fat mass, significant increases in trunk ($P = 0.002$) and total muscle mass (kg) ($P = 0.02$), and a significant reduction in HbA1c ($P = 0.006$). Despite minimal changes in plasma, ADT decreased the concentration of many lipid classes in SkM, notably fatty acids and ceramides with an increase in acylglycerides. Conversely, TRT increased the concentration of most lipid classes in SkM (notably fatty acids, acylglycerides and ceramides) while plasma lipid classes fell, suggesting altered intramuscular lipid handling and redistribution from circulation to tissue. Acylcarnitines declined in both compartments post TRT but increased in SkM following ADT. ADT and TRT exert opposing diametric tissue-specific effects on lipid metabolism. These findings suggest that androgens influence mitochondrial and carnitine dependent fatty acid pathways, although the physiological significance requires further clarification. Ongoing mechanistic work is needed to determine how these adaptations integrate within the broader metabolic response to androgen manipulation.

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P109

Symptomatic hypoglycemia in end-stage renal disease – diagnostic pitfalls and challenges in management

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Background
Hypoglycemia in end-stage renal disease (ESRD) is well described with multifactorial etiology including reduced renal gluconeogenesis, reduced excretion of endogenous insulin, and poor nutrition. Uraemic hypoglycemia can be precipitated by initiation of renal replacement therapy (due to improved insulin sensitivity), insulin therapy, drugs, adrenal insufficiency, liver disease or infections.
Case Presentation
Two patients with ESRD on dialysis and type 2 diabetes mellitus presented with recurrent symptomatic hypoglycaemia. An 80 year old lady with CKD Stage 5 on thrice-weekly dialysis presented with symptomatic hypoglycemia. Ambulatory glucose testing using interstitial glucose monitoring (Libre) showed 84% time in range, 13% low (3–3.8 mmol/l), and 2% very low (<3 mmol/l) blood glucose readings. She was not on any anti-diabetic medications. The second, a woman in her forties with CKD secondary to sarcoidosis on haemodialysis following a failed renal transplant, was on biphasic insulin, which was discontinued due to hypoglycaemia. Both patients had elevated insulin and C-peptide levels, though insulinoma was considered unlikely. Diazoxide was initiated in both patients with symptomatic and biochemical improvement of hypoglycaemia.
Discussion
This case series highlights the diagnostic and management challenges with hypoglycemia in patients with end stage renal disease. Uraemic hypoglycemia

can occur regardless of the patient's diabetes status. Presentation with hypoglycaemia is also a poor prognostic indicator in ESRD. The accuracy of HBA1C can be altered due to a variety of CKD-associated sequelae including anaemia, hence continuous ambulatory glucose monitoring can be useful in these patients. Diazoxide though unlicensed has been described to improve frequency and severity of spontaneous hypoglycaemia in ESRD.

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P110

Investigating the role of direct neuronal innervation of the pancreas by the stomach

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Retrograde tracing studies in rodents have revealed that neurons in the myenteric plexus of the stomach's antrum and in the initial segment of the duodenum extend to the pancreas (1). Through viral tracing, our preliminary data has shown that neurons in the myenteric plexus in the upper duodenum project directly to the pancreas. Furthermore, physical separation of the duodenum from the pancreas abolished the improvement in glucose tolerance observed in mice treated with olive oil (2). However, whether the neurons originating in the antrum of stomach also innervate the endocrine pancreas, and their specific functional role remains unknown. To investigate whether neurons from the gastric antrum also project to the pancreas, pAAV-hSyn-EGFP was injected into pancreas and confirmed EGFP expression in the stomach. Surgical separation of the pancreas from the pyloric region of the stomach was performed and verified histologically. The separation did not affect fasting blood glucose levels or body weight. Separation surgery resulted in a more rapid decline in blood glucose following an oral glucose tolerance test compared with sham-operated controls. No significant effect was observed in intraperitoneal glucose tolrance suggesting a gastrointestinal tract specific mechanism. Gastric distension induced by oral gavage of methyl cellulose or fast-refeed had no significant impact on glucose tolerance. These findings suggest that neurons connecting the stomach and pancreas may normally suppress oral glucose tolerance, and that disrupting this communication enhances the glycaemic response to ingested glucose. This effect appears to be independent of mechanical gastric signals and may represent a novel target for metabolic disease intervention.

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P111

Real world outcomes of adjunctive sodium-glucose cotransporter-2 (SGLT2) inhibitors in adults with type 1 diabetes: a single-centre retrospective analysis

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Background
SGLT-2 inhibitors improve weight and glycaemic control in type 1 diabetics, (1,2) however concerns remain regarding increased diabetic ketoacidosis (DKA) risk. This study aims to evaluate their efficacy and safety as adjuncts to insulin in adults with type 1 diabetes.
Methods
We conducted a retrospective review of adults ($\geq$18 years) with type 1 diabetes prescribed adjuvant SGLT-2 inhibitors at a single centre between February 2018 and September 2021. Clinical data including HbA1c, body weight, and total daily insulin dose were collected before and after SGLT-2 initiation. Paired t-tests were used for statistical analysis.
Results
Eleven patients were included (seven women, mean age 50.3 $\pm$ 15 years), diabetes duration 29.6 $\pm$ 12.2 years. Duration of adjunctive SGLT-2 was 24.8 $\pm$ 11.6 months. Five patients were on 5 mg dapagliflozin, four on 10 mg and two on 25 mg empagliflozin. Mean HbA1c decreased from 74 $\pm$ 21.7 to 65.3 $\pm$ 15.2 mmol/mol ($P = 0.08$). Weight decreased from 83.8 $\pm$ 22.7 kg to 82.7 $\pm$ 25.9 kg ($P = 0.3$), and insulin dose reduced from 48.1 $\pm$ 14.6 to 46.5 $\pm$ 11.8 units/day ($P = 0.6$). One case of thrush (9%) and one DKA (9%) occurred; the latter in a patient not following sick day rules. No urinary tract infections or severe hypoglycaemia were reported.
Conclusion
In this cohort, adjunctive SGLT-2 therapy was well tolerated, improving HbA1c, weight and insulin dose - though not statistically significant, likely due to small sample size. Despite proven benefits, withdrawal of their license in type 1 diabetes limits access to a valuable therapeutic option.
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P112

Dual GLP-1 and GIP therapy for severe post-bariatric surgery hypoglycaemia: a clinical case

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Post-bariatric hypoglycaemia (PBH) is a recognised complication of bariatric surgery; it is estimated that between 25% and 75% of individuals could experience PBH of varying severity. First-line management includes dietary modification; pharmacotherapy is reserved for refractory cases. We present a 38-year-old woman who underwent sleeve gastrectomy in 2022. Her BMI before surgery was 42.6 kg/m^2 and reached a steady BMI of 23 kg/m^2 after two years. She regained 10 kg by the end of 2024 and started tirzepatide from January to March 2025. Shortly after discontinuing tirzepatide, she collapsed without warning, and ambulance-recorded glucose was 2.8 mmol/l. She required an urgent endocrine appointment due to the severity of her symptoms. History revealed hypoglycaemia occurring particularly 2–4 hours after meals, suggestive of PBH. She did not experience hypoglycaemia while fasting. Baseline biochemical tests, including fasting glucose, gut hormone profile, metadrenalines, urine sulphonylurea, short Synacthen test, and IGF1/IGF2 ratio, showed no abnormality. She was commenced on acarbose alongside dietary interventions. Continuous glucose monitoring (CGM) confirmed ongoing severe hypoglycaemic episodes despite strict dietary measures and acarbose. Undetectable glucose readings were recorded on several occasions on both CGM and capillary, linked to near collapses. She was required to keep a glucagon injection at home. Further consultations discussed other options for pharmacotherapy, including somatostatin analogues and diazoxide. Due to side effects associated with diazoxide, this was deemed not a long-term option. Due to current restrictions requiring funding for somatostatin analogue as a high-cost drug, it was not possible to start this immediately. Reintroduction of tirzepatide at a 2.5 mg dose resulted in dramatic clinical improvement within 12 hours, with 100% resolution of all hypoglycaemic episodes. This case highlights a potential therapeutic role for GLP-1/GIP receptor agonists in PBH and the need for further clinical evaluation in larger cohorts.

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P113

Association between hepatic steatosis and vitamin D insufficiency in nonalcoholic fatty liver disease patients

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The study aims to determine the association between hepatic steatosis and vitamin d insufficiency in nonalcoholic fatty liver disease patients. From August 2023 to February 2024, a descriptive study was carried out at the Department of Biochemistry in several locations in Bangladesh and Pakistan. The study was approved by the institution's ethical committee. This study included 108 NAFLD patients with a diagnosis and 100 chronologically and gender-matched controls. SPSS version 23.0 was used to conduct the statistical analysis. To identify the independent predictors of NAFLD, a logistic regression analysis was extended to incorporate possible components from the univariate analyses (a statistically significant value of <0.05 was employed). Laboratory values were demonstrated to rise in the Control group. Fasting blood glucose (FBG) revealed a significant *P*-value of 0.004, while vitamin D serum has a significant value (*P*-value 0.001).

On the other hand, the *P*-value for ferritin, aspartate aminotransferase(AST), and uric acid was all 0.000. The levels of 25(OH)D were shown to be significantly correlated with HDL-C ($P = 0.004$), uric acid ($P = 0.005$), HbA1c ($P = 0.002$), the urine albumin/creatinine ratio ($P = 0.001$), FBG rates (0.031), and the erythrocyte sedimentation rate(ESR) (<0.001). Serum vitamin D levels were shown to be lower in NAFLD cases compared to controls. To assess additional evidence-based research, more investigations are required.

Keywords: hepatic steatosis, vitamin D, insufficiency, nonalcoholic fatty liver disease (NAFLD)

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P114

Long-term LDL-C reduction and treatment persistence with PCSK9 inhibitors: a real-world evaluation from a secondary care lipid service

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Background
PCSK9 inhibitors offer potent LDL-cholesterol (LDL-C) reduction in patients with severe or familial hypercholesterolaemia (FH), yet long-term real-world data on lipid outcomes and treatment persistence remain limited in UK secondary care, where pathway variation and resource constraints often influence adherence.
Methods
This single-centre evaluation in a secondary care lipid clinic included adults initiated on PCSK9i therapy between 2017 and 2024, retrospectively evaluated using Cerner prescribing and laboratory records. Patients with $\geq$12 months of follow-up were included; lipid parameters were assessed at baseline and annually for up to seven years. Primary outcomes were changes in LDL-C and non-HDL-C; the secondary outcome was treatment persistence.
Results
Fifty-three patients (mean age 53 $\pm$ 12 years) were included: 44 received alirocumab and 9 evolocumab. Twenty-one patients had genetically or clinically confirmed heterozygous FH, and 21 patients were treated for primary prevention. Baseline mean LDL-C was 5.0 $\pm$ 1.2 mmol/l, declining to 3.0 $\pm$ 0.8 mmol/l at year 1 (-39 %) and remaining stable between 2.2–2.8 mmol/l (-43 to -56 %) over seven years. Non-HDL-C decreased from 6.4 $\pm$ 1.5 to 3.4–4.1 mmol/l (-36 to -46 %). Treatment persistence declined progressively: for alirocumab, 59 % remained on therapy at year 3, 37 % at year 5, and 27 % at year 7. For evolocumab, persistence was higher initially (100 % at year 5) but 11 % discontinued by year 7. Reasons for discontinuation in both groups were not documented and should be investigated further.
Conclusion
In this seven-year real-world evaluation, PCSK9i therapy achieved durable lipid reductions consistent with clinical-trial efficacy. However, long-term persistence was suboptimal, particularly for alirocumab. These findings highlight that, beyond efficacy, adherence represents the key challenge in delivering sustained lipid optimisation within NHS practice.

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P115

Cardiovascular Risk Assessment Tools in Type 2 Diabetes Mellitus: A Comparative Study from Nigeria

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Background and Objectives
Cardiovascular disease is the leading cause of mortality in Type 2 Diabetes Mellitus (T2DM). Most risk calculators (Framingham, ASCVD, QRISK3) were developed in non-African populations, raising concerns about applicability. We compared these tools in Nigerian T2DM patients to identify the most suitable for local use.
Methods
A cross-sectional study of 223 T2DM patients at LUTH. Data were collected through clinical assessments and review of patient records. Cardiovascular risk was estimated using the Framingham, ASCVD, and QRISK3 risk scores. The agreement was tested with correlation coefficients and Bland-Altman plots
Results
A total of 223 participants were included in the study, with a mean age of 62.80 $\pm$ 9.5 years. Male: Female ratio is 1:1.4. 40.4% of the participants had a duration of DM $<$ 5years. Framingham risk score (FRS) classified 55.1% of the participants as high risk (median 21.6%), QRISK3 classified 47.5% as moderate and 35.0% as low risk (median 12.1%), while ASCVD identified 39.5% as high risk (median 15.0%). QRISK3 correlated strongly with ASCVD ($r = 0.88$). Bland-Altman showed FRS consistently overestimated risk compared to both QRISK3 ($+7.3$%) and ASCVD ($+1.67$%).
Conclusion
Framingham risk score overestimates cardiovascular risk in Nigerian T2DM patients, while QRISK3 and ASCVD show closer agreement. QRISK3 may be a more suitable tool for risk stratification in this population, but prospective validation is needed.

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P116

Chronic GIPR agonism results in human beta cell GIPR desensitisation

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Background
There is renewed interest in the therapeutic targeting of the glucose-dependent insulinotropic polypeptide receptor (GIPR) following the market-leading metabolic improvement induced by glucagon-like peptide-1 receptor (GLP-1R)/GIPR co-agonist tirzepatide. We have previously shown using *ex vivo* and *in vivo* models that chronic exposure to the investigational GIPR agonist GIP108 resulted in significant desensitisation of the mouse pancreatic GIPR, a process that likely minimises its therapeutic effect. As there are recognised differences between mouse and human GIPR trafficking processes involved in desensitisation, we assessed whether the human GIPR is also prone to agonist induced receptor desensitisation in pancreatic beta cells. We also studied desensitisation of the mouse and human GIPR in response to chronic exposure to tirzepatide, shown to signal predominantly through the GIPR in human islets. Desensitisation of the human beta cell GLP-1R with liraglutide was also studied for comparison.
Methods
Mouse GIPR desensitisation was studied in dispersed pancreatic islets from wild-type C57BL/6J mice and *Glp1r*$^{-/-}$ mice. Human beta cell GIPR and GLP-1R desensitisation was studied using validated human beta cell model EndoC-βH5® cells. Cells were transduced with fluorescence-based cADDis cAMP biosensor enabling cAMP responses to be measured using live cell imaging.
Results
24-hour pre-treatment with tirzepatide resulted in significant mouse GIPR desensitisation in islets from wild-type and *Glp1r*$^{-/-}$ mice. Following identification of suitable pre-treatment and re-challenge doses of peptides based on target engagement and stability studies, we observed significant human GIPR desensitisation following 24-hour GIP108 and tirzepatide pre-treatment, and significant human GLP-1R desensitisation following 24-hour liraglutide pre-treatment.
Conclusion
Chronic GIPR agonism resulted in human beta cell GIPR desensitisation, highlighting the need to develop GIPR agonists with reduced desensitisation tendency. This is an important step towards the design of metabolic pharmacotherapies of the highest possible efficacy for the treatment of obesity and type 2 diabetes.

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P117

Maternal incretin hormones can predict insulin resistance in pregnant women

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Background
Gestational diabetes mellitus (GDM) is a significant public health problem with a rising prevalence and a potential impact on maternal and fetal health outcomes. Studies have shown the potential relationship between maternal incretin hormones and gestational diabetes. This study aimed to evaluate the relationship between incretin peptides, gestational diabetes mellitus (GDM), and pregnancy outcomes.

Method
Participants were screened for GDM using the 75 g post-oral glucose load test. Incretin hormones (glucagon-like peptide 1 (GLP1) and glucose inhibitory peptide (GIP)), as well as fasting insulin, were assayed using the sandwich-ELISA technique. Anthropometry was also measured, including maternal weight, height, and blood pressure. Fetal and maternal outcomes were recorded at delivery. The sociodemographic and clinical characteristics of the study population were described. Bivariate and multivariate regression analyses assessed differences in maternal incretin levels between the GDM and non-GDM groups.
Result
The mean age of the participants was 30.59 years; multiparous women comprised 59.1%, and grand multiparas were 34.0%. The prevalence of gestational diabetes based on the 2013 WHO criteria was 14.88%. At baseline (0 mins), the mean values of GIP and GLP-1 were 220.17 ± 159.18 and 53.45 ± 29.71, while at 120 mins (after stimulation), they were 459.91 ± 189.23 and 459.91 ± 373.56 pg/ml, respectively. There was a positive correlation between the basal and stimulated levels of incretin hormones and insulin resistance ($r = 0.275$, $P = 0.006$ for GIP for GLP1 and $r = 0.2589$, $P = 0.0004$ for GIP, respectively).
Conclusion
The findings from this study indicate the need for a larger-scale multi-institutional study to evaluate the role of maternal incretin hormones in the diagnosis of insulin resistance and GDM.

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P118

A case of new onset type 2 DM presenting with DKA in 85-year-old female on immunotherapy for multiple myeloma

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85-year-old female was brought into hospital with history of having gradually worsening conscious level for past 1 week. Past medical history includes Smouldering Myeloma, hypertension, stage 3 CKD and hearing impairment. Patient was receiving Daratumumab, lenalidomide and oral steroids for her MM for past few months. Patient was independent with her ADL till last week when she gradually started to deteriorate with drowsiness and confusion. On presentation to hospital patient was found to have a GCS of 9/15 and initial bloods showed ph. 7.22, hco3 14.6, glucose 24.1 and ketones of 6.4. calcium was 2.31 with adjusted calcium of 2.42, CRP of 27, TSH 1.28. CT head was done that came back normal and rest of bloods were stable. There was no previous history of DM however family said that patient was having positive osmotic symptoms for past 2-3 moths and had lost around 6-8 pounds during this time. Patient was started on treatment of DKA with insulin, fluids and K as per trusts guidelines, Hba1c was done that was found to be 121 mmol/mol. Patient was seen by diabetic team and diagnosed as having new onset of Diabetes likely secondary to immunotherapy with initial presentation with DKA. Patient improved over next 2-3 days and after resolution of DKA patient was started on biphasic insulin and was followed up the diabetic team that showed improvement in HbA1c to 41 mmol/mol. The aim of presenting his case report is to highlight the potential for newer immunotherapy regimes to cause diabetes mellitus and to be vigilant in monitoring of patients who display symptoms of hyperglycemia so that new onset of DM can be diagnosed earlier to prevent development of life-threatening complications such as DKA

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P119

Comparative efficacy of GLP-1 RA vs. SGLT2 inhibitors in slowing chronic kidney disease (CKD) progression - a retrospective study done in northern hospital in pakistan

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Background and Aim
One of the main causes of disease burden worldwide is chronic kidney disease (CKD). Although SGLT2 inhibitors (SGLT2 I) are often used as Reno protective medications. The purpose of this study was to evaluate the efficacy of these two medications SGLT2I and GLP1 A on critical renal outcomes in a high-risk population with CKD and type 2 diabetes.
Methodology
It was a retrospective cohort study done between 2024 to 2025. In this study, 60 patients with T2D and stages 3rd and 4th of chronic kidney disease (eGFR 25 to 59 mL/min/1.72 m2) were selected and data was analysed for 8 months, one group was on a GLP-1 RA such as liraglutide or dulaglutide ($n = 30$) and the other group was on SGLT2i (empagliflozin/dapagliflozin), $n = 30$. tests including eGFR and albuminuria (UACR) were compared for both groups and comparative effectiveness of both classes of drugs were evaluated.
Results
The glucagon-like peptide-1 group had a significant preservation of eGFR, with a mean change of -0.8 mL/min vs -4.2 mL/min in the SGLT2 I group. In contrast, SGLT2 inhibitors resulted in a considerably higher reduction in albuminuria, with a median UACR decline of -52% compared to -38% with GLP-1 RA.
Conclusion
Both drug classes show Reno protective effects but with distinct profiles. GLP-1 RAS are linked to greater stability in eGFR, whereas SGLT2 inhibitors offer a more substantial reduction in albuminuria. Therefore, the choice between these treatments may depend on the specific clinical goal: slowing the decline of eGFR or reducing proteinuria in high-risk patients with type 2 diabetes and chronic kidney disease.

Keywords
Chronic Kidney Disease, Type 2 Diabetes, Urinary Albumin-to-creatinine Ratio, SGLT2 inhibitor

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P120

DKA: diagnostic conundrums of a common presentation on take

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History
A 31-year-old gentleman with morbid obesity, hypertension and congenital blindness presented with 2 days of vomiting and drowsiness.
Examination
On presentation, he was in diabetic ketoacidosis (DKA).
- GCS: 11
- Widespread non-blanching rash
- Abdomen: diffusely tender, soft

Investigation results
- CR$P > 320$
- Creatinine 360
- Neutrophils 17
- Amylase 32
- CXR clear
- Antibodies for T1DM and lipid profile sent

Diagnostic challenges, Management and course
Without a history of Type 1 diabetes, the cause of DKA was unclear. Suspected precipitants included meningitis or intra-abdominal infection. He was started on IV ceftriaxone and aciclovir, with CT imaging arranged. CTAP showed pancreatic tail oedema, suggestive of acute pancreatitis. Despite 8 hours of DKA therapy, acidosis persisted (pH 6.9, HCO_3 4), requiring ICU admission and 72 hours of haemofiltration, after which renal function improved. Further results: triglycerides 35 mmol/l, HbA1c 150, T1DM antibodies negative. Repeat CTAP confirmed necrotising pancreatitis (distal body/tail) with splenic vein thrombosis.
Learning points
1. Rising metabolic syndrome can lead to uncommon DKA triggers.
- Here, undiagnosed type 2 diabetes (HbA1c 150) progressed to type 3c (pancreatogenic) following pancreatitis due to severe hypertriglyceridemia.

2. Hypertriglyceridemia should be considered as a cause of pancreatitis.
3. Splenic vein thrombosis may complicate pancreatitis and the pro-thrombotic state of DKA, emphasising the role of thromboprophylaxis.
4. Fluid resuscitation in morbid obesity:are we underfilling?

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P121

Metabolic-bariatric surgery outcomes in people with pre-surgical mental health diagnoses

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Background
Metabolic–bariatric surgery (MBS) is increasingly performed in patients with obesity and mental health (MH) conditions, yet the interplay between these conditions, weight loss and other outcomes remains unclear.
Objective
To evaluate relationships between preoperative MH conditions and postoperative psychological complications and metabolic outcomes two years after MBS.
Methods
We analysed a cohort of adults who underwent primary MBS at a tertiary bariatric centre from 2021-2024. Multivariable linear and modified Poisson regression models were used to assess weight, metabolic, and psychological outcomes adjusted for age, sex, BMI, type 2 diabetes, and type of bariatric surgery.
Results
After excluding patients who became pregnant or were diagnosed with cancer postoperatively, 482 were included and of these, 217 (45%) had $\geq$1 MH condition diagnosed preoperatively (81.5% women, mean$\pm$SD age 44.6$\pm$11.5 years, mean$\pm$SD BMI 45.2$\pm$8.2 kg/m2). Baseline characteristics were comparable between MH and non-MH groups, apart from a higher proportion of women among those with MH conditions (88% vs 76%; $P < 0.001$). Two years post-surgery, %TWL was similar between patients with and without MH conditions ($P = 0.34$). Likelihood of suboptimal weight loss (<20%TWL) or weight regain did not differ by MH status. Psychotropic medication use remained stable after surgery (R$r = 0.99$, 95% CI 0.88–1.12; $P = 0.87$), while higher baseline BMI modestly increased likelihood of ongoing psychotropic medication use postoperatively (β 1.02 per kg/m^2; $P = 0.01$). Patients with MH conditions had increased risks of postoperative suicidal ideation (RR 9.67, 95% CI 1.53–61.04; $P = 0.016$) and self-harm/attempted suicide (RR 7.00, 95% CI 1.08–45.46; $P = 0.042$).
Conclusions
People with preexisting MH conditions have comparable post-surgical weight loss outcomes to people without MH conditions. Significant associations exist between preoperative MH conditions and postoperative suicidal ideation and self-harm/attempted suicide. These findings suggest that postoperative care should integrate dedicated mental health follow-up to optimise long-term outcomes.

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P122

Human genetic determinants of skeletal muscle and adipose tissue partitioning

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Background
Healthy skeletal muscle and adipose tissue determine physical and cardiometabolic resilience. Age-related attrition of either produces adverse health outcomes, while sentinel disorders demonstrate that their disproportion can be a hallmark either of harm [e.g. sarcopenic obesity (high adiposity, reduced lean mass), or lipodystrophy (reduced adiposity, high muscle mass)] or supranormal function [e.g. myostatin deficiency (increased muscle, low adiposity)]. We hypothesised that the genetic determinants of their relative proportions may yield insights into mechanisms maintaining healthy body composition. We thus conducted bi-trait analysis of whole-body fat-free and fat mass normalized to height (FFMI and FMI respectively), using UK Biobank bioelectrical impedance data.
Methods and Results
Variant-level associations for each trait were first determined ($P < 10^{-3}$), with resulting variants next analysed by cross-phenotype association to identify those with diverging effects on FFMI and FMI ($p_{pairwise} < 5x10^{-8}$). The list was finally filtered for overlap at locus level for both traits. 6 variants were thus identified in men, 5 in women, and 14 in sex-combined analysis. These were assessed for association with a wider raft of cardiometabolic and body composition traits, and the pattern of association compared with that for rare variant burden scores for potentially mediating genes. *PLCE1*, *SLC30A10*, *IRS1*, and *WNT2B* showed concordant association patterns. In a complementary approach, variant-level association with (FFMI-FMI) was studied in exome sequences. Resulting variants ($P < 1x10^{-3}$) were clumped into 500kB linkage disequilibrium blocks, and lead variants within blocks with the highest probability of overlapping association for FFMI and FMI selected. For each variant, gene burden association testing for potential mediating genes was undertaken, using both prior traits and selected serum protein measures. 43 additional genes, and replication of signals for *PLCE1* and *ADAMTSL3* were identified.
Conclusion
These findings give novel insights into the genetic architecture of cardiometabolic resilience and suggest numerous avenues for downstream mechanistic study.

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P123

Exaggerated GLP-1 and satiety responses after gastrectomy: implications for metabolic adaptation

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Gastrectomy is associated with profound metabolic changes, yet the endocrine adaptations underlying post-surgical weight loss remain poorly understood. This prospective observational study aimed to characterise postprandial GLP-1 responses and their relationship to satiety, weight loss, and nutritional status following gastrectomy. Patients undergoing elective gastrectomy for gastric cancer were assessed preoperatively and at 10 days, 6 weeks, and 3 months postoperatively using serial mixed-meal tolerance testing and symptom questionnaires. Significant weight loss was observed at 3 months (mean %BWL 14.4 $\pm$ 2.1, $p < 0.0001$). Postprandial GLP-1 secretion increased markedly from day 10, with a near tripling of GLP-1 AUC ($p = 0.007$) and a four-fold rise in peak GLP-1 concentrations ($p = 0.02$). The GLP-1 response curve maintained its shape across timepoints ($p = 0.14$), indicating increased magnitude but unchanged secretion dynamics. Fasting GLP-1 levels did not change significantly. Satiety scores increased significantly at 6 weeks (mean 50.0 vs 4.8 pre-op, $p = 0.008$), but this effect was not sustained at 3 months. Lack of appetite scores rose transiently postoperatively but did not reach statistical significance ($p = 0.06$). Eating symptoms increased at 6 weeks and 3 months ($p = 0.04$). Biochemical changes included reductions in vitamin E ($p = 0.04$), albumin ($p = 0.02$), total protein ($p = 0.007$). No significant relationships were identified between GLP-1 indices or satiety scores and percentage weight loss. These findings highlight early, sustained exaggerated postprandial GLP-1 secretion following gastrectomy, with a transient rise in satiety. The results provide insight into incretin-mediated endocrine adaptations post-gastrectomy, relevant to metabolic changes observed after upper gastrointestinal surgery.

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Indole-3-carbinol stimulates GLP-1 release and improves glucose tolerance

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The increasing prevalence of obesity and type 2 Diabetes Mellitus (T2DM) is a worldwide health concern. Existing therapeutic approaches face the challenge of side effects and low patient adherence. Therefore, novel treatments are still required. The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor expressed in different cell types and is thought to be involved in inflammatory responses and regulating endothelial barrier integrity. Indole is an organic compound generated following gut microbial catabolism of *L*-tryptophan. Indole and its derivatives are AhR ligands, and their production has been reported to have a negative association with the incidence of T2DM. Activating AhR by indole derivatives is associated with enhanced insulin sensitivity in mice. Previous studies have found that indole can promote the acute secretion of glucagon-like peptide-1 (GLP-1) and the proliferation of GLP-1 secreting cells, and thereby improve glucose tolerance both acutely and in the longer term. However, being considered as an experimental agent, the potential of indole as dietary supplement is restricted. Indole-3-Carbinol (I3C) is a derivative of indole that can be commonly found in cruciferous plants. In this study, the acute glucoregulatory effect of I3C was examined. Enteroendocrine STC-1 cells were cultured and different concentrations of I3C applied. Intraperitoneal glucose tolerance test was performed in mice to elucidate the effect of oral administration of I3C *in vivo*. Our results suggest that I3C can stimulate the secretion of GLP-1

from STC-1 cells *in-vitro* with 10μM having the most significant effect. Oral administration of I3C significantly improved the glucose tolerance acutely *in vivo*, but unlike indole, this effect did not persist for several days. Future research will focus on the mechanism underpinning the glucoregulatory effects of I3C, whether they are dependent on AhR signalling, and whether chronic treatment with I3C has the potential to treat metabolic disease.

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P125

Autosplenectomy in a patient with autoimmune polyglandular syndrome type 2 (APS-2)

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Autoimmune glandular syndrome type 2 is a complex genetic condition where a triad of endocrinopathies are involved namely Addison's disease, type 1 diabetes and/or autoimmune thyroid disorder. The disease predisposes one to a variety of other autoimmune associations. Here we report a rare presentation of a patient with APS-2 presenting with a 7-year history of progressive splenic atrophy leading to auto-splenectomy observed through imaging. We postulate that the underlying cause of this presentation is also of autoimmune nature. While APS-1 has been associated with asplenia and hyposplenism in literature, this is the first report of APS-2 associated with the same. Splenic hypofunction can increase susceptibility to encapsulated bacterial infection, with overwhelming post-splenectomy infection (OPSI) being a significant threat. It is crucial that clinicians recognize the importance of providing guidance on vaccinations, antibiotic chemoprophylaxis, and patient education for individuals with asplenia or hyposplenism. If patients with APS can experience progressive splenic atrophy, we suggest long term follow up with splenic function assessment. It is yet unclear whether pre-emptive screening with pitted red cell count has any clinical impact in this group of patients.

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P126

Reactive hypoglycaemia following fundoplication surgery for hiatus hernia successfully treated with GLP1 agonists

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Background
Fundoplication is a common surgical procedure used to treat severe gastroesophageal reflux disease and large hiatus hernias. Reactive hypoglycaemia, a form of late dumping syndrome characterized by postprandial insulin surges and resulting hypoglycaemia, is uncommon after fundoplication. This case presents a rare instance of this complication in an elderly patient.
Case Description
A 73-year-old male with a large sliding hiatus hernia underwent elective fundoplication following persistent GERD symptoms unresponsive to proton pump inhibitors. The surgery was uncomplicated, and the patient was discharged on postoperative day 2. In the following months, he reported improvement in reflux symptoms and returned to a regular diet. Approximately 4 months postoperatively, the patient began experiencing episodes of dizziness, palpitations,sweating, and confusion occurring 1.5 to 3 hours after meals. These episodes were transient and resolved spontaneously or with carbohydrate intake. There was no history of diabetes mellitus or use of glucose-lowering medications.
Clinical Hypothesis
Reactive hypoglycaemia post-upper GI surgery is most commonly associated with bariatric procedures due to rapid gastric emptying and exaggerated insulin responses.
Diagnostic Pathway
Capillary blood glucose readings during symptomatic episodes revealed hypoglycaemia with values ranging from 2.1 to 3.0 mmol/l. Fasting glucose: 4.9 mmol/l. Postprandial glucose (90 mins): 3.2 mmol/l Insulin level (90 mins): Inappropriately elevated for glucose level C-peptide: Normal. HbA1c: 34 mmol/mol. The symptoms completely resolved with Tirzeperatide.
Discussion and Learning Points
This case underscores the need to consider postprandial hypoglycaemia in the differential diagnosis of unexplained neurological or autonomic symptoms following fundoplication.

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P127

Insulin Antibody Syndrome (Hirata's Disease) in a young female

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Background
Insulin Antibody Syndrome (IAS), is a rare autoimmune condition characterized by spontaneous hypoglycemia due to high titres of insulin autoantibodies in individuals who have not been previously exposed to exogenous insulin.The pathophysiology involves the formation of autoantibodies that bind circulating insulin, creating a large insulin-antibody complex. This binding alters insulin kinetics, leading to delayed insulin release and unpredictable fluctuations in glucose levels.
Case Description
We present the case of a 25-year-old female who was admitted with recurrent symptomatic hypoglycemia in the absence of diabetes or insulin therapy.
Clinical Hypothesis
The pathophysiology involves the formation of autoantibodies that bind circulating insulin, creating a large insulin-antibody complex. This binding alters insulin kinetics, leading to delayed insulin release and unpredictable fluctuations in glucose levels. Clinically, patients may present with recurrent episodes of hypoglycemia, which can range from mild adrenergic symptoms to severe neuroglycopenic events, particularly in the postprandial state.
Diagnostic Pathway
Flash glucose monitoring confirmed reactive hypoglycaemia and insulin antibodies were positive, C peptide was within reference range. Her symptoms eased with frequent, small meals and to avoid simple sugars.
Discussion and Learning Points
Insulin Antibody Syndrome, should be considered in the differential diagnosis of spontaneous hypoglycemia, in non-diabetic individuals with no history of exogenous insulin use. This case highlights the diagnostic challenge of paradoxical laboratory findings of hyperinsulinemia and hypoglycemia in the absence of insulin administration. Early recognition and appropriate immunological testing are crucial to avoid misdiagnosis and unnecessary interventions. In our patient, timely identification of insulin autoantibodies guided a conservative, non-invasive treatment approach, leading to clinical improvement and resolution of hypoglycemic episodes.

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P128

Cholecystokinin and secretin differentially regulate glucose homeostasis

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Cholecystokinin (CCK) and secretin (SCT) are gastrointestinal hormones classically recognised for regulating pancreatic exocrine secretion and digestive processes. Their wider endocrine roles, particularly in modulating insulin secretion and glucose homeostasis, are less well understood. Incretin gut hormones (e.g. GLP-1 and GIP) can act via the circulation and also engage enteric neural circuits, which in turn communicate with peripheral organs like the pancreas. Transcriptomic data reveal that both the CCKA receptor (Cckar) and the SCT receptor (Sctr) are highly expressed in duodenal myenteric plexus neurons, raising the possibility that the enteric nervous system (ENS) may serve as a relay for gut hormone influence on endocrine function and glucose homeostasis. We therefore investigated the effects of CCK and SCT on pancreatic islets and systemic glucose regulation. Static glucose-stimulated insulin secretion (GSIS) assays were conducted in isolated mouse islets, with or without co-culture of longitudinal muscle myenteric plexus (LMMP) neurons. Intraperitoneal glucose tolerance tests (IPGTT) were also performed following hormone administration. *in-vitro*, neither CCK nor SCT altered insulin secretion in isolated islets. However, under neuronal co-culture, SCT significantly enhanced insulin secretion under high-glucose conditions. *in vivo*, the systemic effects

diverged: SCT impaired glucose tolerance, increasing peak glucose, whereas CCK improved tolerance, reducing glycaemic excursions. These findings further support the notion that CCK and SCT may also play endocrine roles beyond their traditional digestive functions. The dual observation that both hormones potentiate insulin secretion *in-vitro* yet differentially regulate glucose tolerance *in vivo* highlights the complexity of gut hormone signalling. Together, these results broaden our understanding of enteroendocrine-islet interactions and suggest new perspectives on gut hormone involvement in glucose homeostasis.

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P129

Small intestinal integrity contributes to glucose homeostasis

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More than two billion people worldwide are overweight or obese. Excess caloric intake triggers local and systemic inflammatory responses[1]. Specifically, in the gut, obesity induces increased permeability and remodelling of the intestinal tissues[2]. The small intestine has a crucial role in the regulation of glucose homeostasis, through its role in the sensing, digestion and absorption of nutrients, and the secretion of insulin-stimulating peptide hormones[3]. However, the mechanisms connecting glucose homeostasis and small intestinal integrity are poorly characterised. To investigate how changes in small intestinal inflammation and permeability influence glucose tolerance, lean C57Black6/J mice were treated with an RNA analogue (Poly I:C) to induce intestinal inflammation and damage, or saline control. In addition, we used Tally Ho mice, a model of obesity and type 2 diabetes. All mice were fed a chow diet and monitored for intestinal permeability using FITC-dextran assay and glucose homeostasis using intraperitoneal glucose tolerance tests (IPGTT). Poly I:C induced intestinal damage as confirmed by histology. Poly I:C treatment in lean mice also induced an increase in intestinal permeability compared to saline-treated mice. Furthermore, Poly I:C induced glucose intolerance in a dose-dependent manner. Diabetic Tally Ho male mice had increased permeability compared to the obese but euglycemic littermate controls. Altogether, our preliminary data suggest that intestinal integrity plays a role in regulating glucose homeostasis.

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P130

Utilising urine as a non-invasive biofluid to assess type 2 diabetes and predict metabolic improvement with bariatric surgery

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Introduction

Diagnosing and monitoring type 2 diabetes (T2DM) requires blood testing, which, although being minimally invasive, requires trained medical professionals. Additionally, bariatric surgery may result in T2DM remission, but this varies between 40-80% of patients. Urine samples offer a non-invasive method which may be suitable to screen, monitor, and predict changes in hyperglycaemia/T2DM following bariatric surgery. We investigated pre- and post-surgery urine samples as a method to distinguish between disease states (obesity and T2DM), bariatric surgery type, and T2DM improvement following surgery.

Methods

Urine samples were collected from female white European participants (age = 52.7 ± 1.39 years; body mass index = 41.6 ± 1.09 kg/m^2; $n = 40$) with T2DM undergoing bariatric surgery, at baseline (pre-surgery), 1-month and 6-months post-surgery. Samples were assessed via mass spectrometry (MS), identifying 2557 proteins in total; Amica software was used to determine differences in (1) obesity status; (2) diabetic status; (3) surgery type; and (4) T2DM improvement.

Results

MS identified differentially expressed proteins based on obesity status (class-1 vs class-2: $n = 46$; class-1 vs class-3: $n = 134$; class-2 vs class-3: $n = 330$) and T2DM status (no T2DM vs T2DM: $n = 75$; no T2DM vs prediabetes: $n = 112$; prediabetes vs T2DM: $n = 385$). One month post-surgery, gastric plication (GP) patients had a different protein profile to laparoscopic adjustable gastric banding (LAGB) and biliopancreatic diversion (BPD) patients; this was lost at 6-months post-surgery. 57 differential proteins were identified in pre-surgery urine based on T2DM improvement at 6-months post-surgery.

Discussion

This highlights urine as a useful, non-invasive biofluid that can distinguish between obesity and T2DM statuses. Moreover, urinary protein profiles differ based on bariatric surgery type, and pre-surgery urine samples may be used to predict T2DM improvement following bariatric surgery. This suggests that urine sampling could be utilised as an additional screening/monitoring tool, which could also aid to stratify patients for personalised support to improve success rates post-bariatric surgery.

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P131

Steroid 5α-reductase network in metabolic dysfunction-associated steatotic liver disease

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Pharmacological inhibition of 5α-reductases (*SRD5A1*) activity is associated with insulin resistance, dyslipidaemia, and hepatic steatosis in humans, while increased susceptibility to steatosis and liver fibrosis have been observed in mice with disruption of *Srd5a1*. We aim to identify the potential *SRD5A1* regulatory networks underpinning metabolic dysfunction-associated steatotic liver disease (MASLD). We used genomic and hepatic transcriptomic data from Genotype-Tissue Expression Project (*GTEx*; $n = 208$, 55.0 ± 13.0 years, 66.9% men) and Stockholm-Tartu Atherosclerosis Reverse Networks Engineering Task (*STARNET*; $n = 522$, 65.0 ± 8.7 years, 70.3% men). Causal inference was used to reconstruct interactions between *SRD5A1* and its downstream targets in liver, using *cis*-expression Quantitative Trait Loci as instrumental variables. Co-expression networks were constructed with weighted correlation network analysis (WGCNA). Functional enrichment was conducted to determine the roles of target genes. The networks were subsequently validated in an independent cohort of MASLD cases and controls (*SteatoSITE*; $n = 469$, 52.5 ± 13.3 years, 52.4% men). We identified 54 *cis*-eQTLs of *SRD5A1* in GTEx and 158 in STARNET liver. At 15% FDR, seven causally regulated genes were found in STARNET, including *SERPINF1* and *GGPS1*, suggesting a role in adiposity and cholesterol metabolism. WGCNA analysis identified 45 modules that were significantly associated with *SRD5A1* expression in GTEx and 21 in STARNET. The top two strongly associated modules were enriched for cholesterol and steroid synthesis, and insulin secretion in GTEx; and complement pathways and lipid metabolism in STARNET. Notably, genes within these modules were differentially expressed across fibrosis stages in MASLD patients, with strongest up- or downregulation seen in *HMGCS2*, *APOC1*, *LIPG*, *ACAT1*, *HMGCS1*, *IL6R, C8B,* and *ST6GAL1,* key genes in the metabolic and inflammatory regulation. Hepatic steatosis and fibrosis induced by disruption of *SRD5A1* may be linked with dysregulation in cholesterol metabolism and inflammation pathways in liver. Future work will map the *SRD5A1* pathways in subcutaneous and visceral adipose.

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P132

Hyponatraemia at st george's hospital

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Background

Hyponatraemia, a potentially life-threatening electrolyte disturbance, is frequently encountered in internal medicine. Prompt recognition and appropriate

management - especially in patients with serum sodium <115 mmol/l or with moderate to severe symptoms - are critical for patient safety. These patients often require high-dependency or intensive care unit (ICU) management.
Method
A retrospective study was conducted at St George's Hospital to assess how hyponatraemia is investigated and managed among medical inpatients. The study included patients admitted between 1st December 2024 and 31st January 2025 with sodium levels below 130 mmol/l. Data collected included demographic information, sodium levels, symptoms, investigations performed, causes, management strategies, time to resolution, and mortality rates. The study also compared patients managed on general wards to those referred to the Critical Care Outreach Team (CCOT) or ICU.
Results
Out of 116 patients, 95 were managed on the ward and 21 were referred to CCOT. Notably, 32.6% of ward patients should have been referred to CCOT but weren't, while 47.6% of those referred did not meet criteria for escalation. Both groups were similar in age, gender, sodium levels on admission, time to sodium normalisation, and mortality. Drowsiness (P-value = 0.002) and lower urine sodium (P-value = 0.002) were more common in the CCOT group. Only a small fraction of patients in both groups received the full recommended diagnostic workup for hyponatraemia (5.26% in the ward group, 9.52% in CCOT). SSRIs (P-value = 0.032) were more commonly implicated in CCOT patients, and hypertonic saline (P-value = 0.038) was used more in this group.
Conclusion
The study highlights gaps in the investigation and management of hyponatraemia. Particularly in escalation practices and completion of recommended investigations for more targeted treatment. It underscores the need for improved adherence to guidelines to ensure timely referral to critical care services and appropriate treatment, including interventions such as hypertonic saline.

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P133

The Tubby Protein as a Transcription Factor Regulating Brown Adipocyte Differentiation

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Brown adipose tissue (BAT) primarily performs non-shivering thermogenesis by metabolising lipids using mitochondrial uncoupling protein 1 (Ucp1). Differentiation of brown preadipocytes is essential for this function, driven by key transcription factors such as Pparg, which promotes lipid storage and sensitivity to insulin and β-adrenergic agonists. The Tubby protein, first identified by its mutant variant in mice for its extreme obesity and diabetes phenotype, is expressed in adipose tissue and has been linked to insulin sensitivity and resistance. Tubby contains a DNA-binding domain and prior work suggests Tubby is a potential transcriptional regulator during BAT maturation. To investigate Tubby's role in brown adipocyte differentiation, we characterised its expression via western blotting as well as immunofluorescence analysis. RNA-sequencing analysis was performed on differentiating brown preadipocytes following Tubby siRNA knockdown to identify potential transcriptional targets, after 24 hours of differentiation. Selected potential target genes were validated by qRT-PCR. Tubby expression was found to be highest throughout the cell at 24 hours after initiation of differentiation, while also translocating to the nucleus, before decreasing in expression until fully matured. Analysis of the RNAseq data identified several essential BAT functional pathways affected by Tubby knockdown, including Ppar signalling and lipolysis. Specifically, expression of key genes such as Pparg and Fabp4, were significantly reduced following Tubby depletion (> 0.5 log2fold change in expression). This data indicates that Tubby is crucial for the appropriate transcriptional cascade required for brown adipocyte maturation. Our findings suggest that the protein Tubby acts as a transcription factor essential for the regulation of brown adipocyte differentiation, potentially through the direct or indirect control of master regulators like Pparg at an early stage in BAT differentiation. Further investigation is needed to fully characterise the DNA-binding activity of Tubby and its precise mechanism of action within the BAT differentiation pathway.

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P134

When hypoglycemia hits early: a rare case of insulinoma post-bariatric surgery and novel tirzepatide therapy in preoperative optimization

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Introduction
Post-bariatric hypoglycemia or late dumping syndrome is a complication of bariatric surgery occurring 1- 3 years post operatively and 1-3 hours post meal. Presentation includes hypoglycemia, lethargy, dizziness and diaphoresis. When hypoglycemia occurs prior to this time frame, other etiologies should be considered. This abstract reviews the presentation of hypoglycemia in the early post-operative stage of laparoscopic sleeve gastrectomy.
Background
A 48-year-old female presented with recurrent hypoglycaemic episodes 11 days following laparoscopic sleeve gastrectomy. Her symptoms included dizziness, confusion, diaphoresis and fatigue. Self-monitoring blood glucose readings confirmed hypoglycaemia. Hypoglycaemia was documented within 24 hours of initiating a 72-hour fast. Laboratory evaluation revealed elevated insulin (216 pmol/l) and C-peptide (1343 pmol/l) levels, with a negative sulfonylurea screen, suggesting endogenous hyperinsulinism. CT and MRI of the pancreas were unremarkable. Endoscopic ultrasound identified an 11–12 mm lesion in the pancreatic head. Fine needle aspiration confirmed insulinoma. Diazoxide therapy was initiated but was subsequently discontinued due to deranged liver enzymes. Whipple's procedure was deferred due to inadequate postoperative weight loss. Tirzepatide was commenced to optimise weight management and with 23 kg loss she currently eligible for surgery.
Discussion
This case underscores the importance of considering insulinoma in patients with early-onset hypoglycaemia following bariatric surgery. In the preoperative period a low-calorie liver shrinking diet improves the mobility of the liver intraoperatively, causing rapid visceral fat reduction, improving insulin sensitivity and likely unmasked the insulinoma. Tirzepatide proved effective promoting weight loss with euglycemia in the setting of hyperinsulinemia. Though there is documented use of incretin mimetic agents in reactive hypoglycaemia and late dumping syndrome, use in the setting of hyperinsulinemia has not been documented. To our knowledge this has been the first successful case. Tirzepatide may be an effective preoperative therapy to facilitate surgical candidacy in patients with morbid obesity and hyperinsulinism.

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P135

Alcohol abuse: an easily missed cause of severe lactic acidosis

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Lactic acidosis defined by a lactate >4 mmol/l, pH <7.35 and bicarbonate < 20mmol/l is the commonest cause of metabolic acidosis in hospitalised patients. It is grouped into type A (hypoperfusion) and type B (non-hypoperfusion). Alcoholic lactic acidosis is a rare type B form. We report an obfuscated severe case in a patient with a history of alcohol abuse.
Case report
36 year old female presented with myalgia, collapse and impaired conscious level. Examination: cachectic, dehydrated, sinus tachycardia 120/minute, blood pressure 100/60 mmHg, tachypnoeic 28 per minute. Alcohol consumption was denied. Investigations: pH 6.76, bicarbonate 3.1 mmol/l, lactate 23.7 mmol/l, ketones 2.3 mmol/l, glucose 5.9 mmol/l, sodium 142 mmol/l, chloride 103 mmol/l, potassium 5.7 mmol/l, urea 3.6 mmol/l, creatinine 111 umol/l, eGFR 48 ml/per min, osmolality 317 mmol/Kg, CRP 2 mg/l, amylase 411 U/l, corrected anion gap 33 mmol/l, toxicology screen negative for ethanol, ethyl alcohol and methanol. The initial diagnosis was antifreeze ingestion (latter two results not available at that time). Intensive fluid resuscitation with Hartmann's, 10% dextrose and fomeprizole resulted in correction of clinical and laboratory abnormalities within 48 hours. Endocrine opinion was sought on the aetiology of the lactic acidosis. The patient confirmed chronic and acute (3 days prior to admission) consumption of whisky with subsequent anorexia.
Discussion
Metabolism of ethanol is to acetaldehyde and then acetate by the NAD+ cofactor enzymes alcohol dehydrogenase and aldehyde dehydrogenase respectively. The conversion results in increased generation of NADH which alters the redox reaction catalysed by lactic dehydrogenase to favour pyruvate to lactate conversion. The half-life of ethanol (4-5h), resulting in its absence on toxicology screen, plus initial denial of its consumption confounded the diagnosis. The rapid recovery was attributed to the absence of co-pathologies.

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P136

Glucocorticoid activation of mono-ADP-ribosylation through parp16 determines er stress response

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Glucocorticoid excess-induced muscle wasting is characterised by activation of the unfolded protein response (UPR) via its three canonical arms (PERK, IRE1, and ATF6) yet underlying causal mechanism remains unclear. Here we examine how glucocorticoids regulate the endoplasmic reticulum (ER) UPR, aiming to mitigate adverse effects of glucocorticoids. We previously identified links between glucocorticoids and ADP-ribosylation, an NAD^+-dependent modification involving mono-(MAR) or poly-(PAR) ADP-ribose. In terminally differentiated murine muscle cells(C2C12s), we show dexamethasone(1μM) inhibits PAR (0.61-fold change ± 0.13 sem, $P < 0.01$; $n = 8$) with a corresponding increase in NAD^+(20% increase, $P < 0.02$; $n = 8$). Conversely, Mono-ADP-ribose increases (1.34FC ± 0.20, $P < 0.001$; $n = 6$) under the same conditions. To understand whether increment of MAR is from breakdown of PAR, we used a PAR gluco-hydrolyser inhibitor and found MAR upregulation is unaffected by inhibition of PAR degradation. This demonstrates MAR is not a breakdown product of PAR, but a distinct signaling modification. Analysis of subcellular fractionations of muscle cells reveals PAR is decreased in ER, mitochondria, and nuclei with dexamethasone (0.75FC ± 0.08), (0.85FC ± 0.07), (0.68FC ± 0.1), respectively. MAR is significantly elevated in all organelles in response to dexamethasone (nucleus: 1.61FC ± 0.30 ; mitochondria: 2.37FC ± 0.68; microsomes: 3.36FC ± 1.18; cytoplasm: 3.28FC ± 1.14, $P < 0.05$; $n = 3$). These data highlight the compartmental-specific signaling of this post-translational modification. Based on dexamethasone-induced elevation of MAR and UPR-stress markers in the ER, we examined transcriptional responses of PARPs1-16 to glucocorticoids finding PARP16 to be most upregulated (1.82FC ± 0.18, $P < 0.05$; $n = 3$). Crucially, inhibiting PARP16 reverses dexamethasone-induced activation of all three arms of UPR (p-eif2a/eif2a: 0.3FC ± 0.31; sXBP1: 0.15FC ± 0.13; ATF6: 0.76FC ± 0.23, $P < 0.05$, $n = 3$), and MAR. Our findings uncover compartment-specific regulation of ADP-ribosylation by glucocorticoids. Importantly, we define PARP16–ADP-ribosylation–Unfolded Protein Response axis as a key pathway driving muscle atrophy.

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P137

Delayed diagnosis of Wolfram Syndrome Type I Spectrum Disorder

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Wolfram Syndrome Type I Spectrum Disorder (WFS1-SD) is a rare autosomal recessive disease caused by mutations of the WFS1 gene located on chromosome 4 p16.1. The disorder comprises early (<16 years) optic atrophy, diabetes mellitus and hearing loss. Additional manifestations are neurological, renal, bladder and psychiatric.

Case report

An 18-year-old male was referred with possible monogenic diabetes. Optic atrophy had been diagnosed at 10 years of age (decreased visual acuity) and type 1 diabetes at 16 years of age (osmotic symptoms and HbA1c 134 mmol/mol). He had never experienced diabetic ketoacidosis and was treated with insulin. A mitochondrial MT-ND 5 mutation of uncertain significance (ClinVan) had been recorded and invoked as the aetiology of the optic atrophy. Examination confirmed BMI 25, visual acuities 6/24-1 right and 6/24+1 left, optic atrophy, no diabetic retinopathy, normal visual fields, dysdiadochokinesia of tongue, arms/hands, bilateral reduction of triceps/supinator reflexes, absent knee/ankle reflexes and flexor plantar responses. Anti-GAD, Islet antigen 2 and ZnT-8 antibodies were negative. A diagnosis of WFS1-SD was considered and confirmed by the finding of two likely pathogenic WFS1 gene mutations. Both were previously reported but not in this combination. His parents were confirmed as carriers and brother normal.

Endocrine investigations

normal basal pituitary function except for slightly low cortisol level but short tetracosactide and insulin tolerance tests confirmed normal cortisol and growth hormone responses. Water deprivation test normal.

Other investigations

audiometry, ECG, echocardiography, MRI heart, MRI pituitary/brain all normal. Exercise ECG stopped due to fatigue at 82% of age-related predicted heart rate.

Discussion

This case demonstrates the need to consider WFS1-SD in patients with the combination of optic atrophy and diabetes mellitus of juvenile onset. The finding of a mitochondrial gene mutation delayed the diagnosis of WFS1-SD. The variation in phenotype is demonstrated by this case.

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P138

Three similar cases of misdiagnosed glycogenic hepatopathy – a cautionary tale

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Glycogenic hepatopathy (GH) is a rare complication of poorly controlled type 1 diabetes characteristically seen in children and young adults. The aetiology is incompletely understood but recurrent extreme fluctuations in glucose levels with hyperglycaemia being over-treated with insulin resulting in hypoglycaemia appears to be pivotal. Transient elevation of transaminases along with hepatomegaly are found coincidental with episodes of abdominal pain, nausea and vomiting. We present 3 cases of GH with similar clinical and investigation features in which the hepatomegaly was attributed to metabolic dysfunction-associated steatotic liver disease (MASLD).

Case 1

female, age 22, HbA1c 148 mmol/mol, labile blood glucose levels, weight 38 kg, BMI 20.4, alanine transaminase (ALT) 466 IU/l, MRI no evidence of fatty infiltration, liver biopsy – histology consistent with GH.

Case 2

male, age 23, HbA1c 129 mmol/mol, labile blood glucose levels, weight 60.3 kg, BMI 20.8, ALT 264 IU/l, MRI no evidence of fatty infiltration, liver biopsy – histology consistent with GH.

Case 3

female, age 21, HbA1c 133 mmol/mol, labile blood glucose level, weight 39.3 kg, BMI 15.2, ALT 164 IU/l, MRI no evidence of fatty infiltration, liver biopsy declined.

Discussion

Following the entry of high glucose levels into hepatocytes, facilitated by the non-insulin dependent glucose transporter (GLUT2), it is phospholorated to glucose-6-phosphate by the enzyme glucokinase which is then converted to glycogen by glycogen synthetase, the latter activated by high insulin levels. This process results in increased glycogen storage in hepatocytes resulting in them swelling and consequent hepatomegaly. The similar features in our 3 patients, particularly the low BMIs, contrast with those of MASLD which include type 2 diabetes and obesity. Avoidance of extreme variations of glucose improved HbA1c with resolution of symptoms and hepatomegaly. Case 3 supports the suggestion that MRI is possibly a reliable substitute for liver biopsy.

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Exploring brown adipose tissue-mediated systemic metabolism using network analysis of total-body PET/CT scans

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Brown adipose tissue (BAT) generates heat through non-shivering thermogenesis, primarily when activated by cold exposure. The presence of BAT, identified by 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography with computed tomography (PET/CT) at room temperature, is associated with improved insulin sensitivity and wider cardiometabolic health. However, the mechanisms mediating this beneficial effect are unclear and may be due to crosstalk between BAT and other organs. We hypothesised that adults with and without detectable BAT would display different organ-level ^{18}F-FDG-uptake patterns, reflecting differences in systemic metabolism. Thirty total-body static ^{18}F-FDG PET/CT scans were analysed from 15 BAT-positive (64.2 ± 13.9 years; 25.0 ± 5.4 kg/m^2) and 15 BAT-negative (64.2 ±

14.4 years; 26.4 ± 5.1 kg/m^2) age, BMI, and sex-matched patients. BAT was identified manually using BARCIST criteria, and >140 tissues were segmented per scan using the Multi-Organ Objective Segmentation Engine (MOOSE) tool. Bone marrow adipose tissue, red marrow and bone were segmented using Hounsfield Unit thresholds. Standardised uptake values (SUVs) were extracted from PET data and used to compare groups, followed by exploration through principal component analysis (PCA) and correlation-based networks in Graphia. Organ-specific ^{18}F-FDG SUVs in key cardiometabolic tissues such as skeletal muscle, liver, white adipose tissue, and the heart were similar between groups. PCA revealed that bone and marrow tissues primarily drove systemic variance in glucose metabolism, but BAT status did not account for variation in the principal components. Network analysis further revealed that BAT-positive participants exhibited more inter-organ correlations in glucose uptake, involving muscle, bone, and heart. In contrast, BAT-negative participants showed correlations largely confined to individual organ systems. In conclusion, while BAT presence was not associated with organ-specific differences in glucose uptake, it was linked to a more integrated metabolic network. Further studies under cold stimulation and/or dynamic imaging may better characterise BAT's systemic influence.

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Development of sub-clinical hepatic steatosis precedes metabolic dysfunction but not obesity in a porcine model of high-fat feeding

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Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) susceptibility varies among people due to its multifactorial nature. We hypothesised that we could induce insulin resistance and steatosis in a fatty breed of pig exposed to short-term high fat feeding. Female Mangalitza pigs (a fatty, slow growing breed) ($n = 6$) were metabolically phenotyped at baseline and during 15-weeks of high fat diet (HFD, 23% saturated fat). Insulin, glucose, NEFA, total cholesterol, liver enzymes and non-invasive blood pressure (NIBP) were monitored. Oral Glucose Tolerance Tests (OGTTs) were performed at baseline, week 7, and week 13. Liver biopsies and MRI were performed at baseline and week15. The HFD significantly increased body fat mass in MRI (from 27 ± 6 to 41 ± 6%) and weight (from 64 ± 6 to106 ± 6 kg). This was accompanied by greater, though not sustained, insulin secretion during OGTT (AUC_{INS} baseline 1075 ± 563.5 vs. week13 3372 ± 1835; $P < 0.05$), which effectively suppressed NEFA. Fasted NEFA initially increased (Baseline:501.5 ± 176.7nmol/l vs. Week 6:1133 ± 366.4nmol/l; $P < 0.05$) before returning to baseline levels (Week15:483.1 ± 127nmol/l). Crucially, triglycerides, total cholesterol, liver enzymes, NIBP, and HOMA-IR remained unchanged throughout the trial. Liver histopathology, however, revealed early signs of pathology, including increased inflammation and ballooning (H&E, MASLD score 1.5IQR1.5 vs 4IQR1.92, $P < 0.05$), collagen deposition (Picrosirius Red, N of pixels 167.91x109 ± 86.25x109 vs 241.17x109 ± 48.88x109,$P < 0.05$), and small lipid droplets (Oil Red O, droplets total area and number), though clinical steatosis did not develop. These pigs became obese yet demonstrated a positive adaptive response to HFD. They were not dyslipidaemic, nor did they develop severe insulin resistance or hypertension, suggesting a resilient phenotype where systemic metabolic health was maintained despite obesity. Liver histopathology, conversely, revealed a subclinical MASLD, suggesting that in this model, liver changes may develop at an early stage, preceding systemic pathology, which could allow to find the earliest drivers of MASLD.

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Insulin Autoimmune Syndrome: Presenting as severe hypoglycemia with recurrent syncope and seizures

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Insulin autoimmune syndrome (IAS), or Hirata disease, is a rare cause of spontaneous hypoglycemia mediated by insulin autoantibodies (IAA). We report a 76 year old Caucasian male with hypertension, ischemic heart disease, and benign prostatic hyperplasia who experienced recurrent syncope and seizure like episodes over two months, leading to three hospital admissions. Initial investigations including CT/MRI brain, EEG, echocardiogram, and Holter monitoring were unremarkable. During the third admission, profound hypoglycemia was documented (serum glucose 2.2 mmol/l), accompanied by markedly elevated insulin (>6945 pmol/l), C-peptide (2.48 nmol/l), and IAA titers (75%, normal < 5.5%). Pancreatic imaging and endoscopic ultrasound excluded insulinoma or other neuroendocrine tumors, and a negative sulfonylurea screen confirmed IAS. Management comprised two days of intravenous hydrocortisone, transition to oral prednisolone, frequent low-carbohydrate meals guided by dietary counselling, and continuous glucose monitoring. Rituximab was considered but not administered due to rapid clinical and serological improvement. Follow up at five months demonstrated declining IAA titers and no further hypoglycemic episodes. Historically most prevalent in Japan (0.017/100,000), IAS is associated with HLA-DR4 (DRB1*0406) and triggers such as sulphhydryl drugs or viral infections. Rising reports among Caucasians likely reflect wider medication use and availability of IAA assays. The pathophysiology involves high capacity, low affinity IAA forming insulin antibody complexes that cause unpredictable glycemic swings. Clinical manifestations range from mild neuroglycopenic symptoms to severe seizures and syncope. Management is challenging but often successful, with an overall spontaneous remission rate of approximately 82% and recurrence in fewer than 5% of cases. This case underscores the importance of considering IAS in patients presenting with unexplained hypoglycemia and highlights the effectiveness of corticosteroids and dietary strategies.

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High-throughput functional screening of INSR intracellular domain variants

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Pathogenic extracellular mutations in the insulin receptor (INSR) produce recessive severe insulin resistance (IR), while intracellular mutations confer autosomal dominant IR explained by trans inhibition of wild-type (WT) INSR by mutant. Few recurrent mutations are described, however, and large-scale sequencing has revealed many "Variants of Unknown Significance" (VUS) that confound genetic diagnosis and stratification for personalised therapies. We recently applied multiplexed assays of variant effects (MAVEs) to evaluate expression, insulin binding and signalling by ~14,000 extracellular INSR variants. We now seek to interrogate ~8,500 INSR variants in the intracellular tyrosine kinase-containing domain essential for signal transmission. Most such variants are classified as VUS. To do this we have adapted our prior MAVE approach. First, we have enhanced the cell line used, an Igf1r knockout mouse embryo fibroblast (MEF) line in which endogenous mouse Insr is knocked down potently, with concomitant expression of mutant human INSR under the control of doxycycline. We have now introduced a separate transposon-encoded WT INSR allele tagged with a bromotag, whose transcription is induced by cumate and whose protein level can be modulated by a small molecule PROTAC (Proteolysis Targeting Chimera). This system has been validated and permits controlled testing of mutant receptor in isolation, and as a heterodimer with WT receptor. As a final step in assay optimisation, we have used RNA-seq to identify a promoter to use in an insulin dose-responsive transcriptional reporter currently being constructed. This will be added to a saturating, plasmid-based barcoded INSR variant library already made before A. barcode-variant phasing by long read sequencing, B. incorporation via Bxb1 at a unique landing pad in target MEFS, and C. MAVEs. This powerful new system will enable functional stratification of all intracellular INSR variants, identifying residues essential for INSR function and dominant negative activity, and panning of candidate therapies against all variants.

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Insulinotropic and metabolic benefits of *Punica granatum* peel extract in obese diabetic mice

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Punica granatum peel has long been used in traditional medicine for managing metabolic disorders such as diabetes. Rich in antioxidant and anti-inflammatory compounds, it may offer therapeutic benefits in alleviating diabetes associated complications. This study evaluated the insulin-releasing and glucose-lowering effects of ethanol extract of *Punica granatum* (EEPG) peel using both *in-vitro* and *in vivo* models. In BRIN-BD11 pancreatic β-cells, EEPG significantly enhanced insulin secretion in the presence and absence of known insulin modulators such as IBMX and tolbutamide, while its effect was partly inhibited by diazoxide and verapamil, indicating involvement of K_{ATP} and calcium channel-dependent pathways. EEPG also promoted β-cell proliferation as confirmed by Ki67 immunostaining. In high-fat-fed (HFF) diet-induced obese mice, oral administration of EEPG (150 and 250 mg/kg) improved glucose tolerance at 30, 60, and 120 min, lowered fasting blood glucose, and reduced food intake over 21 days, with the higher dose demonstrating superior efficacy in normalizing body weight and fluid consumption. The glucose-lowering effect of EEPG was comparable to that of glibenclamide (5 mg/kg). Additionally, EEPG enhanced gut motility and improved the lipid profile by increasing HDL levels and reducing total cholesterol, LDL, and triglycerides, suggesting its potential role in supporting digestive and metabolic functions. Preliminary phytochemical screening indicated that EEPG contains flavonoids, terpenoids, and steroids, which may be responsible for these beneficial effects. Overall, these findings demonstrate that EEPG exerts insulinotropic and antihyperglycemic effects through β-cell stimulation, enhanced proliferation, and regulation of glucose metabolism in diet-induced obese mice. Further studies are warranted to elucidate its underlying molecular mechanisms and active phytoconstituents contributing to its anti-diabetic potential.

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Euglycaemic diabetic ketoacidosis associated with semaglutide use: a case report

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Introduction
Euglycaemic diabetic ketoacidosis (euglycaemic DKA) is an uncommon but serious metabolic disorder characterised by ketoacidosis with normal or mildly raised blood glucose levels. While classically associated with the concomitant use of sodium-glucose cotransporter-2 (SGLT2) inhibitors, the concomitant use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide has also been implicated.
Case study
A 37-year-old woman presented with a one-day history of nausea, vomiting, and malaise. Medical history included type 2 diabetes mellitus and overweight. Medications included metformin and semaglutide. She was previously taking canagliflozin, which had been stopped three months prior, and semaglutide was started three weeks prior to presentation. She was a non-smoker and did not drink alcohol. Examination was unremarkable. She had a body mass index of 39 kg/m2.
Investigation and management
Investigations demonstrated metabolic acidosis with ketosis and mild hyperglycaemia (glucose value:10.7 mmol/l) consistent with euglycaemic DKA. She also had mild leukocytosis with an elevated c-reactive protein level of 8 mg/l. Her renal function was normal. A test for COVID-19 infection was incidentally positive. Her c-peptide and pancreatic autoimmune antibodies were normal. She was given a diagnosis of euglycaemic DKA precipitated by gastroenteritis. She was treated according to the DKA management guidelines and made a rapid recovery. She was discharged on metformin, gliclazide and once a day long-acting insulin (glargine).
Discussion
We have presented a case of euglycemic diabetic ketoacidosis in a patient taking Semaglutide. The interaction between intercurrent illness, reduced intake, and relative insulin deficiency probably precipitated euglycaemic DKA in this patient. Prior SGLT2 inhibitor exposure may have further increased risk, as these agents can predispose to DKA even after discontinuation due to residual metabolic effects. Clinicians should remain alert for euglycaemic DKA occurring in patients taking semaglutide, particularly with recent SGLT2 use.

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An audit on outpatient insulin prescribing practice in an Irish tertiary hospital

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Insulin is a high-risk medication which has the potential for harm if not prescribed correctly. This audit aimed to evaluate the prescription of insulin in the outpatient setting in St Vincent's University Hospital. A retrospective analysis of all patient charts from six days of diabetes clinics in 2025 was carried out. Data of 104 patients (67 men, median age 49.5 years, median HbA1c 57.5 mmol/mol) were available for analysis. Insulin was prescribed for all ($n = 61$) patients with type 1 diabetes mellitus and 37% ($n = 15/41$) with type 2 diabetes mellitus. GLP-1 agonists were prescribed for 10% ($n = 6$) of patients with T1DM and 41% ($n = 17$) of patients with T2DM. 70% ($n = 46$, of which 10 are T2DM) of patients prescribed insulin were on a basal/bolus regimen, 7% ($n = 5$) on a basal- or bolus-only regimen, and 38% ($n = 25$, all T1DM) on an insulin pump. Basal timing was specified in 30% ($n = 15$). Needles were prescribed for 82% ($n = 62$) while needle size was specified in 61% ($n = 38$). Of those on insulin, glucose test strips were prescribed for 90% ($n = 69$), lancets for 81% ($n = 62$), continuous glucose monitoring for 80% ($n = 61$), glucose shot for 92% ($n = 70$), and glucagon for 84% ($n = 58$). Ketone test strips were prescribed for 92% ($n = 56$) patients with T1DM. In our cohort of 76 patients living with diabetes on insulin therapy, we noted high levels of co-prescription of blood glucose monitoring devices and hypoglycaemia treatment but incomplete prescription on basal timing and needle specification. We suggest strategies such as education for prescribers, insulin prescribing checklist, implementation of prescription template and electronic prescribing.

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G protein-coupled oestrogen receptor 1 regulates CPT1a expression in human hepatocytes

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Background
The prevalence and severity of metabolic dysfunction-associated steatotic liver disease (MASLD) rises after the menopause. Preclinical studies have demonstrated that oestrogen signalling regulates metabolic and inflammatory pathways involved in MASLD development in rodents. The precise impact of distinct oestrogen receptor signalling on metabolic pathways involved in MASLD in human hepatocytes is unclear.
Methods
Gene expression levels of oestrogen receptor α (ERα), β (ERβ) and G protein-coupled oestrogen receptor 1 (GPER1) in human hepatoma cell lines (Huh7 and HepG2) and primary human hepatocytes were evaluated using RNA sequencing and western blot analysis. Huh7 cells were treated for 24 hours with oestradiol (E2) or the specific GPER1 agonist (G1), and expression of genes involved in *de novo* lipogenesis (FASN and ACCA) and fatty acid oxidation (CPT1A and PPARα) were assessed using Taqman qPCR. Additional gene expression studies were conducted following siRNA knockdown of GPER1 in the presence and absence of G1.
Results
GPER1 mRNA was highly expressed in Huh7, HepG2 cells, and in primary human hepatocytes. In comparison, in all 3 cell culture models, expression of ERα and ERβ was minimal. mRNA data were endorsed through western blot analysis confirming protein-level GPER1 expression. Treatment of Huh7 cells with 2μM G1 increased CPT1A mRNA expression ($P = 0.02$). Successful knockdown of GPER1 in Huh7 cells (64 ± 1.2% knockdown) reversed the G1-induced upregulation of CPT1A ($P < 0.001$). There were no changes in mRNA expression of FASN or ACCA.
Conclusion
GPER1 is highly expressed in human hepatocytes and has the potential to regulate lipid metabolism. Further study is needed to validate its role in the development of MASLD in humans and specifically its role in the postmenopausal predisposition to MASLD and the putative impact of hormone replacement therapy.

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Deep metabolic phenotyping reveals tissue-specific actions of transdermal oestradiol and oral micronised progesterone in postmenopausal women

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Background
Cardiometabolic risk increases after the menopause, with evidence suggesting an increased prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD). Hormone replacement therapy (HRT) may modify cardiometabolic disease risk in menopausal women and previous studies have focussed on oral combined preparations. Although transdermal oestradiol (E2) with oral micronised progesterone is the current preferred regimen, its metabolic impacts are not well characterised.
Methods
Postmenopausal women ($n = 8$) underwent paired deep metabolic phenotyping before and after 12-weeks of low-dose transdermal E2 and nightly 100 mg oral micronised progesterone. Investigations included liver magnetic resonance imaging to assess hepatic fat content, mixed meal testing (after an overnight fast) incorporating stable isotope tracers ([U^{13}C]palmitate, ^2H_2O), adipose microdialysis, abdominal/gluteal adipose biopsies and dual energy x-ray absorptiometry scanning.
Results
All 8 participants successfully completed the study, but only 3 demonstrated a detectable increase in plasma E2 levels. After treatment, body weight increased ((mean $\pm$ standard deviation) $+0.91 \pm 1.2$ kg, $P < 0.05$), android fat mass increased (375.5 ± 376.2 g, $P < 0.05$) but gynoid fat mass remained unchanged compared to baseline. Circulating liver enzymes were unchanged and although hepatic fat content increased, this did not reach statistical significance ($+0.74 \pm 1.0$ %, $P = 0.11$). Fasting triglyceride concentrations reduced after treatment (-0.22 ± 0.28 mmol/l, $P < 0.05$). Subgroup analysis of participants who exhibited increased E2 levels showed decreased non-esterified fatty acid (NEFA) spillover from adipose tissue after treatment, measured through ^{13}C incorporation from a labelled fatty acid into the plasma NEFA pool.
Conclusions
This is the first study to assess how transdermal E2 and oral micronised progesterone impacts metabolic disease risk using deep metabolic phenotyping. Preliminary analysis suggests that there may be divergent responses in E2-absorbers and non-absorbers, and begins to highlight potential differential impacts of oestrogen and progesterone on adipose tissue function.

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Long-Term Impact of Roux-en-Y Gastric Bypass on Comorbidity and Type 2 Diabetes in Adolescents: A Systematic Review and Meta-Analysis

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Background
The long-term impact of Roux-en-Y gastric bypass (RYGB) on comorbidities in adolescents with severe obesity remains incompletely defined. We conducted a systematic review and meta-analysis to evaluate remission of type 2 diabetes (T2DM), hypertension, and dyslipidaemia after RYGB in this population.
Methods
Searches of MEDLINE, EMBASE, Cochrane, and SCOPUS were performed to July 2023. Eligible studies included patients under 21 years undergoing RYGB with ≥ 2 years of follow-up. Data were pooled using a random-effects model. Primary outcomes were remission of T2DM, dyslipidaemia, and hypertension.
Results
Twelve studies comprising 522 adolescents were included. The mean age was 17.5 years (range 13–21), and 73.6% were female. Mean follow-up duration was 48.4 months. Baseline mean body mass index (BMI) was 50.1 kg/m^2. Preoperatively, 12.2% had established T2DM, 24.3% had hypertension, and 29.7% of patients had dyslipidaemia. T2DM remission was achieved in 85% of patients, with 73% remission of hypertension and 85% remission of dyslipidaemia.
Conclusion
RYGB in adolescents with severe obesity results in substantial remission of type 2 diabetes and obesity associated comorbidities. While metabolic outcomes are favourable, the risk of postoperative complications must also be considered. Further long-term longitudinal studies extending into late adulthood are needed.

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Use of fibroscan assessment to determine MASLD in a diverse paediatric obesity cohort

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Background
Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD), a term used to describe the spectrum of liver features associated with obesity, is seen in one third of adults living in the UK. The persistent accumulation of liver steatosis can lead to scarring causing the development of Metabolic Dysfunction-Associated Steatohepatitis (MASH). MASH is linked to genetic predisposition and ethnicity, with higher rates in South Asians. FibroScans are being increasingly used as a non-invasive, quick ultrasound-like test to detect MASLD in adults. Its use in paediatrics is limited. We assessed the utility of FibroScans in a single tier 3 paediatric Complications of Excess Weight (CEW) clinic in East London.
Methods
Over the last 6 months, we offered FibroScans to patients attending CEW (referral criteria BMI SDS > 3.3 with associated co-morbidity). MASLD was indicated by a result of CAP ≥ 248dB/m and stiffness < 7.5kPa, and MASH was indicated by CAP ≥ 248 dB/m and stiffness > 7.5kPa. Results were obtained from routine blood tests (including liver function tests and HbA1C).
Results
Out of the 9 children (3 females, 6 males) aged 9-17 yr (mean $= 12$ yr) with BMIs from 28.2-42.6 kg/m^2 (mean $= 34.9$), 8 presented had Fibro-Scan measurements consistent with MASLD/MASH. CAP scores ranged from 210-348 dB/m (mean $= 289.3$) and liver stiffness ranged from 4.4-19.6 kPa (mean $= 7.7$). 5/9 children had Fibro-Scan results representing steatosis alone and 3/9 representing fibrosis. In contrast, only 2/9 patients showed deranged LFTs, ALT ranged from 17–244 U/l (mean $= 65$). Ethnicities of the children were Black, Asian and Middle Eastern.
Conclusion
Our findings indicate that MASLD is likely an underrecognized condition within the diverse paediatric obesity cohort of East London. Our findings demonstrate that LFTs do not consistently capture steatosis or fibrosis. Hence FibroScans may offer an alternative/ adjunctive non-invasive clinical tool in paediatric obesity clinics to enable early detection of MASLD.

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Real-World Experience of Semaglutide (Wegovy) Effectiveness in Weight Loss in an NHS Tier-3 Weight Management Service

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Background
In 2023, NICE approved Semaglutide for the treatment of obesity in adults with BMI $\geq$35 kg/m^2, with at least one weight-related comorbidity, within Tier-3 weight management services. Continuation beyond 6 months requires $\geq$5% weight loss, with a maximum duration of 2 years.
Objective
To evaluate real-world effectiveness and tolerability of **Wegovy** in an NHS Tier-3 weight management service.
Method
A retrospective study of adults starting Wegovy between January 2024 and August 2025 in Musgrove Park Hospital, Taunton with data collection of demographics, weight, BMI, treatment duration, and discontinuation through electronic records.
Results
Of 181 patients (mean age 51.3 $\pm$ 12.4 years; 66 % female), baseline weight was 142.1 $\pm$ 34.9 kg and BMI 50.1 $\pm$ 10.5 kg/m^2. At 6 months, 116/181 (64%) had weight data: mean weight loss 9.5 $\pm$ 5.2%. 27/181 (14.9 %) discontinued during the first 6 months (side effects 14/181, 7.7 %; $<$5 % weight loss 8/181, 4.4 %; poor adherence 5/181, 2.8 %). 38/181 had been on treatment $<$6 months and, 16/181 (8.8 %) discontinued Wegovy between 6–12 months (bariatric surgery 4/181, 2.2 %; swapped to tirzepatide 5/181, 2.8 %; complications 3/181, 1.7 %; conception planning 2/181, 1.1 %; target weight 1/181, 0.6 %; death 1/181, 0.6 %). At 12 months, 65/181 had follow-up weight data, with mean weight loss of 13.5 $\pm$ 6.5%, and 138/181 (76.2%) remained on treatment.
Discussion
In comparison with global studies, weight loss at 12 months is similar (13.5% vs 14.9%)[1]. Treatment persistence at 6 months is significant 81% vs 46.3%, [2]while discontinuation due to side effect is 7.7%. Despite sporadic availability of semaglutide in NHS, this can be effective management.
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Successful outpatient treatment of diabetic foot osteomyelitis with dalbavancin – a case report
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Dalbavancin is a Lipoglycopeptide antimicrobial that can be considered in the treatment of Diabetic Foot Osteomyelitis (DFO). When administered through intravenous infusion on day 1 and day 8, Dalbavancin maintains therapeutic concentrations within the cortical bone for up to 8 weeks. Here we present an 86-year-old female who attended the Diabetic Foot ProtectionService at Regional Hospital Mullingar with active ulcers of her left foot, at the lateral border of her metatarsophalangeal joint (4.5 cm x 5 cm), hallux interphalangeal joint (1.5 cm x 1.5 cm) and second digit interphalangeal joint (2 cm x 2 cm). Past medical history was significant Type 2 Diabetes Mellitus and Chronic Kidney Disease stage 3b. Inflammatory markers were elevated (CRP 104 mg/l (ref, $<$ 5)), white cell counts 13.28x10^9/l (ref, 4 - 10)). DFO was confirmed clinically as all ulcers probed to bone. The patient completed multiple courses of oral antibiotics over 8 weeks without clinical improvement. Dalbavancin was given in the outpatient setting (1g on day 1, 500 mg on day 8). Dalbavancin treatment was associated with a significant improvement in inflammatory markers (CRP 9 mg/l, WBC 9.27x10^9/l), and ultimately wound healing. Five months post administration, the ulcers have reduced in size (metatarsophalangeal (1.5 cm x 3.8 cm), hallux (0.2 cm x 0.2 cm) and second digit in remission). In this case study Dalbavancin was shown to successfully treat DFO. Dalbavancin has significant potential benefits over standard antimicrobial treatments, potentially eliminating the need for lengthy oral or intravenous antibiotic courses, reduced burden on Outpatient Parenteral Antimicrobial Therapy services, and avoidance of inpatient admission
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Evaluating adherence to lipid management guidelines in adults with type 1 diabetes: a clinical audit of primary prevention practices
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Background
People with type 1 diabetes (T1DM) are at a significantly increased risk of cardiovascular disease (CVD) and stroke compared with the general population. Statin therapy effectively reduces this risk. According to NICE guidelines (NG238), statin treatment for primary prevention should be offered to adults with T1DM who are aged over 40 years, have diabetes for more than 10 years, have established nephropathy, or have other CVD risk factors. NICE also recommends an annual lipid profile for all adults with diabetes.
Aim
To evaluate adherence to NICE guidelines on statin prescribing and annual lipid profile monitoring in adults with T1DM attending Doncaster and Bassetlaw Teaching Hospitals.
Methods
A retrospective audit was conducted of 78 adults with T1DM (aged $>$18 years) attending Doncaster and Bassetlaw Teaching Hospitals between February 2024 and February 2025. Electronic health records were reviewed to assess eligibility for statin therapy and completion of lipid profile testing within the previous 12 months.
Results
Among 78 patients, 7 were aged $<$20 years, 31 were aged 20–39 years, and 40 were aged $\geq$40 years. Twenty-two had diabetes duration $>$10 years, 10 had established nephropathy, and 4 had a previous myocardial infarction (MI). Based on NICE criteria, 56 patients met indications for statin therapy, but only 21 (37%) were prescribed statins. Among these, 5 patients with nephropathy and 1 with prior MI were not on treatment. Lipid profile monitoring was completed in 56 of 78 patients (72%) within the preceding year.
Conclusion
Adherence to NICE recommendations for statin prescription and annual lipid monitoring in adults with T1DM was suboptimal. Following the audit ,eligible patients were started on statins as per NICE criteria. To improve compliance, we recommend increased clinician awareness through educational posters and inclusion of the date of diabetes diagnosis in clinic letters as a prompt for statin review.
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P153

The pharmacology of biased anorectic gut hormone-derived treatments
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Background
Obesity and diabetes are among the greatest public health challenges for the coming decades. Current glucagon-like peptide-1 receptor (GLP-1R) agonists are effective for Type 2 diabetes and obesity but are often limited by dose-dependent nausea, potentially linked to β-arrestin recruitment. Ex-Asp3 and Ex-Phe1 are modified exendin-4 analogues with single amino acid substitutions near the N-terminus. Ex-Phe1 functions as a partial and G protein–biased GLP-1R agonist that reduces receptor desensitisation *in-vitro* and nausea-like behaviour *in vivo*. This study aimed to investigate the role of β-arrestin-2 in modulating GLP-1R signalling and to determine how its knockout (KO) affects responses to Ex-Asp3 and Ex-Phe1, with a particular focus on appetite regulation, which has not been investigated in detail.
Methods
Glp1r-Cre $\times$ Arrb2 fl/fl mice were generated to knock out β-arrestin-2 specifically in GLP-1R-expressing cells, including anorectic neurons. Crossover intraperitoneal glucose tolerance tests and food intake studies were performed in knockout and littermate control mice to assess the impact of β-arrestin-2 knockout on appetite and glucose regulation following GLP-1R agonist administration.
Results
β-arrestin-2 KO did not markedly alter feeding or glucose responses, suggesting compensatory or redundant mechanisms.
Discussion
Several factors may explain the limited phenotype observed in β-arrestin-2 knockout mice, including incomplete knockout, compensation by β-arrestin-1, or developmental adaptations. Alternatively, β-arrestin–dependent effects may emerge only under specific conditions such as high fat diet exposure, or may involve β-arrestin–independent pathways.
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P154

The efficiency of point-of-care blood ketone monitoring in a central London hospital

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Introduction
Point-of-care testing Ketone Monitoring (POCT KM) in the Emergency and Integrated Care setting is one of the most common investigations carried out, allowing for early recognition of life-threatening conditions such as Diabetic Ketoacidosis. Since its introduction, trust guidelines, which were established based on the recommendations by the National Institute for Health and Care Excellence (NICE), have been developed to assist with appropriate implementation of testing as well as indicate when to continue monitoring.
Objectives
Our study aimed to assess if POCT KM was carried out in adherence to trust guidelines; understand why the use of ketone was greater than anticipated; and address how to prevent incorrect monitoring.
Method
This retrospective study assessed adults on inpatient wards during April 2025, looking at their age, past medical history and indication for POCT KM based on the current guidelines found on the Intranet.
Results
This study concluded that of the 193 inpatients that were analysed, 61% (n = 119) of all POCT KM was not indicated according to guidelines.
Of these, the most common rationale for testing was:
- Capillary blood glucose CBG was >15 but the patient was not unwell/non-consecutive reading of >15 CBG (38%, n = 45).
- Ketones are taken when CBG <15 (30%, n = 36).
- Inappropriate continuance of ketone monitoring following initially correct rationale (11%, n = 13)

Conclusion
Unnecessary POCT KM contributes to ineffective use of staff time, increased patient anxiety from over-investigation, as well as a financial burden upon the Trust. This study concludes that the main intervention to help improve adherence to the guidelines would be focused teaching for nursing staff regarding when POCT KM is indicated, as well as for on-call staff surrounding hyperglycaemia management.

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P155

Reversing obesity-induced type 2 diabetes in the NONcNZO10/ltJ polygenic mouse model: a multi-omics perspective from the liver

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Background
The mechanistic basis of type 2 diabetes remission is challenging to model in humans. Insight into disease pathogenesis can be effectively studied in bespoke polygenic diabetes-susceptible models such as the NONcNZO10/ltJ mouse. We showed that this model develops impaired glucose tolerance and increased *de novo* lipogenesis (DNL) when fed a high sucrose diet (HSD) and that was reversed by calorie restriction (CR). Here, we provide a deeper molecular insight via comprehensive multi-omics analysis of the liver to elucidate molecular mechanisms underlying disease progression and remission.
Methods
NONcNZO10/ltJ mice (n = 12) were fed HSD for 12 weeks, after which half continued on HSD while the other half were switched to CR diet (30%) for 12 weeks. At 24 weeks, mice were euthanized, and liver tissues were snap-frozen at –80°C. Omics profiling—including transcriptomics, lipidomics, metabolomics, and kinomics—was performed using standardized protocols and analysed using in-house workflows.
Results
RNA-seq identified 334 differentially expressed genes (DEGs; 202↑,132↓) involved in many pathways including fatty acid metabolism (21 genes), neutral lipids storage (11 genes), long-chain fatty acid synthesis (9 genes), and regulation of lipid metabolic process (16 genes). Lipidomic and metabolomic analysis identified 44 lipids (19↑,25↓), and 58 compounds (33↑,25↓) significantly changed. Kinomic analysis identified 15 protein tyrosine kinases (PTKs; 10↑,5↓) and 19 serine/threonine kinases (STK; 16↓,3↓). Multi-omics data integration (transcriptomics, kinomics, and metabolomics) identified 38 enriched pathways, 10 of which were common across all three datasets. Notably, the sphingolipid signaling pathway emerged as a key shared pathway, involving critical targets such as *Degs1l, Mapk12, Fyn, Pik3r1,* and *Pik3r3*.
Conclusions
Our data identified several lipid-related hepatic targets significantly altered by CR in NONcNZO10/ltJ mice. These are currently being validated to clarify their roles in the DNL pathway and their potential as therapeutic targets.

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P156

IgG4-related disease presenting with new-onset diabetes

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IgG4 related disease (IgG4-RD) is a rare, multi-organ immune-mediated disorder which manifests as fibro-inflammatory lesions, primarily involving the pancreas, biliary tract, kidneys, lacrimal glands, salivary glands, retroperitoneum, and rarely causing hypophysitis and thyroiditis. We present a 53-yr-old male who was referred with a new diagnosis of diabetes with polyuria, polydipsia, 16 kg weight loss over 3 months, intermittent abdominal pain and diarrhoea. He had a history of coronary artery disease. On examination, acanthosis nigricans and lipodystrophic features were absent. Right axillary and left submandibular lymph node were palpable. He had an HbA1c of 119 mmol/mol, negative islet autoantibodies, abnormal liver function tests [ALT 141 U/l(7-40 U/l); ALP 679 U/l (30-130 U/l)]and low faecal elastase. Viral and autoimmune hepatitis screening was negative. CT scan revealed homogeneous pancreatic enhancement, biliary dilatation, and lymph node involvement. IgG4 levels were elevated [1.73 g/l (range 0-1.30 g/l)}, leading to a new diagnosis of diabetes secondary to hitherto undiagnosed IgG4-related autoimmune pancreatitis (AIP). MRCP indicated focal pancreatitis and severe intrahepatic cholangiopathy. A lymph node biopsy showed reactive follicular hyperplasia. He was treated with prednisolone and insulin therapy. Due to azathioprine intolerance, mycophenolate mofetil was introduced as a steroid-sparing agent. Liver function improved, and subsequent imaging showed significant improvement in cholangiopathy. IGG4-RD can present with pancreatobiliary complications, often misdiagnosed due to symptom overlap with tumors, infections, or immune-mediated diseases. Diagnosing IgG4-related disease (IgG4-RD) as a cause of Type 3c diabetes is challenging but crucial, as corticosteroids and immunosuppressants can lead to radiological, biochemical, and serological improvements. IgG4-RD should be suspected when pancreatitis coexists with salivary or lacrimal gland inflammation, retroperitoneal fibrosis, or renal involvement. Imaging shows a diffusely enlarged pancreas with ductal strictures. Effective management requires a systematic approach, high suspicion, and multidisciplinary team involvement.

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P157

Modelling Biased Agonism at the GLP-1R Using C-terminal Modifications

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Rationale – Obesity is a major global health challenge in the face of accessible nutrient-rich meals and increasing sedentary lifestyles. While glucagon-like peptide-1 receptor (GLP-1R) agonists are therapeutically effective, high rates of nausea and vomiting (up to 40%) often cause treatment discontinuation. Certain G protein-biased GLP-1R agonists may offer a promising therapeutic strategy by favouring beneficial G protein signalling over β-arrestin pathways, potentially enhancing efficacy while minimising internalisation-mediated side effects.
Rationale – To isolate the functional consequences of bias independently of ligand pharmacology, we employed a hGLP-1R mutant sequence modifications that inhibit its phosphorylation to recapitulate G protein-biased activation. We compared the mutant and wild-type receptors in HEK293 cells using the native ligand GLP-1 and two oppositely biased agonists (Exendin-F1 and Exendin-D3), measuring internalisation, β-arrestin recruitment, Gas activation and signalling readouts in HEK293 cells.
Key findings and Conclusion – The "phosphodeficient" receptor mutant exhibited reduced arrestin recruitment and internalisation upon stimulation with GLP-1 and β-arrestin-biased Ex-D3, to similar levels achieved with G protein-biased Ex-F1 in

wild-type receptor. Consequently, this "arrestin-away" cellular phenotype of the mutant receptor results in markedly enhanced ligand-induced kinase activation and cAMP signalling. These findings support the potential of receptor-mediated G protein-bias to improve drug responses for GLP-1-based obesity treatments.

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P158

Transcranial super-resolution ultrasound imaging as a tool to visualise neuronal activation patterns in the brain following peripheral administration of GLP-1 receptor agonists

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Energy homeostasis is a major focus of biomedical research due to the prevalence of obesity affecting over 890 million adults globally. The brain plays a central role in energy homeostasis through key neural circuits and endocrine signalling governing appetite regulation and satiety. Modern pharmacotherapeutics targeting gut hormone receptors, such as glucagon-like peptide-1 receptor agonists (GLP-1RAs), have emerged as effective adjunctive therapies in obesity management. However, the precise neural mechanisms underlying GLP-1RAs remain unclear, in part due to the relatively low spatial and temporal resolution of the current non-invasive neuroimaging methods. Contrast-enhanced ultrasound (CEUS) enables non-invasive assessment of the cerebral haemodynamics. Super-resolution ultrasound (SRUS) is an ultrasound imaging technique that localises and tracks the microbubbles (MBs), used as contrast agents, to achieve structural vascular maps with high spatial resolution and allows for quantitative blood flow analysis. We describe studies investigating SRUS as an imaging platform to investigate the effects of GLP-1RAs on the brain during the progression of metabolic disease. Images of satiety regulating brain regions are acquired using a high-frequency ultrasound scanner following an intravenous injection of MBs. The MB signals are extracted using singular value decomposition and localised using a cross-correlation algorithm. The localised MBs are used to construct a super-resolution map of the vasculature. Subsequently, the MBs are tracked across time to extract blood flow parameters. GLP-1RAs activate specific brain regions in wild type mice and the polygenic Tally Ho (TH) mouse model in which males develop diabetes and females develop obesity. Super-resolved neuronal activation maps of control and TH mice before and after peripheral administration of GLP-1RAs, can be used to assess the effects of GLP-1RAs as obesity develops. These studies suggest the potential utility of CEUS and SRUS to longitudinally and non-invasively assess dynamic changes in blood flow parameters which putatively map to neuronal activation patterns.

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P159

Triglyceride-glucose (tyg) index cut-off for identifying metabolic syndrome in nigerians

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Background
Triglyceride-glucose (TyG) index, a product of triglyceride and fasting plasma glucose, is a novel tool that can identify people with metabolic syndrome (MS). It has been shown that TyG index can identify MS among Nigerians, but its cut-off is unknown. We aim to determine the (TyG) index cut-off for MS in a Nigerian population.
Methods
Cross-sectional health screening was conducted between among staff and students of Ekiti State University/Ekiti State University Teaching Hospital, Nigeria, Ado-Ekiti. The analysis included 173 men and 300 women, aged >18 years. Anthropometric indices and blood pressure were measured by standard protocol. Fasting lipid profile and blood glucose were determined. TyG index was calculated, and MS defined according to the harmonized criteria. The TyG index cut off for MS was determined with the Receiver Operating Characteristic (ROC) curves.
Results
The mean age of the participants was 39.2 (11.4) years. Metabolic syndrome was more prevalent among women (22.0 vs 11.6%, $P = 0.005$). In both genders, there was significant positive correlation between TyG index and waist circumference (men, r= 0.178, $P = 0.019$; women, $r = 0.172$, $P = 0.003$)), and fasting plasma glucose (men, $r = 0.453$, women, $r = 0.438$, $P < 0.001$). The Tyg index cut-off for identifying MS in men was >8.60 (95%CI, >8.55 to >8.80), corresponding to a Youden index J of 0.67; AUC 0.89, $P < 0.0001$ (sensitivity 100%, specificity, 67.3%). The Tyg index cut-off for identifying MS in women was >8.90, (95%CI, >8.81 to >8.96) corresponding to Youden index of J of 0.50; AUC 0.89, $P < 0.0001$ (sensitivity 60.6%, specificity, 89.747%)
Conclusions
TyG index is effective in identifying MS, and its cut-off is >8.60 and >8.90 in men and women respectively.

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P160

Factors impacting hospital length of stay in older adults on insulin: a single-centre observational study

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The proportion of older adults and the prevalence of diabetes are increasing globally. As functional and cognitive capacities decline with age, diabetes management becomes increasingly challenging particularly for those requiring insulin. This study aimed to identify factors associated with an increased hospital length of stay (LOS) in older adults with diabetes. A retrospective review of all patients with diabetes aged ≥ 75 years on insulin at time of admission to hospital during a 1-year period (July 2023-2024) was carried out. 117 patients (26% Type 1/lADA/Pancreatic diabetes and 74% Type 2) were included. On admission, older people on insulin had poor diabetes control, with a mean HbA1c of 71 mmol/mol. The average LOS was 19 days. There was a high prevalence of cognitive (16%) and functional (47%) impairment among older people on insulin and 53% of admissions were primarily diabetes related. Those with functional or cognitive impairment had a longer length of stay than those who did not (23 days vs 12 days, $P = 0.002$). Only 26% of individuals with a documented functional or cognitive impairment self-managed their insulin; 47% relied on community supports (either a public health nurse or family members) and 27% lived in a residential care home. 62% of admissions in this cohort were diabetes related. By comparison, for those without cognitive or functional impairment, 98% self-managed their insulin, and 37% of admissions in this cohort were diabetes related. Cognitive and functional impairment are prevalent in older adults with diabetes on insulin admitted to hospital; they are associated with a significantly longer hospital length of stay and frequently require community supports for insulin administration. This study emphasises the importance of individualised multi-disciplinary management strategies and enhanced community engagement in these cases.

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P161

Protective Role Of Garcinia Kola Against Cadmium Chloride-Induced Pancreatic Dysfunction And β-Cell Apoptosis In Wistar Rats

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Background
Cadmium chloride ($CdCl_2$) is a pervasive environmental toxicant that provokes pancreatic oxidative stress, mitochondrial-dependent apoptosis and β-cell dysfunction, with downstream hyperglycemia and islet disorganization.
Methods
Twenty-five adult male Wistar rats ($n = 5$/group) were allocated: Group 1 (control, feed/water); Group 2 ($CdCl_2$, 3 mg/kg i.p., three doses on alternate days); Group 3 (Garcinia kola ethanolic extract, 100 mg/kg orally for 14 days); Group 4 (co-treatment: $CdCl_2$ + G. kola); Group 5 (post-treatment: $CdCl_2$ then G. kola). Body weights were recorded during the study. At termination fasting blood was collected for glucose measurement, animals were humanely euthanized by cervical dislocation, and pancreata were excised, weighed, and divided: portions homogenized for oxidative (e.g., MDA, SOD), inflammatory (e.g., TNF-α) and hormonal assays (insulin, glucagon, somatostatin); remaining tissue was fixed for histology and Bcl-2 immunohistochemistry.
Results & Discussion
$CdCl_2$ produced progressive body-weight loss, pancreatic atrophy, fasting hyperglycemia and lowered circulating insulin with histological acinar/islet degeneration; these changes corresponded with a shift toward pro-apoptotic signaling (decreased Bcl-2 / increased Bax-ratio) described for cadmium exposure. Garcinia kola treatment consistent with kolaviron and other G. kola

reports showing antioxidant, anti-inflammatory and hypoglycemic actions partially or fully restored pancreatic weight, improved glycemic and hormonal profiles, reduced oxidative markers and enhanced Bcl-2 immunoreactivity, effects strongest in co- and post-treatment groups. Mechanistically, the extract's biflavonoid-rich fraction likely attenuates ROS/JNK-mediated mitochondrial apoptosis and modulates inflammatory mediators, permitting islet recovery.
Conclusion
Ethanolic Garcinia kola extract mitigates $CdCl_2$-induced pancreatic injury via antioxidant, anti-inflammatory and anti-apoptotic pathways.

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P162

Case series on patients with post bariatric reactive hypoglycaemia followed up in Medical Obesity Clinic at Princess Royal University Hospital

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Background
Approximately 3 million people living in the UK are affected by severe obesity. Post bariatric reactive hypoglycaemia (PBH) is an increasingly recognised complication. PBH is estimated to occur in 10–30% of patients following Roux-en-Y gastric bypass (RYGB) surgery. We have compiled a few challenging patients with PBH managed with various pharmacotherapeutic agents at our centre.
Results
Case 1: 69F had RYGB (2014) presented with PBH (1.9 -2.5 mmol/l). A trial of Acarbose was discontinued following gastrointestinal intolerance. Hypoglycaemia significantly improved with Octreotide 50 mg twice daily. Case 2: 56F had single anastomotic gastric bypass SAGB (2014) converted to RYGB (January 2019), developed worsening hypoglycaemia (November-2019, 2.9mmol/l) confirmed on prolonged oral glucose tolerance test (OGTT). There was minimal response to dietary changes and acarbose. Hypoglycaemia improved with liraglutide 1.2 mg daily (2025). Case 3: 45F SAGB (2022), converted to RYGB (2022) finally had a partial gastrectomy-2023, presented with hypoglycaemia (March-2023) improved with diet and reversal of surgical procedure in parallel. Case 4: 34F developed severe hypoglycaemia refractory to dietary changes (1.8mmol/l) following gastric bypass (2019). Mixed meal test MMT was diagnostic. She developed gastrointestinal intolerance with acarbose and Octreotide injections; improved on Diazoxide transiently. Treatment was escalated to Liraglutide. Case 5: 27F had RYGB (2020), presented with hypoglycaemia confirmed on MMT; had gastrointestinal side effects with acarbose; injections site issues with Octreotide later improved with Liraglutide 1.2 mg daily. Case 6: 43M, had gastric bypass (2022), developed PBH diagnosed with MMT, commenced on combination of dietary modification and acarbose, experienced improvement of hypoglycaemia.
Conclusion
There are no medications that have a specific license for management of PBH. A standardised national guideline outlining a stepwise approach to medical management would be highly beneficial. Continuous glucose monitoring systems are valuable for patients with hypoglycaemic unawareness and in monitoring treatment response.

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Neuroendocrinology and Pituitary

P163

Sellar extraventricular neurocytoma: the great pituitary adenoma mimic

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Background
Extraventricular neurocytoma of the sellar region (EVNSR) is exceptionally rare, with ~30 cases reported. These tumours often mimic pituitary adenomas on imaging; but, differ in endocrine dysfunction, hyponatremia, and histopathological findings.
Cases
We describe two patients with EVNSR managed at a UK tertiary centre.
Case 1: An 82-year-old man with a history of headaches and progressive visual decline. MRI showed ~30 mm sellar/suprasellar mass invading the cavernous sinus and encasing the left ICA. Transsphenoidal debulking was performed (May 2025), but the tumour's fibrous, adherent nature and intra-operative instability prevented full resection. Postoperatively, he developed SIADH (sodium nadir 125 mmol/l) managed with fluid restriction. Histology confirmed a neuronal tumour (synaptophysin/NeuN positive, Ki-67 3–4%) with non-matching methylation class. Residual tumour remains under clinic review. **Case 2:** A 33-year-old man presented in 2020 with headache, lethargy, constipation, and hyponatraemia. MRI revealed a 23 mm sellar/suprasellar lesion displacing the optic chiasm. Urgent transsphenoidal surgery was undertaken for visual field deterioration. Intra-operatively, tumour was soft/gelatinous with adherent areas; at redo surgery (Dec 2024) dense fibrosis allowed partial resection. Histology demonstrated a neuroendocrine/neurocytoma-like tumour (synaptophysin/NeuN/ChromograninA positive, Ki-67 5–7%, no matching methylation class), with electron microscopy revealing dense secretory granules. He developed GH and cortisol deficiency and intermittent SIADH. Despite repeat surgery and somatostatin analogue therapy, the tumour progressed; radiotherapy planned.
Discussion
Both cases highlight the diagnostic challenge of EVNSR, which often masquerades as pituitary macroadenoma. Key issues include cavernous sinus invasion, non-diagnostic methylation profiles, and SIADH from AVP secretion. Gross total resection is rarely feasible, recurrence is common, and adjuvant options remain limited, with variable SSA response and a role for radiotherapy.
Conclusion
EVNSR is a rare but important differential diagnosis of atypical sellar lesions. Hyponatraemia, neuronal immunoprofile, and non-diagnostic methylation arrays should prompt suspicion.

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P164

CNS relapse of diffuse large B-cell lymphoma presenting with panhypopituitarism and diabetes insipidus: a case report

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A 64-year-old man with a history of diffuse large B-cell lymphoma in remission presented with confusion, blurred vision and hypotension. MRI revealed an enhancing mass lesion involving the hypothalamus and optic chiasm; separate from the pituitary gland but with infiltration of infundibulum, suggesting a relapse of CNS lymphoma. Two days into chemotherapy, he developed polyuria with a 24-hour urine output of 10 litres, hypernatraemia of 150 mmol/l and serum osmolality of 300 mOsm/kg, suggesting diabetes insipidus. While receiving hydration for his chemotherapy, a water deprivation test could not be performed safely. He was empirically started on desmopressin 100 microgram TDS to which he responded with a sodium of 141 mmol/l at discharge. Seven days later, he represented with neutropenic sepsis, hypotension and hyponatraemia of 120 mmol/l. Desmopressin was initially suspended but restarted when polyuria reappeared of 11 litres/day. Repeat 9 am cortisol of 110 nmol/l with hypotension and persistent hyponatraemia prompted suspicion of adrenal insufficiency, although previous Short synacthen test was not indicative of adrenal insufficiency, he responded promptly to hydrocortisone. Subsequent pituitary profile revealed panhypopituitarism; TSH 0.02 mIU/l, FT4 9.2 pmol/l, FT3 <2 pmol/l, ACTH 7 ng/l, FSH 0.7 IU/l, LH <0.1 IU/l, IGF-1 8.9 nmol/l. He is currently well having completed chemotherapy and autologous bone marrow transplant; maintained on hormone replacement therapy with daily levothyroxine 50 microgram, hydrocortisone 10 mg,10 mg,5 mg, and desmopressin 200 microgram TDS. This case illustrates a rare but critical presentation of CNS lymphoma relapse; where hypothalamic infiltration led to severe panhypopituitarism and central diabetes insipidus. The challenge in achieving fluid balance and sodium equilibrium in a case of panhypopituitarism, in an unwell patient with multi-system involvement is highlighted. Combining aggressive chemotherapy with targeted hormone replacement can achieve favourable outcome in such complex cases.

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P165

Syndrome of inappropriate antidiuresis (SIAD) secondary to high-grade neuroendocrine prostate cancer (NEPC): a rare presentation

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81-year-old male was admitted with malaise and hyponatremia of 118 mmol/l within 24 hours of undergoing transurethral resection of the prostate (TURP), performed to alleviate lower urinary tract obstructive symptoms associated with normal PSA prostate cancer. Initially, TURP syndrome secondary to absorption of hypotonic irrigation fluid causing acute water intoxication was thought to be responsible. However, clinical evaluation demonstrated a SIAD picture; euvolemic state, serum osmolality of 255 mOsm/kg, urine osmolality of 915 mOsm/kg, and urine sodium of 87 mmol/l. The patient was discharged with instructions for fluid restriction and outpatient monitoring but worsening hyponatremia led to readmission. CT CAP was largely unremarkable except for a calcified, enlarged prostate and enlarged iliac lymph node and brain imaging was normal. Despite attempts with fluid restriction and demeclocycline, sodium levels showed minimal improvement. A further review of prior urological investigations revealed malignancy and prostate biopsy findings consistent with high-grade neuroendocrine carcinoma (95%). Serum chromogranin A was markedly elevated (384 pmol/l), supporting the diagnosis of active NET (Neuro endocrine tumour). A bone scan showed metastatic skeletal lesions. Given the aggressive nature of the tumour, palliative chemotherapy with carboplatin and etoposide was initiated, along with androgen deprivation therapy (ADT). Unfortunately, the patient's condition deteriorated, and a repeat CT scan revealed widespread organ metastases. Following a multidisciplinary discussion and palliative team review, the patient was sadly transitioned to End of life care This case highlights a rare association between SIAD and NEPC. SIAD is an extremely rare paraneoplastic manifestation in prostate cancer, with the reported cases involving aggressive adenocarcinoma or neuroendocrine pathology. Clinicians should consider this explanation beyond the classic association with small cell lung cancer, in cases of unexplained and persistent hyponatremia and SIAD.

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P166

Acromegaly – a single centre retrospective analysis of outcomes post radiotherapy

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Background and aim
Radiotherapy is an established treatment modality in the management of acromegaly, often used third-line, when surgery and medication don't achieve remission. A few studies report outcomes from limited follow-up and no prognostic factors for treatment response were identified. We aimed to assess clinical outcomes of patients with acromegaly, who underwent radiotherapy and are currently under our follow-up.
Methods
We retrospectively collected demographic, radiological, treatment, biochemical and clinical outcomes on all patients with acromegaly under our follow-up, who received radiotherapy. Descriptive statistics and regression analysis were used for analysis.
Results
Forty-five of 155 patients (29%) with acromegaly completed radiotherapy. The majority of cases were fractionated, a minority received stereotactic and proton beam radiotherapy (7/45). Median age at diagnosis was 36.5 years (IQR 26.3-47.8). Mean follow-up was 10.5 years (range 2-28). Cure was achieved in 13/45 patients (28.9%), defined as no medication needed in 6/45 (13.3%) and medication stopped anywhere from immediately post radiotherapy to 17 years follow-up in the remaining 7/39 (17.9%). Medication de-escalation was achieved in 11/45 patients (24.4%) between 2-24 years follow-up. In 10/45 (22.2%) patients, disease stability was achieved on stable medication doses. In 11/45 (24.4%) of patients, medication was escalated for increased disease activity. Reduction in tumour volume was observed in 14 patients between 6 months to 6 years post radiotherapy, 35.7% of reductions reported at 1 year. In 9/45 (20%) patients hormone deficiencies developed from 2 months to 16 years post radiotherapy, with 4 patients having multiple pituitary axes affected.
Conclusion
Radiotherapy improved disease control in 53% cases. Given such response, potential for medication de-escalation and a more cost effective treatment pathway, radiotherapy should be considered earlier in appropriate cases, with appropriate counselling on the risks and establishment of long-term follow-up.

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P167

Histological and biochemical analysis of pituitary surgeries performed over a decade

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Methods
A retrospective cross-sectional analysis of 152 patients who underwent endoscopic endonasal transsphenoidal surgery (EETS) in University Hospitals Coventry and Warwickshire over a 10-year period from 2013 to 2024.
Results
Histology, endocrine dysfunction and recurrence of pituitary adenoma were reviewed in 64 males (42.1%) and 88 female patients (57.9%). Presentations included visual field disturbance, incidentaloma, acromegaly, headaches and Cushing's disease. Histology showed that 133 (87.5%) were macroadenomas and 14 (9.2%) microadenomas.

Tumour classification based on histology

	Number	Percentage
Non-functioning Gonadotroph adenomas	72	47.4 %
Somatotroph adenomas	25	16.4 %
Non staining adenomas	12	7.9 %
Corticotroph adenomas	12	7.9 %
Plurihormonal adenomas	11	7.2 %
Silent corticotroph adenomas	4	2.6 %
Cyst	4	2.6 %
Prolactinoma	1	0.7 %
Thyrotroph adenoma	1	0.7 %
Miscellaneous	11	7.2 %

Recurrence requiring re-do surgery occurred in 17 (11.2%) patients. Post-operative complications were similar to that reported in literature. Of note, we found that recurrent tumours had a low Ki-67 index of 0-3%.
Discussion
Pituitary adenomas account for about 15% of all intra-cranial tumours. Pituitary adenomas that do not cause a characteristic hormone hypersecretion syndrome (null cell and the majority of gonadotroph adenomas) are referred to as non-functioning pituitary neuroendocrine tumours (PitNETs). Gonadotroph adenomas are pituitary adenomas derived from steroidogenic factor 1 (SF-1) lineage, and remain the most common subtype of non-functioning pituitary neuroendocrine tumours (PitNETs). Surgical resection is the preferred first-line treatment for all functioning pituitary adenomas except prolactinomas.
Conclusion
Histology analysis in this patient cohort is consistent with existing literature on incidence of pituitary adenomas. Although medical therapy offers effective treatment for functional tumours in specific situations, transsphenoidal surgery continues to provide optimal outcomes for non-prolactin secreting adenomas with a low incidence of major morbidity.

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Diagnostic pitfalls in endogenous hyperinsulinemia hypoglycemia: a rare case of insulin autoimmune syndrome

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Insulin autoimmune syndrome is a rare cause of spontaneous hypoglycemia caused by insulin antibodies directed against endogenous insulin. A woman in her 70s presented with subacute onset of recurrent episodes of fasting and postprandial hypoglycemia fulfilling Whipple's triad with no weight gain. There was no history of gastric bypass surgery. Initially, insulinoma was

considered. During spontaneous hypoglycemia of 2.4 mmol/l, insulin and C-peptide levels were markedly elevated with a negative sulfonylurea screen ruling out exogenous insulin administration and factitious hypoglycemia. A 72-hour supervised fast and mixed meal test showed early-onset hypoglycemia with high insulin and C-peptide levels. Imaging including MRI and DOTATATE PET-CT revealed no evidence of neuroendocrine tumors. Insulin IgG antibodies were found to be significantly high. Considering rarity of condition, MDT decided to repeat supervised fast and PEG precipitation showed insulin antibodies interference confirming diagnosis of insulin autoimmune syndrome.

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P169

Hypophysitis masquerading as pituitary macroadenoma: clinical diagnostic challenge

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Introduction
Hypophysitis is a rare pituitary inflammatory disorder that can mimic macroadenomas, often presenting as a pituitary mass. Clinical differentiation remains a challenge; often misdiagnosed preoperatively and the definitive diagnosis established only through postoperative histopathological examination.
Case
51-year-old lady with a history of primary hypothyroidism (on stable dose of levothyroxine for >10 years), rheumatoid arthritis (no treatment), POF, and hypertension was admitted with a 4-month history of fatigue, low-mood, persistent headache, unintentional weight loss, abdominal pain, nausea, vomiting, decreased appetite and postural symptoms. Endoscopy and CT (abdomen/pelvis) performed prior to admission did not show any significant pathology. She was misdiagnosed as depression. Blood tests on admission interestingly revealed secondary hypothyroidism (TSH-0.04mU/l), low T3-<2pmol/l, T4-8.5pmol/l). Hence, a full pituitary profile was carried out. Random cortisol(<28nmol/l) and ACTH(3.5nmol/l) were low with inadequate short Synacthen test response (basal-cortisol <28, post-synacthen cortisol-117 nmol/l) and low prolactin (34 mU/l). Hydrocortisone was initiated immediately with subsequent increased dose of levothyroxine. MRI (pituitary) revealed a heterogeneously enhancing pituitary mass (1.3x1.6x1.3 cm), suggesting macroadenoma, which was not present previously on MRI performed 14-months ago for anosmia. Further discussion at the pituitary MDT suspected hypophysitis, due to a thickened pituitary stalk and hyper-enhancing lesion. Further testing for ACE and IgG was negative. Complete resolution of the pituitary mass on interval MRI scan 3 months later confirmed the suspected diagnosis of hypophysitis, without needing a biopsy for histopathological confirmation.
Conclusion
- Prompt recognition of shift from primary to secondary hypothyroidism led to the diagnosis of hypopituitarism accounting for her presenting symptoms, and subsequent pituitary imaging.
- Although rare, hypophysitis should be considered as a differential diagnosis to avoid unnecessary surgery.
- MDT plays a crucial role in case of diagnostic dilemma and interval imaging is highly recommended.
- This case highlights the diagnostic challenge of distinguishing hypophysitis from macroadenoma clinically.

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P170

Evaluation of 1.8% Hypertonic Saline Use in Acute Severe Hyponatraemia: An Audit of Patients Admitted to a Medical High Dependency Unit

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Introduction
Acute severe hyponatraemia is a medical emergency. Three percent hypertonic saline is recommended to increase sodium by 4–6mmol/l to reduce cerebral oedema. Many UK centres, including our own, use 1.8% saline, although there is no evidence to support this. Overcorrection may cause osmotic demyelination syndrome (ODS), particularly when sodium increases by >10 mmol/l in 24 hours, or >8 mmol/l in those with additional risk factors.
Aims
To assess the use of 1.8% saline, including indication, monitoring, correction rates, ODS episodes, and 30-day mortality.
Method
Retrospective review of patients admitted to a single-centre medical high dependency unit with hyponatraemia as the primary diagnosis between July 2019 and November 2024.
Results
Thirty-seven patients were identified (median age 64 (IQR 18)); median admission sodium was 110 (IQR 8) mmol/l. Risk factors for ODS were present in 65%. Biochemical investigations were performed in almost all cases: urine osmolality 100%, urine sodium 97%, serum osmolality 95%. Monitoring included urinary catheterisation in 68%, arterial access in 41%, and central venous access in 24%. Twenty-nine patients received hypertonic saline, appropriately indicated in 27. Median 24-hour sodium rise was 10 (IQR 7) mmol/l; 48% had an increase >10 mmol/l, and 83% of patients with risk factors ($n = 18$) rose >8 mmol/l. Fourteen patients (58%) required multiple boluses. The rate of sodium rise >10 mmol/l was lower in those given multiple boluses compared with a single bolus (35% vs 63%). Sodium increased by <4 mmol/l in four patients (14%), all receiving multiple boluses. ODS was not suspected in any cases, and there was no 30-day mortality.
Conclusion
Despite close monitoring, the rate of overcorrection with 1.8% saline was high, though lower in patients given multiple boluses. Further studies are needed to compare outcomes using 1.8% and 3% saline for severe symptomatic hyponatraemia.

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P171

Osilodrostat therapy and 11C-methionine PET to IMprove corticotroph pituitary Adenoma detection and Localisation in patients with Cushing's disease (OPTIMAL); study design and rationale

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Background
Up to one-third of ACTH-secreting pituitary adenomas are occult on standard MRI. Functional imaging with ^{11}C-methionine PET/CT can improve adenoma localisation in MRI-negative or equivocal cases. Osilodrostat, a potent 11β-hydroxylase inhibitor, lowers cortisol and may raise ACTH via reduced negative feedback, potentially increasing adenoma metabolic activity and tracer uptake.
Objective
To determine whether short-term pre-operative osilodrostat enhances detectability of corticotroph adenomas on ^{11}C-methionine PET/CT and increases conspicuity on conventional MRI.
Methods
Single-arm, prospective observational study ($n = 15$ adults) with confirmed Cushing's disease and absent/equivocal pituitary lesion on MRI. Participants undergo baseline ^{11}C-methionine PET/CT co-registered with MRI, then commence osilodrostat with titration to achieve eucortisolaemia over a period of 3–4 months, guided by biochemical monitoring including free cortisol measurements (urine and saliva). After a sustained period of eucortisolaemia, imaging is repeated. **Primary endpoint:** within–patient change in adenoma SUVmax values pre- vs post-treatment; a >20% increase is predefined as clinically meaningful. **Secondary endpoint:** within–patient change in MRI adenoma visibility/conspicuity. **Exploratory endpoints:** markers of bone turnover and hypercoagulability, plus clinical and quality-of-life measures. PET and MRI will be independently read by two experts radiologists with third-reader adjudication as required. Where imaging reveals a definitive surgical target, transsphenoidal surgery will be offered per MDT consensus; safety/tolerability of osilodrostat will be recorded.
Expected impact
If pharmacological optimisation with osilodrostat augments ^{11}C-methionine PET/CT signal and MRI conspicuity of corticotroph adenomas, this priming strategy could improve surgical targeting in MRI-negative or equivocal Cushing's disease.

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P172

Rivaroxaban Prophylaxis for VTE Prevention in ACTH-Dependent Cushing's Syndrome: Safety and Effectiveness in a Single-Centre Retrospective Cohort

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Background
Venous thromboembolism (VTE) risk is substantially elevated in ACTH-dependent Cushing's syndrome (CS), yet optimal prophylaxis strategies remain undefined. In 2019, our centre introduced oral rivaroxaban 10 mg once daily for patients with ACTH-dependent CS.
Objective
To evaluate whether a protocolised prophylactic rivaroxaban approach is safe and associated with fewer VTE events.
Methods
Single-centre retrospective cohort study of adults with ACTH-dependent CS (pituitary and ectopic) managed from January 2012 to January 2025. Outcomes before protocol adoption (pre-2019; no routine prophylaxis) were compared with those after implementation (post-2019). VTE was confirmed radiologically. Bleeding was classified as major or minor by standard definitions. Haematological indices and adherence were recorded.
Results
Seventy patients were included (29 pre-2019; 41 post-2019) with comparable baseline characteristics; pituitary-dependent Cushing's disease predominated (26/29 pre-2019; 34/41 post-2019). In the pre-2019 cohort, 4/29 patients (13.7%) experienced six VTE events, occurring both pre-operatively (up to eight months before surgery) and within one month post-operatively. After protocol implementation, 39 patients received rivaroxaban prophylaxis; no new or recurrent VTE occurred. Five patients had prior VTE before endocrine assessment and initiation of rivaroxaban. No major or minor bleeding complications were observed. Haematological parameters remained stable, and all patients completed the prescribed prophylaxis course (median duration: 7.9 months).
Conclusions
This is the first study to evaluate oral rivaroxaban prophylaxis for VTE prevention in ACTH-dependent CS. Compared with a 13.7% VTE rate before 2019, introducing rivaroxaban prophylaxis was associated with complete absence of new or recurrent events and no observed bleeding complications. These findings support early initiation at diagnosis and continuation through the peri- and postoperative period in ACTH-dependent CS.

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P173

A rare case of isolated ACTH deficiency (IAD) following COVID

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Background
Isolated adrenocorticotrophic hormone (ACTH) deficiency (IAD) is a rare cause of secondary adrenal insufficiency. Its symptoms can overlap with post-viral or long-COVID fatigue, making recognition challenging.
Case Presentation
A 35-year-old man was referred to endocrinology clinic for persistent and worsening fatigue and mild cognitive impairment following COVID infection in 2021, during which he was unwell for 6 days but did not require hospital admission or oxygen. Initial testing showed morning cortisol 166 nmol/l, with normal electrolytes, glucose, and inflammatory markers. He denied exogenous steroid use, trauma, infection, or drug misuse. He was not taking regular medications apart from prior finasteride use and topical dihydrotestosterone-blocking shampoo for hair loss. Repeat assessments demonstrated persistently reduced cortisol (108 nmol/l) and low ACTH ($<$ 6 ng/l) with other pituitary axes stable. MRI pituitary with contrast was normal. The findings were consistent with isolated ACTH deficiency. He responded well to low-dose prednisolone, with marked symptomatic improvement.
Conclusion
IAD is a rare disorder. Post-COVID IAD cases have been reported only sporadically. In this case, the temporal association may suggest a possible COVID-related aetiology. Proposed mechanisms include molecular mimicry between SARS-CoV-2 peptides and ACTH, cytokine-mediated hypothalamic–pituitary suppression via IL-6/TNF-α, and possible direct viral or microvascular damage to the hypothalamic–pituitary axis[1,2]. Clinicians should consider IAD as a differential in patients with persistent post-COVID fatigue. Early recognition enables timely glucocorticoid replacement and optimised clinical management.
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P174

A rare case of triple endocrine dysfunction following immune checkpoint inhibitor therapy

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An 80-year-old woman was diagnosed with malignant epithelioid mesothelioma on 26/02/2025 following presentation with a left pleural effusion. Thoracoscopy with biopsy confirmed the diagnosis, and an indwelling pleural catheter (IPC) was inserted on 26/03/2025 for recurrent effusions. She was started on combination immunotherapy with ipilimumab and nivolumab, receiving her first cycle on 15/05/2025. Following her second cycle, thyroid function tests showed initial thyrotoxicosis that later evolved into hypothyroidism with a free T4 of 6 pmol/l. She was diagnosed with immune checkpoint inhibitor (ICI)-induced thyroiditis and commenced on thyroxine replacement. After her fourth cycle on 17/07/2025, she was admitted with dizziness, confusion, and palpitations. Investigations revealed hyponatremia (Na 113 mmol/l), low cortisol (31 nmol/l), and evidence of secondary adrenal insufficiency consistent with ICI-induced hypophysitis. Pituitary profile results (FSH 3.2 IU/l, LH $<$0.3 IU/l, IGF-1 6 µg/l, prolactin $<$50 mIU/l) supported the diagnosis. She was started on hydrocortisone, resulting in clinical and biochemical improvement. A month later, she re-presented with fatigue and lethargy. She was alert and hemodynamically stable. Biochemical investigations showed blood glucose 27 mmol/l, pH 7.22, bicarbonate 17.3 mmol/l, and ketones 6 mmol/l, consistent with diabetic ketoacidosis (DKA). She was admitted to the high-dependency unit and managed according to DKA protocols, alongside intravenous hydrocortisone for adrenal insufficiency. Her C-peptide was low (7 pmol/l), confirming absolute insulin deficiency. A diagnosis of ICI-induced diabetes presenting with DKA was made. Immune checkpoint inhibitors can cause diverse endocrine immune-related adverse events, most often involving the thyroid, pituitary, adrenal, and pancreatic glands. While single gland involvement is relatively common, multiple endocrine dysfunctions are rare, affecting approximately 1–2% of patients, particularly with combination therapy. Triple endocrinopathies such as thyroiditis, hypophysitis, and diabetes mellitus are extremely uncommon, with an estimated incidence of around 0.02%.

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P175

Unmasking of Idiopathic Parkinson's Disease (PD) following cessation of Cabergoline in a patient with Macroprolactinoma

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Introduction
Dopamine agonists (DA) are treatment of choice in Prolactinoma. We report a patient manifesting symptoms and signs of PD following temporary cessation of Cabergoline for Macroprolactinoma.
Case
A 68-year-old gentleman was referred to Endocrinology following an incidental finding of 1.7 x 1.7 x 2 cm mass in pituitary fossa on CT Head. Patient was asymptomatic, denied headache or visual disturbances and clinical examination was unremarkable. Biochemistry demonstrated elevated Prolactin (PRL) of 42460 mIU/l (range 73-403) with rest of pituitary function being normal. Cabergoline 500*u*g twice weekly was started for Macroprolactinoma. His PRL level came down to 330 mIU/l. However, he developed symptoms of anxiety which failed to respond to standard treatment. Cabergoline was considered the culprit agent; it was tapered and stopped. He then developed visual hallucinations, unsteady gait, difficulty initiating movement and legs feeling like "lead" and "frozen". He was referred to Neurology and diagnosed with Idiopathic PD and commenced on Levodopa. His neurological symptoms improved but PRL continued to rise. Bromocriptine was added and was well tolerated and resulted in biochemical remission and shrinkage of adenoma on CT.
Discussion
This case highlights an interesting and unique phenomenon of unmasking symptoms of PD following withdrawal of DA therapy which has not been

previously documented in literature. This is different from the established entity of DA withdrawal syndrome seen in patients with diagnosed PD following DA withdrawal. Cabergoline either as monotherapy or in combination with Levodopa is effective for managing motor symptoms of PD. It is probable that the neurological symptoms that appeared after Cabergoline cessation in our patient are either due to unmasking of preexisting PD or a coincidental occurrence, but it is important for clinicians to be aware of this possibility.

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P176

A rare case of ectopic ACTH production and carcinoid syndrome from a metastasized small bowel neuroendocrine tumour

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Neuroendocrine tumours (NET) resulting in Cushing's and Carcinoid syndrome(s) are rare. We present a case of a NET producing both ACTH and Serotonin with ensuing complexities in management. A 68 year old female, presented with a 5day history of weakness and increased stoma output requiring ITU admission for persistent hypokalaemia (K + 2.2 mmol/l). Two months prior, she was diagnosed with a small bowel adenocarcinoma with liver metastases requiring palliative chemotherapy, on a background of extensive bowel surgery for Crohn's disease. Investigations into her hypokalaemia revealed elevated levels of 9am cortisol (>1650nmol/l), ACTH (256.2ng/l), and 24hr urinary free cortisol (>3189nmol/l), consistent with ACTH dependant hypercortisolaemia. Apart from endogenous steroid induced hyperglycaemia, her clinical features of Cushing's syndrome were minimal. A block and replace regime with adrenolytic Metyrapone and Hydrocortisone quickly normalised her cortisol and potassium levels. Review of her histopathology with neuroendocrine stains returned positive for synaptophysin, chromogranin A and CD-56, in keeping with a poorly differentiated NET, Ki 67 index 94%. Targeted chemotherapy with Oxaliplatin and Capecitabine was initiated. Further investigations showed elevated levels of Chromogranin A (280pmol/l) and Urine 5-HIAA (310umol/24hrs) in keeping with Carcinoid syndrome. Sandostatin LAR was started but she developed increased stoma output requiring gut rest and parenteral nutrition. Somatostatn analogue therapy was discontinued as it had no impact on her stoma output. A NM Octreotide SPECT CT scan confirmed evidence for somatostatin receptor positive liver metastases. The NET MDT outcome confirmed the rarity of octreotide avidity in a poorly differentiated NET and suggested the possibility of resuming somatostatin analogues. This and the role for any peptide related radiotherapy will be considered by the NET MDT at next review. This case highlights the need to investigate for multiple hormonal secretion from metastatic NET and the complexities in management when dual pathology is present.

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P177

A case of insulinoma in an elderly man: diagnostic and treatment challenges

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Introduction
Insulinomas are rare neuroendocrine tumours (NET) derived from the beta islet cell of the pancreas. It is more frequent in women in their fifties compared to men. The diagnosis and treatment of insulinomas in the frail elderly with poor cognition plus multiple comorbidities can be challenging. A delayed diagnosis increases both morbidity and mortality.
Case
An 82-year-old man presented with an episode of confusion and hypoglycaemia (glucose 2.4 mmol/dl). He had been experiencing these symptoms for ten years and weight gain of 20 kg. He was a frail with reduced cognition and dependent on his wife for his activities of daily living. His medical history included pulmonary embolism, polymyalgia rheumatica and hypertension. At presentation he had an elevated c-peptide level of 2.39 nmol/l and insulin level of 287 pmol/l. He declined further investigation but reappeared after having another fall with hypoglycaemia. A subsequent 72-hour fasting test demonstrated hypoglycaemia (2.1mmol/l) with an elevated serum c-peptide (2.17 nmol/l) and proinsulin (25.9 pmol/l). Liver, adrenal and thyroid function were normal. A computerised tomography scan of his abdomen demonstrated a 20-mm solid lesion in the tail of his pancreas, giving a likely diagnosis of an insulinoma. Because of his medical history he was treated conservatively with dietitian input (starch and multiple small meals) and diazoxide. He remains well.
Discussion
This case highlights the challenges and treatment of hypoglycaemia in older individuals with complex medical issues and how crucial it is to consider uncommon causes like insulinoma. Elderly patients often present with atypical symptoms or subtle signs that can easily be overlooked or misinterpreted. Diet and diazoxide can give good symptom control, and somatostatin analogues are an alternative. Surgery can be considered in selective cases with risks and benefits assessed.

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P178

Secondary hypogonadism in adulthood: late presentation of congenital obstructive hydrocephalus with pituitary stalk distortion

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Background
Congenital obstructive hydrocephalus is rarely diagnosed in adulthood and may present with atypical endocrine manifestations. Pituitary stalk distortion or vascular compromise can result in hypopituitarism.
Case Presentation
A 25-year-old male with a history of ankylosing spondylitis presented with headache, fatigue, reduced libido, and diminished morning erections. He reported normal childhood development and pubertal onset at age 12, but minimal facial hair and difficulty growing a moustache. Initially, his libido was preserved, but over the preceding two years, he developed progressive loss of body hair, weight gain, gynecomastia, and loss of sexual drive.
Investigations
On examination, his height was 180 cm and BMI was 32.8. He had bilateral gynecomastia, normal testicular volume, and Tanner stage 5 secondary sexual characteristics. There were no overt signs of endocrinopathy. Biochemical evaluation revealed borderline low total testosterone (8.9 nmol/l; reference: 8.3–30), low LH (1.3 IU), and low FSH (0.9 IU), with normal cortisol, thyroid, and prolactin levels. Pituitary MRI demonstrated congenital obstructive triventricular hydrocephalus secondary to a fourth-ventricular web, with significant pituitary stalk distortion.
Management
Following multidisciplinary review, endoscopic third ventriculostomy with Rickham reservoir insertion was performed. Postoperatively, testosterone and gonadotropin levels remained low (total testosterone 8.5 nmol/l, calculated free testosterone 0.220 nmol/l, with persistently low LH 1.6 IU and FSH 0.7 IU). Initially, clomiphene or HCG therapy was discussed due to immediate plans for conception. Subsequently, after the patient confirmed fertility was no longer desired, testosterone replacement therapy was commenced.
Conclusion
This case demonstrates that congenital hydrocephalus may remain compensated until adulthood and present with endocrine dysfunction. It further highlights that vascular compromise to the hypothalamic-pituitary axis is likely the underlying mechanism, emphasising the importance of neuroimaging.

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P179

Development of hypopituitarism after fractionated pituitary radiotherapy for pituitary disease: a single-centre audit

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Introduction
Modern pituitary radiotherapy utilises techniques such as intensity modulated radiotherapy (IMRT) to reduce damage to healthy tissue. Rates of hypopituitarism

vary significantly between studies (from 10% to greater than 40%). In this audit, we evaluated the frequency and timing of hypopituitarism in our centre in patients undergoing radiotherapy for pituitary tumours.
Methods
A retrospective review of all adult patients undergoing pituitary radiotherapy at a single centre between 2011 and 2018. Exclusion criteria included missing baseline or follow-up biochemistry. We recorded demographics, previous surgery, histology and radiotherapy technique from radiotherapy records and clinic letters. Each pituitary axis was documented as intact or deficient at baseline, and annually for 5 years post-radiotherapy. Deficiency was defined similarly to previous studies and Endocrine Society guidelines. Women over 50 years were excluded from gonadotrophin analysis.
Results
40 patients fulfilled the above criteria of whom 33/40 received IMRT and 7/40 conformal radiotherapy. Of these, 55% were female with a mean age of 47.8 years and 39/40 had undergone previous pituitary surgery. Most tumours were adenomas (58% non-functioning) with 3 craniopharyngiomas. 43% of patients developed at least one new hormone deficiency by 5 years.

Table 1. Percentage of patients developing new hormone deficiency post-radiotherapy (n = number of patients included in analysis).

	Years after radiotherapy				
	1	2	3	4	5
ACTH ($n = 20$)	30	35	35	35	35
TSH ($n = 24$)	12.5	20.8	20.8	29.2	29.2
Gonadotrophins ($n = 15$)	33.3	33.3	40	40	40
Growth hormone ($n = 28$)	17.9	17.9	17.9	17.9	17.9

Discussion
Our data shows that ACTH, gonadotroph and GH deficiency occurred mostly within the first year, with ACTH deficiency being diagnosed earlier than expected. The retrospective design and non-standardised assessments may introduce ascertainment biases (including potential over-diagnosis). Nevertheless, we suggest clinicians remain vigilant for hypopituitarism, with potential focus on ACTH deficiency within the first 1-2 years post-IMRT.

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P180

Ectopic ACTH-producing pulmonary carcinoid tumor presenting with cushing syndrome

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A 26-year-old woman presented with progressive features of Cushing syndrome, including weight gain, amenorrhea, proximal muscle weakness, and purple striae. Biochemical testing revealed elevated morning serum cortisol concentrations (31 mg/dL [855 nmol/l]) and nonsuppressible cortisol on low-dose dexamethasone suppression test. Plasma ACTH was markedly elevated (121 pg/mL [26.6 pmol/l]). High-resolution computed tomography of the chest identified a lesion in the left lower lobe, and octreotide scintigraphy confirmed uptake consistent with a neuroendocrine tumor. Resection specimen demonstrated a typical carcinoid tumor immunoreactive for ACTH and CD56. Following lobectomy, the patient required hydrocortisone replacement due to hypothalamic–pituitary–adrenal axis suppression. Postoperative urinary free cortisol normalized, and ACTH decreased to 32 pg/mL (7.1 pmol/l). This case emphasizes the importance of considering ectopic ACTH syndrome in patients with hypercortisolism and negative pituitary imaging, and highlights the value of multidisciplinary management.

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P181

Breast cancer and Venous Thromboembolic disease (VTE) in patients with Multiple Endocrine Neoplasia type 1 (MEN 1) in The Sheffield NET Centre, European Neuroendocrine Centre of Excellence

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Background
MEN -1 is caused by a pathogenic variant in the tumour suppressor gene leading to a tumour development. Registry data quotes an increased risk in breast cancer and thromboembolic disease. Recent best practice guidance does not currently recommend breast cancer screening in this group. The Dutch registry data reports invasive breast cancer in 12 of 190 females (with MEN-1) with a relative risk of 2.83 and approximately 6 % developing breast cancer. With respect to VTE, the lifetime risk has been has been estimated to be 2 fold higher with a pooled prevalence of 11.1% in MEN-1.
Objectives
To review our practice: recording: demographic data, genetic MEN 1 diagnosis, incidence of breast cancer and VTE.
Methodology
Interrogation of the Sheffield NET database was performed filtering for 'multiple endocrine neoplasia' and MEN 1 patients selected. Evidence of breast cancer and VTE was then reviewed.
Results
164 patients were listed as having a form of multiple endocrine neoplasia. 67 were confirmed to be gene positive. 8% of all patients underwent triple assessment (examination, mammography and biopsy) for breast cancer. 3% with MEN-1 were found to have a diagnosis of breast cancer (5 patients). A total of 13 patients (8% of total) had a thromboembolic event, where 9 were MEN-1 gene positive, 3 of these patients developed both a DVT and PE. 2 patients with the MEN-1 gene developed both breast cancer and TED.
Conclusion
In this limited dataset Sheffield NET Centre has a small proportion of patients who presented with breast cancer or VTE. Clinicians should carefully review any family history of breast cancer and advise patients on self-examination. Looking forward a worldwide study is needed to inform if earlier breast screening is warranted and useful. In the future AI may prove to be useful in assessment of MEN surveillance interval imaging.

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Outcomes of hospitalized patients with severe hyponatremia: findings from the pilot of HypoNa-RESCUE, a multicentre observational study

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Background
Hyponatremia guidelines recommend limiting of sodium correction rate to prevent osmotic demyelination syndrome (ODS). However, emerging evidence suggests ODS is rare, and rapid sodium correction is associated with reduced mortality. There is currently no standardized surveillance system to detect ODS. We set up a multicentre surveillance model to explore trends in severe hyponatremia management. Using data from this, we compared length of hospital stay (LOS) between patients who underwent rapid ($>$10mmol/l/24 hours) and slow correction ($\leq$10mmol/l/24 hours).
Methods
A multicentre observational retrospective study was conducted from January-May 2025 across two tertiary UK hospitals. Patients admitted with severe hyponatremia (serum sodium $<$ 125mmol/l) from January-December 2024 were included. Through expert consensus, we established a surveillance system called HypoNa-RESCUE (Understanding Trends in Hyponatremia Management through Rapid Evaluation and Surveillance of Critical Urgencies in Endocrinology Model) to facilitate data collection. Data on demographics, precipitating factors, management, and outcomes of hyponatremia were collected. Data were analysed using SPSS and presented as appropriate in frequency or median and interquartile range [IQR].
Results
A total of 767 admissions were included in pilot analysis with a baseline median age of 71.0 [IQR, 61.0-81.0] years, and Charlson Comorbidity index of 4.0 [3.0-5.0]. Most common aetiology for severe hyponatremia was drug-induced (21.4%) . Most patients were asymptomatic (65.6%). Median sodium on admission was 121 [118-123] mmol/l, increasing to 130 [125-134] mmol/l at discharge. Hypertonic saline was used in 2.3% of admissions, and 4.7% were managed in intensive care. 45 (8.9%) patients had rapid correction, and 458 (91.1%) had slow correction. There was no significant difference in median LOS between rapid vs slow correction (7.0 [3.3-15.0] vs. 6.0 [3.0-14.0] days, $P = 0.496$).
Conclusion
Pilot data suggest that either correction strategy did not affect LOS. Future work will explore differences in mortality and frequency of ODS, which may inform prospective trials.

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Reversible central adrenal insufficiency in a patient with high dose loperamide use post bowel surgery

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Background
Loperamide, a peripherally acting μ-opioid receptor agonist, is commonly used for diarrhoea management and control of high output stomas. Due to limited CNS penetration from P-glycoprotein efflux at the blood brain barrier, it is considered safe at therapeutic doses. However, in supra therapeutic doses, loperamide may cross the blood brain barrier and suppress the hypothalamic pituitary adrenal (HPA) axis, leading to central adrenal insufficiency (CAI). Such cases remain exceptionally rare (1).
Case Presentation
A 56-year-old woman presented with persistent hypotension, profound fatigue, and marked unintentional weight loss after emergency surgery with loop ileostomy for small bowel necrosis. Initial symptoms were attributed to postoperative stress and volume depletion. She was self administering loperamide up to 64 mg/day, four times the recommended maximum, to manage high stoma output. Despite adequate fluid and electrolyte optimisation, symptoms persisted. Endocrine evaluation demonstrated CAI (Table 1). Other pituitary axes were intact. Pituitary magnetic resonance imaging found a small 3.4 mm incidental Rathke's cleft cyst deemed benign and stable with no mass effect.
Table 1

Parameter	Baseline	30 mins	60 mins
Cortisol	113 nmol/l (119-618)	453 nmol/l	532 nmol/l
ACTH	5 pg/mL (7.2-63.3)		
DHEAS	0.6 μmol/l (0.9-7.4)		

Management and Outcome
Hydrocortisone replacement therapy led to rapid clinical improvement. Loperamide was tapered down to recommended limits. Over 12 months, adrenal function normalised (0/30 min cortisol 527/864 nmol/l), permitting successful hydrocortisone withdrawal.
Conclusion
This case highlights a rare but reversible form of CAI secondary to supratherapeutic loperamide use. Clinicians should maintain vigilance for drug induced HPA axis suppression in patients with unexplained fatigue or hypotension. Prompt recognition, steroid replacement, and rationalisation of therapy are critical for preventing morbidity and ensuring full endocrine recovery.
Reference
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Hypertonic saline test: a salty journey from a 'feared' procedure to a safe, effective diagnostic for arginine vasopressin deficiency

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Background
Distinguishing arginine vasopressin deficiency (AVP-D) or resistance (AVP-R) from primary polydipsia (PP) is clinically challenging. The water deprivation test (WDT) is widely used but is labour-intensive, time-consuming, and yields a higher rate of equivocal results. The hypertonic saline-stimulated copeptin test (HST) offers greater diagnostic accuracy in differentiating AVP-D from PP. We describe the establishment of HST as routine care in our endocrine centre, addressing concerns about safety and feasibility.
Methods
Discussions were held at monthly endocrine service meetings before adoption. A consultant endocrinologist and specialist nurse co-developed a clinical protocol and patient information leaflet. Initially, one test per month was carried out, later increasing to two per month. Patients underwent HST as outpatients, with monitoring of symptoms and serum sodium before, during and after stimulation. Technical success was predefined as post-stimulation sodium >149 mmol/l. Copeptin levels determined diagnostic category (complete AVP-D, partial AVP-D, PP, or AVP-R).
Results
Twenty-six patients (19 women, 7 men; median age 43 years) were studied. All achieved technical success (100%) with post-stimulation sodium >149 mmol/l. No complications were reported; all patients were discharged the same day with normal sodium levels. Mild to moderate transient symptoms were documented but resolved. Diagnoses: 3 (11.5 %) complete AVP-D, 2 (7.7 %) partial AVP-D, 20 (76.9 %) PP, and 1 (3.8 %) AVP-R based on baseline copeptin.
Conclusion
Implementation of HST as an outpatient diagnostic is feasible and safe when adequate protocols, personnel training, and monitoring are in place. The 100 % technical success rate, absence of complications, and clear diagnostic outcomes support HST as a highly efficient alternative to WDT. We propose copeptin stimulation tests be considered part of the standard approach for the evaluation of hypotonic polyuria, when basal laboratory tests are indeterminate.

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Involvement of GM3 gangliosides in acromegaly associated insulin resistance

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Background
Acromegaly is a multi-system, multi-morbidity disease caused by a pituitary tumour that oversecretes growth hormone (GH); subsequently elevating levels of its effector hormone, insulin-like growth factor-1 (IGF-1). A significant number of patients with acromegaly develop insulin resistance and diabetes mellitus, the mechanism of which is not fully understood. GM3 gangliosides (GM3) have previously been mechanistically linked to insulin resistance in patients with diabetes mellitus.
Aim
We aimed to configure the role of GM3 in acromegaly-associated insulin resistance in 3T3-L1 adipocytes, a mouse adipocyte cell line.
Methods
3T3-L1 adipocytes were exposed to GH (1 μM) and/or IGF-1 (1 μg/ml) for 48h. Insulin signalling was assessed by Western(mmuno)blot of AKT phosphorylation. Membrane order was assessed through measures of membrane polarisation by confocal microscopy of DI-4-ANEPPDHQ fluorescence. GM3 content in cellular extracts was measured by NMR spectroscopy. The expression of *ST3GAL5* (which encodes for GM3 synthase, the enzyme responsible for GM3 synthesis) was assessed by qPCR.
Results
Exposure of 3T3-L1 adipocytes to elevated concentrations of GH and IGF-1 led to lowered phosphorylated AKT to total AKT levels, indicating impaired insulin signalling. This effect was associated with altered membrane fluidity (1.8 ± 0.1 fold, $p \leq 0.01$) and increased (1.75 ± 0.2 fold, $p \leq 0.05$) cellular levels of GM3 in the cells. Exposure to elevated GH concentrations also led to increased (1.4 ± 0.1 fold, $p \leq 0.01$) expression of *ST3GAL5*.
Conclusions
Taken together, these data indicate that exposure to GH and IGF-1, as seen in acromegaly, inhibits insulin signalling in 3T3-L1 adipocytes potentially via alterations in plasma membrane fluidity caused by increased GM3 content.

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Spindle cell oncocytoma presenting with mass effect and panhypopituitarism. a case report

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Background
Spindle cell oncocytomas (SCOs) are rare, benign primary tumours of the posterior pituitary gland, characterized by a proliferation of spindle-shaped cells. They are low-grade non-neuroendocrine neoplasms and are often diagnosed as non-functioning pituitary adenomas until the immunohistochemistry shows the

characteristic findings, lack of pituitary hormone immunoreactivity and lineage-specific transcription factors.
Case
We report the case of a 66-year-old female who presented with adrenal insufficiency and was found to have bitemporal hemianopia. Pituitary MRI confirmed a pituitary lesion with chiasm compression. She was confirmed to have panhypopituitarism. Her case was discussed in the pituitary multidisciplinary team meeting, with radiologically appearances of a pituitary adenoma. The patient underwent trans-sphenoidal resection of the tumour. Intraoperatively the lesion appeared typical of an adenoma. Part of tumour was left behind as adherent to the posterior diaphragma sellae. Histopathology showed a SCO, neoplastic cells had positive immunoreactivity for TTF-1, focal expression of EMA and negative expression of pituitary transcription factors (SF1, T-Pit, Pit-1). The Ki-67 proliferation index was 15 to 20%. Further characterisation by DNA methylation studies confirmed the histopathological diagnosis. Vision improved after surgery. Post-operative MRI showed a left sided sellar residuum but the large bulk of tumour removed decompressing the optic chiasm. 6 monthly surveillance scans showed no growth of the tumour.
Conclusions
SCOs of the pituitary are rare tumours mostly presenting with progressive symptoms of pituitary dysfunction and or mass effects, particularly visual disturbances. Most reports indicate a peak incidence in the fifth and sixth decades. Early diagnosis and surgical resection are key to improve patient outcomes. Histopathological evaluation remains crucial for confirming the diagnosis. Imaging features are nondescript. Surgical resection is the treatment of choice in most of cases, although hypervascularity and adherence can hinder complete excision. Radiotherapy is reserved for recurrences. Despite a generally favourable prognosis, recurrence necessitates long-term follow-up.

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Haplotypes for disease-causing aip variants are geographically spread across the UK and ireland, but do not influence disease severity

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Background
Mutations in the *AIP* gene cause Familial Isolated Pituitary Adenomas (FIPA). While two specific *AIP* mutations in Northern Ireland and England suggest a shared ancestor, the clinical impact of this shared ancestry remains unknown. We aimed to analyse common AIP mutations, determine their origin from shared ancestors and assess their impact on clinical features.
Methods
We analysed 389 carriers with 54 unique *AIP* mutations from the International FIPA Consortium. We also reviewed the UK Biobank population cohort for additional families. We determined shared ancestral origins using identity-by-descent analysis of array genotyping data. We then compared clinical features between carriers with and without a shared ancestral haplotype.
Results
We identified four recurrent mutations in multiple unrelated families in the FIPA consortium with additional families in the UK Biobank: p.R304* (97 carriers / 35 pedigrees), p.F269_H275dup (21 carriers / 13 pedigrees), p.R271W (9 carriers / 8 pedigrees), and p.R81* (4 carriers / 2 pedigrees). Analysis showed 23/35 (66%) families with the p.R304* variant shared a single haplotype. Of these, 16 (70%) families originated from Northern Ireland, and 3 (13%) from Scotland, and 4 (17%) from England. Additionally, 11 (85%) families with the p.F269_H275dup variant shared a haplotype and were all from England. In contrast, p.R271W and p.R81* variants showed no evidence of a shared ancestral origin. Clinical comparison of p.R304* carriers with ($n = 106$) and without ($n = 27$) the shared haplotype revealed no significant differences in individuals with and without adenoma, age at diagnosis/symptom onset, tumour size, tumour invasiveness, or need for multiple surgeries ($P > 0.05$).
Conclusion
The p.R304* and p.F269_H275dup *AIP* variants originate from shared ancestral haplotypes with distinct geographical distributions across the UK and Ireland. However, the shared ancestry does not appear to significantly alter disease severity suggesting the absence of major modifier variant in the *AIP* gene.

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The challenges of a rapidly progressive pituitary metastasis

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Background
Pituitary metastasis, although rare, is life-threatening often presenting with visual disturbances, hypopituitarism and AVP deficiency. The most common primary sites are breast and lung carcinomas. We highlight such a case of non-small cell lung cancer (NSCLC) presenting with pituitary metastasis.
Case Presentation
A 52-year-old, ex-smoker, presented with headaches, visual disturbances and profound fatigue. Biochemistry confirmed hypopituitarism: Na 144mmol/l, LH <0.5iu/l, FSH <0.5iu/l, Testosterone <0.3nmol/l Cortisol 99nmol/l, IGF1 143ng/mL, Growth hormone 0.9 mg/l, TSH 0.06mIU/l, fT4 7.4pmol/l, Prolactin 74mIU/l. Pituitary MRI demonstrated a 17mm heterogeneous intra and suprasellar mass, compressing the optic chiasm and consistent with a pituitary macroadenoma. Hormone replacement with hydrocortisone, thyroxine and testosterone was initiated. Within two weeks, he re-presented with worsening headaches, confusion, polydipsia and polyuria and was subsequently started on desmopressin. Repeat MRI revealed rapid interval growth, raising suspicion of an infiltrative pathology. CT CAP identified a 5 cm lung mass, histologically confirmed as NSCLC. Following pituitary and lung MDT discussions, the pros and cons of debulking surgery were discussed with the patient and his partner. They opted for surgery despite significant risks, with the hope of post-operative chemotherapy. Craniotomy with EVD, followed by a second surgery was needed for maximal tumour resection. Post operatively, he remained confused with difficult sodium/AVP-D management. A 'smart catheter' was used to assist with fluid balance. Unfortunately, he did not tolerate chemotherapy, and palliative care supported his terminal period. His partner was thankful for the extra time surgery provided, as he would have died much sooner without surgery.
Conclusion
This case illustrates the aggressive progression of NSCLC-related pituitary metastasis, challenges in surgical decision-making, AVP-D management, and palliative care in panhypopituitarism. Rapid-onset symptoms with a heterogeneous pituitary mass on MRI warrant urgent follow-up MRI and CT CAP. Any pituitary mass presenting with AVP-D should prompt consideration of metastatic malignancy.

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Acromegaly management and outcomes: a 47-year single-centre experience

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Background
Acromegaly is usually caused by a pituitary adenoma, resulting in excess growth hormone (GH) with high insulin-like growth factor-1 (IGF-1) levels. Neurosurgical, radiotherapy, and pharmacological treatment options have advanced. We evaluated outcomes of 71 patients over 47 years.

Table 1: treatment outcomes

Treatment Modality	Number of patients	Number of macro-adenomas	Number of micro-adenomas	Biochemical remission or control
Surgery alone	11	6	5	10
Surgery + radiotherapy	6	3	2	7
Surgery + medical therapy	12	8	3	6
Surgery + radiotherapy + medical therapy	29	19	7	20
Radiotherapy + medical therapy	1	1	0	1
Medical therapy alone	10	5	5	6
No therapy necessary (pituitary apoplexy)	1	1	0	1
Insufficient data	1	1	0	0
Total	71	44	22	51

Methods
Retrospective review of all diagnosed with acromegaly between 1978–2025. Data were obtained from electronic and paper records. Biochemical remission was defined as nadir GH <1 μg/l and normal age-adjusted IGF-1.
Results
71 patients (59.2% males) included (mean age 58.6 $\pm$ 1.8 years). Macroadenomas present in 44/71 (62%); microadenomas in 22/71 (31%); remaining 5/71 (7%) with unknown tumour size. Dopamine agonists (DA) were prescribed in 25/71 (35.2%); somatostatin analogues (SSA) in 21/71 (29.6%); Pegvisomant in 3/71 (4.2%); 6 achieved remission with medical therapy alone. 51 patients achieved biochemical remission (table 1); 34/51 (66.7%) required multimodal treatment. 9/58 (15.5%) required GH replacement post-operatively. Discordance between GH and IGF-1 results occurred in 38/71 (53.5%) patients.
Conclusion
Across over four decades of practice, 51/71 (71.8%) of patients achieved biochemical remission or control. Persistent discordance occurred in 53.5% patients, contributing to ongoing challenges in monitoring and defining cure.

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Inflammatory pituitary mass in a young female, treated as pituitary abscess caused by *cutibacterium acnes*

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Background
Pituitary abscess is a rare but potentially life-threatening cause of a sellar mass accounting for around 1% of pituitary lesions. Presenting features may be nonspecific with absent systemic infection signs. *Cutibacterium acnes* is an uncommon cause of pituitary abscess.
Case Presentation
A 16-year-old previously healthy female presented with seven months of severe headaches. She experienced spots of visual loss in the left eye, which progressed at six months to complete visual loss in the left eye. Secondary amenorrhea was noted. MRI revealed a 17 mm sellar lesion with necrotic centre compressing the left optic chiasm. Biochemistry confirmed panhypopituitarism (cortisol 85 nmol/l, fT4 5.0 pmol/l, oestradiol <98 pmol/l, prolactin 269 mIU/l), with normal inflammatory markers (WBC 5.7x10^9/l, CRP 3 mg/l). After initiation of hydrocortisone and levothyroxine, she underwent urgent endoscopic transsphenoidal resection of the sellar lesion. Thick yellow purulent material was encountered, and culture grew *Cutibacterium acnes*. Histopathology demonstrated granulomatous hypophysitis with mixed lymphohistiocytic infiltration. She received six weeks of intravenous ceftriaxone and oral metronidazole. Postoperatively, she developed transient diabetes insipidus requiring desmopressin. Her headaches improved, vision normalised, and follow-up MRI showed no residual lesion. She remains hypopituitary on treatment.
Discussion
Cutibacterium acnes infections are typically indolent and may provoke only minimal inflammatory response, obscuring diagnosis. Diagnosis of pituitary abscess was based on positive culture and antibiotic response. The histological finding of granulomatous hypophysitis does not directly support a diagnosis of *C. acnes* abscess. There was no evidence of additional systemic illness such as TB or sarcoidosis. Idiopathic granulomatous hypophysitis remains a possible differential diagnosis.
Conclusion
This case demonstrates an acute presentation of an inflammatory pituitary mass in a teenager treated as *Cutibacterium acnes* pituitary abscess with good clinical outcome. Idiopathic granulomatous hypophysitis remains a differential, warranting further evaluation if recurrence occurs.

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CAM2029 octreotide subcutaneous depot maintains control of IGF-I and symptoms of acromegaly across a 4-week dosing interval and for intervals greater than 28 days: data from the ACROINNOVA 1 trial

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Waning biochemical and symptom control has been reported in patients with acromegaly towards the end of dosing intervals with standard-of-care (SoC) injectable somatostatin receptor ligands. CAM2029 is a long-acting octreotide subcutaneous depot designed for monthly self-administration. In the 24-week (W), Phase 3 ACROINNOVA 1 trial (NCT04076462), CAM2029 (20 mg every 4W [$\pm$1W]) demonstrated superior biochemical control (insulin-like growth factor I [IGF-I] $\leq$ upper limit of normal [ULN; per age and sex]) vs placebo (72.2% vs 37.5%; $P=0.0018$) in patients controlled with SoC at screening. We report analyses of IGF-I and symptom control over a 4W dosing interval. The final CAM2029 dose was received at W20; the end of trial (EOT) was scheduled for W24. IGF-I levels and Acromegaly Index of Severity (AIS; key acromegaly symptoms evaluated by the clinician with the patient) scores were assessed at W20 before administration of CAM2029, W22 and W24/EOT (intervals $\leq$28 days). Some patients experienced delays in their planned W24/EOT visits, resulting in later assessments (intervals $>$28 days). Forty-two patients (87.5%) randomized to CAM2029 completed treatment. 45.2% (19/42) underwent W24/EOT assessment $\leq$28 days post-dose. Mean IGF-I/ULN values remained controlled across W20 (0.83), W22 (0.77) and W24/EOT (0.80). Mean AIS overall scores were stable from W20 (4.7) to W22 (4.2) and W24/EOT (3.6). 54.8% (23/42) of patients had dosing intervals of $>$28 days (maximum 42 days; mean 33.4 days). Mean IGF-I/ULN values were controlled across the $>$28-day dosing interval (0.81, 0.84 and 0.78 at W20, W22 and W24/EOT, respectively). CAM2029 also maintained stable mean AIS overall scores across W20 (4.3), W22 (4.3) and W24/EOT (4.7) in those with later assessments ($>$28 days). CAM2029 maintained stable biochemical and symptom control throughout the 4W dosing interval, including in patients whose intervals extended $>$28 days. These data reinforce CAM2029's potential to address unmet needs among patients with acromegaly.

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Lost to follow-up: the challenge of managing a treatment-resistant giant prolactinoma

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Background
Giant prolactinomas are uncommon pituitary tumours that can cause marked hormone excess and mass effect. Dopamine agonists are usually very effective, but some patients develop resistance or side effects when treated at high doses for long periods.
Case
A 21-year-old man presented with progressive visual loss and headaches. MRI showed an 8-cm sellar mass invading both cavernous sinuses and the tentorium. His serum prolactin was 794,560 mIU/l. He was started on cabergoline 14 mg per week—well above standard dosing—and was lost to follow-up for almost a decade. When reviewed again, his prolactin remained elevated (15,000 mIU/l) and MRI demonstrated persistent invasive disease. He also described compulsive gambling and excessive spending, consistent with a dopamine-agonist-related impulse control disorder. Echocardiography excluded valvular disease. The pituitary multidisciplinary team advised tapering cabergoline and reconsidering radiotherapy, given limited surgical options and incomplete biochemical response.
Discussion
This case highlights the problems that can arise when long-term cabergoline therapy is not closely monitored. Resistance to dopamine agonists and the emergence of behavioural side effects can complicate management and require a reassessment of treatment goals.

Conclusion
Giant prolactinomas resistant to dopamine agonists remain difficult to manage. Ongoing endocrine, neurosurgical and psychiatric follow-up is essential to balance tumour control with treatment safety.

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Primary pituitary lymphoma in a patient with C1 esterase inhibitor deficiency and MGUS: a diagnostic challenge

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Background
Primary pituitary lymphoma (PPL) is exceptionally rare and often mimics non-functioning pituitary adenomas (NFPAs) radiologically. Recognition is crucial to avoid misdiagnosis and inappropriate treatment. C1 esterase inhibitor deficiency has been associated with lymphoproliferative disorders and may predispose to PPL. Therefore, in patients with C1 esterase inhibitor deficiency presenting with pituitary lesions, PPL should be considered in the differential diagnosis.
Case
A 68-year-old lady with known C1 esterase inhibitor deficiency and MGUS presented with a 5–6-year history of intermittent facial and neck swelling, headaches, and transient visual obscuration. The swelling, often preceded by fatigue and myalgia, had been attributed to atypical angioedema. Extensive investigations revealed an incidental 1 cm sellar mass compressing the optic chiasm, radiologically compatible with a non-functioning pituitary adenoma. Given the visual involvement, she underwent endoscopic endonasal debulking in February 2024. Histology revealed sparse CD20-positive B-cell aggregates with Ki-67 $<5\%$, consistent with extranodal marginal zone lymphoma (MALT type). Diagnosis was confirmed by molecular clonality testing. Systemic staging with CT thorax, abdomen, and pelvis showed no disseminated disease. She required no adjuvant therapy and remains under surveillance with endocrinology follow-up. Serial MRI scans have confirmed no recurrence to date.
Conclusion
Primary pituitary lymphoma should be considered when assessing atypical sellar lesions, especially in patients with underlying risk factors. Its clinical and radiological features can closely resemble non-functioning pituitary adenomas, and tumour grade cannot be reliably inferred from growth patterns on surveillance MRI. Definitive diagnosis requires histopathological confirmation. In this case, visual compromise necessitated surgery. A true wait-and-watch approach will rarely be undertaken, as such lesions are typically assumed to be NFPAs until growth or chiasmal compression warrants intervention. Pragmatically, patients are monitored until progression necessitates surgery. A multidisciplinary approach remains essential for accurate diagnosis and optimal management.

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Rare AIP exon 2–3 large deletion linking acromegaly and thyroid carcinoma: first case series from Albania

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Background
Germline *AIP* mutations are a rare cause of familial isolated pituitary adenomas (FIPA), and large deletions present in only ten known kindreds worldwide. We describe the first Albanian family harboring a pathogenic *AIP* exon 2–3 deletion, presenting with growth hormone (GH)–secreting adenomas and an associated thyroid carcinoma.
Methods
Two affected siblings underwent detailed clinical, biochemical, radiological, and histopathological assessment. Germline *AIP* analysis was performed using methods able to detect copy number variants. In the patient with metastatic thyroid carcinoma, tumor DNA was analyzed by next-generation sequencing (NGS) for additional somatic variants.
Results
The index case, a woman diagnosed with acromegaly at 39 years after 20 years of symptoms, had a 16×11 mm somatolactotroph adenoma and achieved long-term remission post-surgery. Her brother, diagnosed at 42 years, had a $23\times15\times10$ mm macroadenoma invading the cavernous sinus, partially responsive to octreotide LAR. He also developed Hürthle-cell thyroid carcinoma, later radioiodine-refractory with lung metastases. NGS of the thyroid tumor revealed somatic variants in *MSH6*, *TP53*, *SMARCA4*, and *HLA-B* deletion. Germline testing confirmed a heterozygous *AIP* exon 2–3 deletion in both siblings.
Conclusions
This kindred represents the first genetically confirmed *AIP* large deletion family in Albania. The phenotype did not differ substantially from other *AIP* mutation carriers. These findings highlight the importance of performing tests for large deletions in *AIP* gene assessment and allow cascade family screening to enable detection of variant carriers and clinical screening.
Keywords
AIP large deletion, familial acromegaly, thyroid carcinoma, Albania, FIPA

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P195

The role of Sox11 in hypothalamic-pituitary development and the pathogenesis of hypogonadotropic hypogonadism

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Introduction
Gonadotropin-releasing hormone (GnRH) is the master hypothalamic hormone regulating the reproductive axis. GnRH insufficiency causes absent puberty with low levels of sex steroids, known as hypogonadotropic hypogonadism (HH). Recently, pathogenic variants in *SOX11 (SRY-box transcription factor 11)* were identified to underlie a novel neurodevelopmental disorder with congenital HH. SOX11 is expressed in both the developing pituitary and hypothalamus, but its role in reproductive development and function is unknown. This project aims to investigate the mechanisms by which SOX11 deficiency effects hypothalamic-pituitary-gonadal axis biology using cellular and mouse models.
Methods
We have generated two new transgenic lines to genetically delete *Sox11*. These mice models have tissue specific knockout of *Sox11* in the pituitary gland ($Prop1.2i^{Cre/+}$;$Sox11^{Flox/Flox}$;$Rosa26^{Tomato/+}$) and in GnRH neurons ($GnRH^{Cre/+}$;$Sox11^{Flox/Flox}$;$Rosa26^{Tomato/+}$). Additionally, we have generated Gn11 CRISPR-Cas9 cell lines to examine the effect of knockdown of *Sox11* expression in a developing GnRH neuronal cell line.
Results
Tissue expression studies showed Sox11 localisation in wildtype pituitary and hypothalamus at embryonic day 18.5. Western blot and immunofluorescence staining demonstrated Sox11 protein expression in immature (Gn11) and mature (GT1-7) GnRH neurons, and also in non-reproductive neuronal (SHY5Y) cell lines. In mice with tissue-specific knockout of Sox11 in the pituitary gland, histology of postnatal day 1 hypothalamic-pituitary axis revealed morphological abnormalities of the pituitary as compared to control mice. The $Prop1.2i^{Cre/+}$;$Sox11^{Flox/Flox}$;$Rosa26^{Tomato/+}$ pituitary mouse model showed a significant delay in balanopreputial separation (males, $P = 0.0086$), vaginal opening (females, $P = 0.0100$) and first estrous (females, $P = 0.0086$), compared to control littermates, consistent with delayed timing of sexual maturation and puberty onset. Body weight was not significantly different at the time of puberty onset between knockout or control mice. Ongoing analysis will further examine both knockout mouse and cellular models.
Conclusion
These data suggest that Sox11 deficiency leads to defective pituitary development with delayed puberty in males and females.

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Drug induced liver injury following low-dose tolvaptan for SIADH: a rare adverse event prompting a change in monitoring

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Tolvaptan, a vasopressin V2-receptor antagonist, is licensed for managing hyponatraemia in the syndrome of inappropriate antidiuretic hormone (SIADH). We report a rare case of drug-induced liver injury (DILI) following low-dose Tolvaptan. A 51-year-old female with SIADH had symptomatic hyponatraemia despite fluid restriction and sodium supplementation. Tolvaptan was initiated at 3.75 mg twice weekly, uptitrated to once daily, in preparation for elective surgery. Baseline liver function tests (LFTs) were normal. After six weeks, serum sodium normalised (122 mmol/l to 134 mmol/l), however ALT rose from 14U/l to 405U/l (normal range 0-32). Synthetic liver function and clinical examination remained normal. The patient had no history of liver disease, alcohol excess, or use of hepatotoxic drugs or CYP3A4 inhibitors. A non-invasive liver screen was negative. Tolvaptan was stopped and her LFTs normalised within 6 weeks. A yellow card report was completed and a drug allergy recorded. DILI is a recognised complication of high-dose Tolvaptan, particularly at high doses (60-120 mg/day) used in autosomal dominant polycystic kidney disease (ADPKD), where it can lead to liver failure (1). This has led to strict counselling and LFT monitoring guidelines in ADPKD, however whilst the BNF recommends LFT monitoring, guidelines do not exist for the use of low-dose Tolvaptan in SIADH. The pathogenesis of Tolvaptan-induced DILI remains unclear, although host-dependent susceptibility appears important regardless of dose (2). Those developing DILI should stop the drug, and recurrence risk is high if restarted (1). Here we show that clinically significant DILI can occur with low-dose Tolvaptan with no reliable predictors of susceptibility. All patients receiving regular Tolvaptan should undergo LFT monitoring irrespective of dose. We recommend monthly LFTs for 18 months, then 3-monthly thereafter. Patients should be counselled on potential risks, and any signs of liver injury should prompt immediate discontinuation.

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P197

Cushing-like but not Cushing Disease

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A 30-year-female with history of progressive weight gain noticed since menarche reduced weight to 104 kilograms from 148 kilograms with lifestyle modifications. Her weight has now become static since the last 1 year. She noticed few extra facial hair and mild acne. She has irregular menstrual cycles for last 4 years, treated with COCs but stopped since last 6 months. She denied any extremity weakness, easy bruising or stretch marks over the body. Her medical history was positive for hypothyroidism (on 300 mg levothyroxine), severe anemia, severe vitamin D deficiency, HLA-B27 positive status. Her GP ordered evaluation for obesity / Cushing disease. Initial biochemical evaluation revealed FT_4 15 pg/mL (10–22)(CLIA), FSH 234 mIU/mL(CLIA), LH 200 mIU/mL(CLIA), Total Testosterone 127 ng/dl(CLIA), prolactin 319 ng/mL (< 25)(CLIA), ACTH 95 pg/mL (<46)(CLIA), 8am serum cortisol 126 µg/dL (5–25)(CLIA), TSH 40 mIU/mL(CLIA)with normal potassium. Additional tests revealed HPLC - β-thalassemia trait, anti-tTG IgG positivity, anti tTG IgA negative, anti-IF positivity, low ferritin. High cortisol / ACTH levels prompted an MRI pituitary which revealed a 3*6 mm anterior pituitary microadenoma, TNTS was planned for Cushing Disease by neurosurgeon. Patient was then referred to Endocrinology Department for perioperative management. On examination patient had abdominal obesity, insulin resistance but no Cushing stigmata. The absence of discriminatory features prompted reevaluation. A LDDST was advised which paradoxically yielded ACTH 145 pg/mL and serum cortisol 240 mg/dL, reinforcing biochemical–clinical discordance. Comprehensive steroid profiling by LC–MS/MS demonstrated normal cortisol / metabolite concentrations, confirming spurious hormonal elevations due to heterophile antibody. Other pituitary hormones were re-evaluated with PEG precipitation and LC-MS/MS methods and hormonal levels were within normal limits. Surgery was withheld and the lesion was reclassified as a non-functioning pituitary incidentaloma.

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P198

When suppression stimulates: persistent testosterone elevation from gonadotrophin-releasing hormone agonist therapy in prostate cancer

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Introduction
Gonadotrophin-Releasing Hormone (GnRH) agonists are the mainstay of androgen deprivation therapy (ADT) in prostate cancer. They act through continuous stimulation of pituitary GnRH receptors, leading to receptor desensitisation, suppression of gonadotrophin release, and achievement of castrate testosterone levels. Persistent testosterone elevation during therapy is rare and may represent paradoxical pituitary stimulation rather than pharmacological ineffectiveness. Understanding such responses is crucial for accurate endocrine interpretation and oncological decision-making.
Case Presentation
A 70-year-old man with T3a Gleason 9 prostate adenocarcinoma commenced ADT with Decapeptyl (11.25 mg) in June and August 2023. Following the second dose, testosterone and FSH rose—peaking at 42.3 nmol/l and 18.7 U/l (NR 1–12) respectively—with a concurrent PSA increase. Other pituitary hormones were normal. MRI demonstrated a 21×19×18 mm pituitary macroadenoma. As gonadotrophins and testosterone remained elevated for several months, an FSH-secreting adenoma (FSHoma) was considered. Multidisciplinary endocrine review concluded that the biochemical profile was most consistent with paradoxical gonadotrophin stimulation secondary to GnRH agonist exposure rather than autonomous secretion. The GnRH agonist was discontinued after the second dose because of sustained hormonal elevation. Over 3–4 months, testosterone and FSH gradually normalised. The patient subsequently underwent radical radiotherapy for prostate cancer and was commenced on bicalutamide, a non-steroidal androgen receptor blocker. Follow-up pituitary MRI in 2024 showed adenoma reduction, with stability confirmed in 2025. Inoperable gastric cancer was diagnosed later in 2024.
Conclusion
This case highlights a rare but clinically significant paradoxical response to GnRH agonist therapy, where persistent gonadotrophin stimulation maintained testosterone production despite intended suppression. The mechanism likely reflects transient pituitary hypersensitivity rather than true androgen resistance. Recognition of this phenomenon is essential to prevent misinterpretation as treatment resistance, avoid inappropriate escalation, and guide timely endocrine evaluation and multidisciplinary management in patients with unexpected biochemical patterns.

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P199

Audit of testing for growth hormone deficiency (GHD) in teenage and young adults (TYA) and adults previously treated with cranial radiotherapy at a Tertiary Oncology Hospital

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Background
Biochemical diagnosis of Growth Hormone Deficiency (GHD) in UK adults(>18yrs) follows NICE criteria (2003) with diagnostic GH on dynamic stimulation test (DST) of <3ng/mL. Local guidance requires 2xDSTs with peak GH <3ng/ml (ITT first-line, GST/AST 2nd-line) for diagnosis in those age>24yrs, and <7ng/ml in 17-25yrs. Recently published criteria[1] highlight updated BMI and age-based cut-offs for the aforementioned DSTs.
Objectives
To assess compliance to NICE criteria and local guidance and determine impact of age/BMI-based cut-offs on GHD diagnosis.
Methodology
Retrospective audit of 50 patients ($n = 46$ included, 24F, mean age 32yrs (17-71yrs)), identified from GH dataset (2005-2024), using local electronic patient record for demographics, clinical data, treatment history, DST results (registered with local audit committee 4358). Inclusion criteria: age>17yrs and undergoing DSTs for GHD diagnosis. Pseudoanonymised data was collected (Microsoft Excel).
Results
Data for 46/50 ($n = 9$TYA, $n = 37$adults) were available for analysis. 41/46 had history of tumour/cancer and radiotherapy (Tumour diagnosis: brain astrocytoma/-glioma/medulloblastoma 24/41, pituitary 6/41, nasopharyngeal 4/41, leukaemia 2/41, other 5/41). 29/46 were on GH replacement, 28/29 met NICE criteria ($n = 14$ >18 yrs, $n = 15$ 18-24yrs). First DST: ITT(19/46), GST(20/46), AST(7/46). Mean BMI 27 kg/m2(range17-37). Application of age/BMI-based cut-offs didn't change

diagnosis in TYA group. 37 patients were >25yrs; 23/37 having 2xDST. Mean(SD) BMI 28.8(5) kg/m2. DST results showed differences between diagnosis using the NICE vs Yuen 2023 criteria (Table), with 26 patients meeting NICE criteria vs 18 meeting Yuen cut-offs.

Table

1st DST	NICE GH<3ng/ml	Yuen cut-offs
ITT(n = 14)	13	13
GST(n = 18)	10	4
AST(n = 5)	3	1

Conclusion

A high compliance is shown to the NICE criteria. Weight and age-based cut-offs have a significant impact on GH diagnosis in those >25yrs when GST is used as first-line diagnostic test.

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P200

Case report: pharmacological and non-pharmacological therapies in the management of refractory hypoglycaemia secondary to malignant insulinoma

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Malignant insulinoma is a rare pancreatic neuroendocrine tumour. Challenges with management include the clinical implications and management of refractory hypoglycaemia. A 42 year old gentleman presented with behavioural changes secondary to point-of-care-confirmed hypoglycaemia of 1.8mmol/l associated with neuroglycopaenia. Subsequent biochemistry revealed inappropriately normal C-peptide 2.64 mg/l (0.80-5.20), insulin 13.81 mIU/l (3.40-19.60) and elevated pro-insulin 138pmol/l (3.4-20.4) with paired fasting serum glucose 2.8mmol/l confirming insulin-dependent hypoglycaemia. Imaging showed a poorly defined heterogenous mass at the pancreatic body and tail. Endoscopic ultrasound with sampling from fine needle aspiration confirmed a pancreatic neuroendocrine neoplasm with poorly-differentiated features, staining positively for SSTR2A, chromogranin, and synaptophysin. He was treated with first line temozolamide/capecitabine neoadjuvant chemotherapy, followed by temozolamide monotherapy. After a therapeutic trial of short acting somatostatin analogue (Octreotide), he was commenced on Lantreotide for hypoglycaemia. Continuous glucose monitoring (CGM) was used to monitor hypoglycaemia and assess response to treatment. Time below range (TBR) prior to chemotherapy was up to 7%. Management of symptomatic fasting hypoglycaemia included clinical nutrition input, diazoxide, and glucocorticoids, which were later reduced due to hyperglycaemia. He underwent subsequent extensive surgical resection with histology showing grade 3 NET, Ki67 up to 40%, ENETS stage pT4N2, R0. Due to radiological recurrence of disease and worsening hypoglycaemia, TBR 18%, nocturnal cornstarch was introduced in combination with high protein snacks nocte resulting in temporary normalisation of fasting blood glucose. He was commenced on everolimus and lutetium peptide receptor radionucleotide therapy (PRRT), without further episodes of hypoglycaemia to date, TBR 0%. The management of hypoglycaemia in malignant insulinoma can be challenging. The use of CGM devices has improved the ability to establish patterns for targeted treatments. The use of cornstarch as a non-pharmacological option for treatment of refractory hypoglycaemia in malignant insulinoma was successful as a bridge to further pharmacological treatments in this case.

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P201

Parotid gland tumours in acromegaly: rare coincidence or IGF-related association?

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Background

In acromegaly, chronic GH hypersecretion with secondary IGF-1 excess sustains proliferative signalling and stimulates widespread growth-factor activity. Although tissue overgrowth is typical, salivary-gland involvement is rarely reported.

Case reports

The first, a 69-year-old woman, was assessed in 2019 with acromegalic features and elevated IGF-1 (3.7 × ULN). MRI showed a pituitary macroadenoma and an incidental right parotid tumour (4.3 × 2.8 × 2.8 cm) with well-defined margins, not clinically apparent, possibly masked by cervical enlargement from underlying multinodular goitre. Transsphenoidal adenomectomy confirmed a somatotroph adenoma (Ki-67 = 3%). GH hypersecretion persisted despite combination therapy with lanreotide and cabergoline; biochemical control was achieved with pegvisomant. The parotid tumour was surgically removed in 2022, and histopathology confirmed pleomorphic adenoma. The second, a 60-year-old woman, presented at the end of 2018 with acromegalic features and elevated IGF-1 (2.4 × ULN). Clinical examination identified a left parotid mass. Cranial CT demonstrated a 2 × 2.5 × 1.4 cm, well-circumscribed parotid tumour, along with a concomitant pituitary microadenoma. Following the diagnosis, cabergoline was initiated. Parotid tumour excision in 2019 confirmed pleomorphic adenoma, followed later that year by transsphenoidal pituitary surgery. Histopathological examination confirmed a GH-secreting adenoma with focal PRL co-expression (Ki-67 = 2%). Lanreotide therapy achieved and maintained biochemical control, with sustained remission after discontinuation in 2022.

Discussion

Pleomorphic adenoma, the most frequent benign tumour of the salivary glands, predominantly affects the parotid. Although IGF-1 excess in acromegaly is associated with increased tumour prevalence, evidence for salivary involvement is limited. PLAG1-driven IGF2 upregulation in pleomorphic adenoma suggests a plausible local mechanism that may act synergistically with systemic IGF-1 signalling to promote tumour growth.

Conclusion

These cases suggest a possible interaction between systemic GH/IGF-1 excess and local PLAG1-driven pathways in benign salivary-gland tumour formation, supporting consideration of parotid assessment during acromegaly follow-up.

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P202

Peptide receptor radionuclide therapy (PRRT) as a treatment option in metastatic ovarian neuroendocrine tumour with carcinoid syndrome and treated carcinoid heart disease: a case report

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Background

Primary ovarian neuroendocrine tumours (NETs) are rare and may secrete serotonin, causing carcinoid syndrome and occasionally carcinoid heart disease (CHD) through direct release of vasoactive peptides. The NETTER-1 trial showed that ^177Lu-Dotatate (PRRT) significantly improves progression-free survival in progressive advanced midgut NETs on somatostatin analogues and is NICE-recommended. Evidence for PRRT in metastatic ovarian NETs with SSTR expression is lacking, though data from large CUP-NET cohorts demonstrate clinical efficacy. A multidisciplinary and personalised approach remains essential.

Case Summary

A 58-year-old woman with type 2 diabetes and asthma presented with presumed postmenopausal symptoms and bleeding. Ultrasound revealed a 13 cm pelvic mass (2021). Preoperative echocardiography for planned hysterectomy unexpectedly showed carcinoid heart disease with thickened, retracted tricuspid valve leaflets and moderate pulmonary regurgitation. She reported long-standing flushing, diarrhoea, fatigue, and pedal oedema. Urinary 5-HIAA (536 µmol/24 h) and chromogranin A (1275 pmol/l) were markedly elevated, confirming carcinoid syndrome. She underwent uneventful tricuspid and pulmonary valve replacement with coronary bypass (2022), followed by pelvic mass resection (2023). Histology confirmed an insular-type ovarian carcinoid (Grade 1, Ki-67 <1%). After 12 months of stability, follow-up ^68Ga-DOTATATE PET-CT (2024) demonstrated hepatic and pulmonary metastases (Krenning 4) with normal markers (5-HIAA 20 µmol/24 h), complicating surveillance. Following NET MDT review, she received compassionate PRRT, which was well tolerated, and follow-up continues.

Discussion and Conclusion

Ovarian NETs are rare. PRRT use in metastatic ovarian NETs is based on limited case reports and extrapolated data but is supported by ESMO 2024 and ENETS guidelines. Early recognition, somatostatin receptor imaging, and multidisciplinary coordination are vital to optimise outcomes. This case illustrates overlapping menopausal and carcinoid symptoms, with carcinoid heart disease diagnosed incidentally. Achieving both tumour and hormonal control is crucial. Compassionate PRRT proved beneficial, underscoring the need for global collaboration to strengthen evidence and ensure access to functional imaging for accurate assessment and follow-up.

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Nursing Practice

P203

Safe prescription frequency for steroids and other vital medications

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Patients' anecdotally reported concern around the ease of getting vital endocrine medications, particularly extended prescriptions. NICE Guidelines for the Identification & Management of Adrenal Insufficiency[1] stresses the importance of a good medication supply, including sick day dosing and travel. Guidance also suggests individualising for patients and involving them in decisions[2]. A systemic review of 3 month vs 28-day supply is seen to be cost effective[3]. A 4-week on-line survey was conducted by the Pituitary Foundation (PF) and Addison's Disease Self-Help Group (ADSHG) in June 2025 and received 1724 responses (1399 PF, 325 ADSHG) around medications, including steroids, desmopressin, levothyroxine, testosterone, oestrogen. Most people received less than 3 months' supply (97% PF, 78.8% ADSHG), with over half only getting one month's supply (60% PF, 55% ADSHG). 33% of patients with short repeats had previously approached their GP for longer. Common refusal reasons included: medicine wastage, stockpiling, supply issues, concern over patient safety, local policy, no reason. Other concerns included slow turnaround (5-7 days), difficulty sourcing hydrocortisone sodium phosphate, delays in hospital communication, and a lack of awareness of the possibility. The PF and ADSHG will raise awareness with professionals through promotion alongside creating templates for professionals and patients, encouraging clinic letters to highlight the need for 3-month supply. Current engagement with the NHSE National Clinical Director for prescribing aims to increase length to a minimum of 56 days with additional 'sick day' supply 'one off' prescriptions easily available. The survey emphasises how pressing this is for patients and the importance of the patient voice.

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Reproductive Endocrinology

P204

Hematological, hormonal and immunomodulatory activities of aqueous extract of *Solanum nigrum* (Linn.) leaf on *Plasmodium bergei* NK65 Infection in gravid mice: a focus on Placental malaria

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Placental malaria is one of the prominent conditions resulting in poor pregnancy outcomes. It is characterized by the sequestration of Plasmodium falciparum-infected erythrocytes and the infiltration of immune cells into the placental interstitium, changing its colour to black due to the deposition of malaria pigment. This study aims to investigate the hematological, hormonal and immunomodulatory activities of aqueous extract of *Solanum nigrum* leaf on *Plasmodium bergei* NK65 infection in Gravid Mice. Twenty female gravid albino mice (24.73g ± 2.15) were randomly divided into 4 groups (I-IV) of five animal each. Group I served as control and group II-IV received distilled water, 500/25 mg/kg body weight of Sulfadoxine-pyrimethamine and 100 mg/kg of AESNL orally for 3 days, respectively. A thin Blood Film smear was carried out to estimate the number of parasitized red blood cells. The animals were sacrificed under di-ethyl anesthesia on day 18 of gestation and the fetus was weighed and preserved in Bouin solution, while the placenta and spleen were in 10% formalin. The result obtained revealed that there was a significant increase ($P < 0.05$) in the serum immunological parameters (Tumor necrosis factor-α and interleukin-6), the maternal % parasitemia and weight of the spleen while a significant decrease ($P < 0.05$) in the serum progesterone and fetal weight were obtained in the untreated group compared to the control. The administration of 100 mg/kg AESNL decreased, white blood cell count, serum tumor necrosis factor-α and interleukin-6 concentration, increased the serum progesterone concentration, increased fetal weight, decreased spleen weight, decreased maternal % parasitemia and improved the theilery developmental features of the infected mice. The findings of this study reveals that AEoSNL elicited hormonal, hematological and immunomodulatory activities against NK65 infected gravid mice at the dose investigated, therefore, it can be explored in the development of antimalarial drug targeting placenta malarial subject to further experimentations.

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P205

A Retrospective Review of Functional Hypothalamic Amenorrhoea in the University Hospitals of Leicester Endocrine clinic

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Background
Functional hypothalamic amenorrhoea (FHA) is associated with reduced bone density and impaired fertility due to prolonged oestrogen deficiency. Existing data describe White populations, with limited knowledge of ethnic variation in FHA. Leicester has a diverse population, 43% Asian. Polycystic Ovarian Syndrome (PCOS), is the commonest cause of secondary amenorrhoea, and is recognised to have increased prevalence in Asians.
Aims
We aimed to assess bone density, management strategies and pregnancy outcomes in patients with FHA. We wished to compare ethnic variation in FHA to that of the PCOS cohort in our clinic.
Methods
A retrospective review of individuals diagnosed with FHA (2000–2025) using our electronic patient record system. Ethnicity data in individuals with FHA were compared with that of the UHL PCOS population (diagnosed 2007–2022), using two-proportion Z-test analysis.
Results
75 FHA patients were identified, mean age 25.8 years, BMI 20.5 kg/m^2. Characteristics; low BMI (<18.5 kg/m^2) 77.3%, excessive exercise 21.3%, and psychological stress 2.7%. Although 76% ($n = 56$) were recommended for DEXA, only 45.3% ($n = 34$) underwent scanning. Of these, 29.3% had reduced bone density, with documented fractures in 10.7%. 6.7% received Bisphosphonates. Pregnancy occurred in 20.0%, miscarriage rate 20.0%, 6.7% required fertility treatment. Hormonal therapy was prescribed in 68%; HRT (29.3%), transdermal oestrogen (45%), oral contraceptive pill (42.7%). Most patients were White British (94.7%), by contrast, only 60.6% of PCOS patients were White, a statistically significant difference 28.9% (95% CI: 23.0–34.8%).
Discussion
Monitoring of bone health was inconsistent, and transdermal oestrogen was infrequently prescribed. FHA predominantly affected White British women, despite Leicester's ethnic diversity, suggesting biological susceptibility alongside cultural factors.
Conclusion
We highlight significant ethnic differences between FHA and PCOS populations. Genetic susceptibility to FHA warrants further translational research. A structured checklist to guide clinicians may improve a holistic approach to FHA management in the endocrine clinic.

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P206

Research priorities for Polycystic Ovary Syndrome: results of a James Lind Alliance priority setting partnership

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Background
Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder with significant metabolic, reproductive and psychological manifestations. Co-production of research priorities is vital in ensuring that research addresses questions that really matter for people with PCOS as well as healthcare professionals (HCPs). We sought to identify the most important areas for research for people with PCOS by establishing a James Lind Alliance (JLA) Priority Setting Partnership (PSP).

Methods
Using standard JLA methodology, we conducted an online survey to gather research questions from a diverse group of stakeholders. We created summary questions and cross-checked these against existing evidence to identify gaps in the literature. Unanswered questions were included in a second survey for shortlisting by stakeholders. A prioritisation workshop will be held to establish the top 10 research priorities.
Results
The first survey yielded 1339 questions from 523 respondents (434 people with lived experience [3% 16-20 years, 35% 21-30 years, 39% 31-40 years, 15% 41-50 years, 8% >50 years; 79.6% White, 8.9% Asian, 3.5% Mixed or Multiple, 3.5% Black], 84 HCPs, 78 others). We formed 55 summary questions, of which 51 were unanswered and included in the second prioritisation survey (374 respondents; 3452 unanswered questions selected and ranked). The 27 top-ranked questions will be taken to the final workshop, held using modified Delphi and nominal group techniques. The top 10 research priorities will be determined by people with lived experience of PCOS ($n = 15$) and HCPs ($n = 15$).
Conclusion
This is the first JLA PSP focused on an endocrine disorder. We identified the most important areas for research for PCOS in the UK, as determined jointly by people with lived experience of PCOS and HCPs. Researchers, funders and policymakers should use these findings to shape the research agenda for PCOS, with the aim of improving meaningful outcomes in this common disorder.

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P207

Prokinectin receptor 2 (PROKR2) gene mutation in a man with primary hypogonadism

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Introduction
The prokinectin signalling pathway plays an important role in olfactory development, sexual development and fertility. The prokinectin receptor 2 (*PROKR2)* is associated with gonadotropin releasing hormone deficiency (isolated hypogonadotropic hypogonadism and Kallmann syndrome). Inheritance is autosomal recessive, requiring two copies of the gene mutation, one from each parent, to develop the disease (homozygotes). Disease can occur if the *PROKR2* gene mutation is combined with a mutation in another gene (oligogenic inheritance) or a different mutation in the *PROKR2* gene (digenic inheritance). Undescended testes (cryptorchidism) can also occur with varying frequency depending on the pattern of inheritance. We describe a man with cryptorchidism, primary hypogonadism who tested positive for the *PROKR2* gene mutation.
Case study
A 32-year-old man presented with infertility due to azoospermia secondary to testicular failure (primary hypogonadism). Medical history included bilateral orchidopexy for cryptorchidism in childhood. He was not on any medication. He was born to a consanguineous marriage. He did not smoke or drink alcohol. Physical examination revealed bilateral small testes and gynaecomastia. He had normal body and fascial hair. Initial investigations demonstrated low testosterone levels with raised gonadotropin levels, characteristic of primary hypogonadism. Genetic testing demonstrated a *PROKR2* missense variant of uncertain clinical significance. His mother demonstrated the same gene variant. The patient and his partner were referred to infertility clinic and medical genetics for further counselling and family screening.
Discussion
There are no previous reports of isolated cryptorchidism leading to testicular failure with elevated gonadotropin levels in relation to the *PROKR2* gene mutation. Homozygotes with two copies of the *PROKR2* gene mutation typically present with reduced gonadotropin levels due to gonadotropin releasing hormone deficiency. The man in this case may have another unknown gene mutation combined with the *PROKR2* gene mutation contributing to this atypical presentation

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Kisspeptin best distinguishes polycystic ovary syndrome (PCOS) from functional hypothalamic amenorrhoea (FHA) in lean women with oligo/amenorrhoea without hyperandrogenism

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Background
Polycystic ovary syndrome (PCOS) is the commonest endocrine disorder in women, but accurate diagnosis is challenging. To diagnose PCOS, two of three features are required: 1.Hyperandrogenism, 2.Oligomenorrhoea, 3.Polycystic ovarian morphology on ultrasound (PCOM). The second commonest subtype of PCOS is 'phenotype-D' comprising of oligomenorrhoea and PCOM. Its presentation overlaps with that of functional hypothalamic amenorrhoea (FHA), who also have amenorrhoea, 45-50% have PCOM, and rarely have hyperandrogenism. Herein, we compared detailed reproductive profiles of lean women (BMI <25 kg/m^2) with PCOS phenotype-D (PCOS-D) vs FHA with PCOM (FHA-PCOM).
Methods
Women with FHA-PCOM ($n = 16$) or PCOS-D ($n = 17$), aged 18–35yrs, underwent early-follicular (or random if amenorrhoeic) assessment of LH-pulsatility (10-minutely sampling for 8hrs) and of responses to intravenous boluses of kisspeptin and GnRH. PCOM was defined as $\geq$20follicles-per-ovary, or anti-Müllerian hormone >23pmol/l where ultrasound was unavailable. Data were presented as mean/median and compared by t-test or Mann–Whitney U test as appropriate.
Results
PCOM was present in all women with PCOS-D and in 41% of FHA. The most discriminatory features between PCOS-D and FHA-PCOM were LH-pulse amplitude (1.18 *vs* 0.45 IU/l; $P < 0.0001$), fT3 (4.06 vs 3.26 pmol/l; $P < 0.0001$), follicular-LH (6.47 vs 2.73 IU/l, $P = 0.0003$), inhibin B (89.3 vs 43.0 ng/l, $P = 0.0085$), androstenedione (5.61 vs 3.83 nmol/l, $P = 0.0120$) and oestradiol (115 vs 87 pmol/l, $P = 0.0149$). FSH responses to GnRH were higher in FHA-PCOM than PCOS-D (6.79 vs 2.26 IU/l; $P = 0.003$). Gonadotrophin rises after kisspeptin were higher in FHA-PCOM than PCOS-D: LH (13.63 vs 5.00 IU/l; $P = 0.0405$), and FSH (10.79 vs 1.74 IU/l; $P < 0.0001$). Peak FSH rises after kisspeptin differentiated FHA-PCOM from PCOS-D with an auROC of 0.92; $p<0.0001$.
Conclusion
Kisspeptin challenge test was the most reliable discriminator to distinguish between FHA-PCOM and PCOS-D and can improve the accuracy of diagnosis in challenging cases.

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Case report – severe hyperandrogenaemia in a post-menopausal female

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Hyperandrogenism in postmenopausal females is rare and always mandates investigation. It may be due to an ovarian or adrenal source of androgen production. A 75-year-old post-menopausal woman was referred by her dermatologist for investigation of severe hyperandrogenaemia (testosterone 30.6nmol/l, RI <1.4; LH and FSH undetectable), on background of polycythaemia (previously felt to be idiopathic). She had a 3-year history of androgenic alopecia (resistant to spironolactone and minoxidil) and virilisation (Ferriman Gallwey score 32/36, Ludwig scale 3/3). DHEAS levels, overnight dexamethasone suppression testing, and adrenal imaging were normal. Both ovaries were enlarged, with multiple small follicles and a mildly thickened endometrium on pelvic MRI. Pathology from a subsequent hysterectomy and bilateral salpingo-oophorectomy revealed a steroid cell tumour of the left ovary. Following surgery, the patient lost 5 kg in weight, testosterone level fell (<0.4nmol/l), LH and FSH rose (30, 23 IU/l respectively), polycythaemia resolved (Hgb 14.4g/dl), and her plethora, hirsutism and alopecia improved (Ferriman Gallwey score 17/36, Ludwig scale 2/3). The patient had presented to multiple physicians over years, with conditions potentially related to hyperandrogenaemia, prior to measurement of testosterone concentration. Investigations suggested an ovarian source of androgens, and although imaging did not identify a suspected tumour, the height of elevation of testosterone was most in keeping with a steroid-producing ovarian tumour, so oophorectomy was the best course of action. Her case highlights the need to consider unusual causes of hirsuitism and polycythaemia and the need for prompt investigation and management of post-menopausal hyperandrogenaemia.

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P210

Identification of highly discriminatory serum markers able to identify undisclosed androgen abuse in men who self-report androgen cessation: a prospective, community-dwelling study

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Background
Androgen abuse is associated with a threefold increase in mortality, primarily due to cardiovascular disease, with significant psychiatric and reproductive morbidity. Men are often reluctant to disclose androgen abuse to healthcare professionals, making clinical management highly challenging. World Anti-Doping Agency (WADA)-accredited laboratories use urinary testosterone-to-epitestosterone (T/E) ratio to detect undisclosed androgen abuse, but this is unavailable in the NHS. Identifying reliable, routinely available serum biomarkers of undisclosed androgen abuse could provide a feasible alternative to urinalysis, helping clinicians manage men withdrawing from androgen abuse.
Methods
A prospective, ethics-approved study recruited ninety-three community-dwelling men self-reporting cessation of androgen abuse. Fasting morning serum and urine samples were collected. Urine steroid profiles were analysed by the London-based WADA-accredited laboratory, with T/E ratio determined by tandem gas chromatography-mass spectrometry.
Results
Undisclosed androgen abuse was identified by a raised T/E ratio in 23% (21/93) of men self-reporting androgen abuse cessation. Men with undisclosed androgen abuse had higher serum testosterone (30.1 ± 13.7 vs 14.0 ± 8.0nmol/l; $p < 0.0001$), oestradiol (183 ± 73 vs 103 ± 10pmol/l; $p < 0.0001$), and haemoglobin (168 ± 16 vs 158 ± 13g/l; $p = 0.006$), and lower LH (0.6 ± 1.3 vs $2.6 \pm 1,4$IU/l; $p < 0.0001$), and FSH (0.5 ± 0.8 vs 3.1 ± 1.8IU/l; $p < 0.0001$) compared with men with confirmed androgen cessation. Serum FSH (AUC = 0.93, $P < 0.0001$) was highly discriminatory for undisclosed androgen abuse. FSH levels > 1.0IU/l indicated a 96% probability that concealed androgen abuse was excluded. Serum oestradiol (AUC = 0.91, $P < 0.0001$), LH (AUC = 0.88), and testosterone (AUC = 0.85) showed good discrimination for undisclosed androgen abuse.
Conclusion
In the largest study of its kind, using state-of-the-art toxicological analysis, we report that 23% of men continue undisclosed androgen abuse despite self-reporting cessation. However, our data reveal that routinely available serum markers could identify most of these men. Our data may have potential to help clinicians support men to safely withdraw from androgen abuse.

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The psychological challenges and available resources for patients with Turner Syndrome (TS); are we meeting International Recommendations and our patients' needs?

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Background
Patients with TS are more likely to experience poorer social and emotional well-being and mental health problems. Clinical practice guidelines for Turner Syndrome (2024) recommend psychological screening and evidence-based interventions to improve well-being and mental health. The well-established TS service at Oxford Centre for Diabetes, Endocrinology and Metabolism has no provision for psychological support. Our project aimed to assess psychological needs in the TS cohort.
Method
A questionnaire using validated measures of mental and health well-being was approved by the quality improvement team and offered to patients attending clinic.
Results
The survey was completed by 52 patients with TS. 75% (38/52) reported that TS had negatively affected their mental health; 23% (12/52) had been referred to mental health services, and 15% (8/52) had been diagnosed with a mental health problem. Causes of psychological distress included fertility and low self-esteem. Unmet psychological needs were reported in 15% (8/51); anxiety, low mood and isolation were commonly reported. On a measure of anxiety (Hospital Anxiety and Depression Score) 44% (22/50) reported symptoms in the mild to severe range. On a measure of social functioning, (Work and Social Adjustment Scale Score) 30% (15/51) reported a moderate or severe level of impairment. The Multidimensional Body-Self Relations Questionnaire assessed body image concerns. This showed lower mean scores than reference populations in the areas of appearance evaluation (2.51), appearance orientation (3.28) and body areas satisfaction (2.76). Overall health was assessed with the 5Q-5D visual analogue scale, a score of <80 was present in 48% (24/51) compared to 32% in a UK reference population. Interest in attending a psychology clinic was 25% (13/52), 30% of patients (21/52) were "unsure".
Conclusion
In this cohort of patients with TS, mental health problems were common. This project supports the development of psychological services for patients consistent with international guidelines.

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Circulating leptin levels are higher in lean women with polycystic ovary syndrome than in those with hypothalamic amenorrhoea

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Background
Leptin, secreted from white adipocytes, links metabolic and reproductive function by acting as a signal of energy sufficiency. Leptin concentrations are proportional to BMI as a surrogate for adiposity. Women with polycystic ovary syndrome (PCOS) often exhibit adipose dysfunction, including hypertrophic white adipocytes and reduced brown adipose activity. In contrast, women with hypothalamic amenorrhoea (HA) have reduced adipose tissue mass. Herein, we examine whether leptin concentrations differ between women with PCOS or HA.
Methods
The study included 148 women aged 18–35 years: 46 healthy controls, 36 with HA, and 66 with PCOS. The PCOS group was stratified by BMI into lean (BMI < 25 kg/m^2; $n = 35$), overweight (BMI 25–29.9 kg/m^2; $n = 14$), and obese (BMI ≥30 kg/m^2; $n = 24$). Leptin concentrations were measured using a two-site DELPHIA immunoassay. Median (IQR) leptin levels are reported throughout. Group differences in serum leptin concentrations were assessed using the Kruskal-Wallis test, and associations with BMI and insulin were assessed using linear regression.
Results
Across the cohort, leptin concentrations increased with BMI ($r = +2.99$, $r^2 = 0.77$; $P < 0.0001$). Compared to healthy controls [12.3 (5.63, 18.55)], leptin was significantly lower in HA [4.7 (2.80–8.50); $P = 0.017$] but higher in PCOS [24.1 (10.88–47.7); $P = 0.003$]. In women with PCOS, leptin increased across BMI subgroups ($P = 0.0004$). In lean women, (BMI <25 kg/m^2), leptin levels discriminated lean PCOS from HA [lean PCOS: 11.7 (6.45–64.30), HA: 4.7 (2.80–8.50)] with an AUC of 0.79 ($P < 0.0001$). Across the full cohort, leptin predicted insulin concentrations ($r = +3.62$, $r^2 = 0.34$; $P < 0.001$).
Conclusion
Leptin concentrations reflect adiposity but were disproportionately higher in PCOS than HA despite similar anthropometry, suggesting either relatively increased adipose mass or hypersecretion of leptin due to additional stimuli such as insulin, androgens, and inflammatory factors. Taken together, leptin shows discriminatory potential in lean women to distinguish PCOS from HA.

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Investigating the effect of anabolic-androgenic steroids on the female reproductive system: a cross- sectional study

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Background
The global prevalence of anabolic-androgenic steroid (AAS) use among women has been estimated at 1.6% and is rising. AAS use is associated with adverse effects on multiple body systems including the cardiovascular and psychiatric system. Female specific adverse effects include menstrual irregularity, hirsutism, voice deepening, androgenic alopecia and clitoromegaly. In men AAS use results in suppression of the hypothalamic-pituitary-gonadal axis which can take months to years to recover. However, the impact of AAS on the female reproductive system is under researched. Here we report preliminary data from our ongoing study aiming to address this research gap.
Methods
Ethics-approved cross-sectional study of 30 women: no AAS use (Control; $n = 13$); current AAS use (Current; $n = 6$); past AAS use (Past; $n = 11$). Blood samples taken included reproductive hormone levels, haematological, hepatic, and lipid profiles. Urine samples for toxicology testing has been saved. Details about AAS use and menstrual cycles were collected using a standardised questionnaire. Women completed validated questionnaires to assess wellbeing, mental health, and sexual function.
Results
Current AAS users were significantly more likely to experience menstrual irregularity (2/13, 15.4%, Control; 5/6, 83.3%, Current; 2/9, 22.2%, Past; $P < 0.01$). Current users had lower serum FSH compared with past users (median FSH: 2.2IU/l [IQR 0.2-5.6], Current; 7.4IU/l [6.0-9.9], Past; $P = 0.03$) and lower SHBG compared with controls (median SHBG: 77mmol/l [47–90], Controls; 17mmol/l [8.1–29], Current; $P < 0.01$). Current users also had significantly higher serum testosterone levels (median total testosterone: 1.0nmol/l [0.78–1.3], Control; 18.0nmol/l [3.9–65.0], Current; 0.9nmol/l [0.67–1.3], Past; $P < 0.01$).
Conclusions
This study demonstrates that menstrual irregularity, and FSH suppression is observed during AAS use in women and, for the majority, this normalises with cessation of use. Our preliminary data highlights the possible short, and long-term adverse reproductive effects of AAS use in women.

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Immunotherapy induced fluctuations in sex hormone levels or a perimenopausal phenomenon?

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Introduction
Immune checkpoint inhibitors have become well-established in the treatment of various cancers. Immune-related adverse effects (irAEs) are well recognised, particularly of the endocrine system. There is limited information on how they may impact sex hormones. A small study demonstrated increased oestradiol levels in men, but there have been no reported cases in women. Timing of onset of irAEs is highly variable and can occur up to 27 months after their use. Our case raises the question of whether the observed changes in estradiol levels are simply due to normal perimenopausal fluctuations or a delayed effect induced by immunotherapy.
Clinical case
A 43-year-old woman was diagnosed with breast cancer in May 2023. Her obstetric history was G1P0+1, which ended in abortion. From the age of 18, she was on the Evra contraceptive patch, which was discontinued following her cancer diagnosis. She described brief interruptions in contraception use, which was usually accompanied by resumption of menstruation. Her cancer treatment, including Pembrolizumab was discontinued in November 2023 due to severe colitis and development of primary hypothyroidism. In June 2025, she suddenly had a menstrual period. Her bloods showed an FSH 43IU/l, LH 86IU/l and oestradiol 927pmol/l. Both pituitary MRI and adrenal CT were normal. Transvaginal ultrasound showed two right-sided ovarian cysts measuring 13 and 26mm. CA-125 was negative. After two menstrual periods, she did not experience further bleeding and repeat biochemistry showed raised gonadotropins with an undetectable oestradiol level.
Discussion
The onset of menstrual periods occurred 19 months after Pembrolizumab was discontinued. We question whether the two delayed menstrual periods occurred as a form of irAE transient ovarian hyperstimulation or impending primary ovarian failure either masked by contraception or induced by immunotherapy. This case highlights the importance of careful biochemical monitoring when on immunotherapy and need of further studies.

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Mapping the biomechanical landscape of the ageing murine ovary using atomic force microscopy

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Background
Ovarian ageing involves progressive extracellular matrix remodelling, resulting in increased stiffness, fibrosis and disrupted ovarian function. Biomechanical studies using nano-indentation and atomic force microscopy (AFM) have demonstrated stiffness changes between young and aged ovaries; however, the evolution of these mechanical properties across reproductive transitions remains unknown. Understanding these shifts is crucial to delineate how the ovarian microenvironment adapts to hormonal and structural changes throughout life.
Aim
To investigate changes in ovarian stiffness across reproductive transitions using AFM and to elucidate the contributions of distinct ovarian structures to these biomechanical properties.
Methods
Mouse ovaries were collected at six distinct ages representing pre-puberty (14, 21 days), reproductive maturity (3, 6 months), and ageing (12, 18 months). AFM-based indentation was used to quantify stiffness as Young's Modulus. Analyses assessed: **(1)** intra-organ stiffness variation, **(2)** reproducibility across biological replicates, and **(3)** differences between age groups. Concurrent optical mapping enabled spatial correlation between stiffness and ovarian substructures. $n = 4$ biological replicates per group.
Results and discussion
Assessment of ovarian stiffness across reproductive transitions indicated that Young's Modulus was highest in pre-pubertal and aged ovaries with median values of 271.1 Pa and 148.0 Pa, respectively. While stiffness increases prior to gonadotrophin exposure and again as oestrous cyclicity is disrupted/arrested, ovaries at reproductive peak displayed the lowest stiffness (median of 90.4 Pa), suggesting a softer microenvironment during this stage. Within individual ovaries, spatial heterogeneity in stiffness was observed at all ageing timepoints. Importantly, this variation could not be explained solely by cortex–medulla differences, indicating that heterogeneity may be driven by variations in follicle subtype and the surrounding stromal microenvironment. Together, these results reveal dynamic changes in ovarian stiffness across reproductive transitions and underscore the importance of future studies to map the structural, mechanical, and extracellular matrix determinants underlying these alterations.

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Bilateral Leydig cell tumours in a post-menopausal woman presenting with alopecia

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Background
Hyperandrogenism in postmenopausal women is uncommon and warrants thorough evaluation due to the potential for androgen-secreting tumours. Leydig cell tumours are rare ovarian neoplasms that typically present with virilising symptoms and biochemical evidence of hyperandrogenism.
Case Presentation
We report the case of an 80-year-old Caucasian woman referred for evaluation of progressive androgenic alopecia and markedly elevated testosterone levels (16

nmol/l). Investigations showed a high free androgen index and low-normal sex hormone-binding globulin, without signs of virilisation beyond alopecia. Gonadotrophins were low for postmenopausal levels, and oestradiol was elevated. Computed tomography revealed a bulky right ovary and a left adrenal adenoma. Although dehydroepiandrosterone sulfate was mildly raised, the degree of testosterone elevation strongly suggested an ovarian source. She underwent bilateral salpingo-oophorectomy. Histology confirmed a 20 mm Leydig cell tumor in the right ovary and Leydig cell hyperplasia in the left. Post-operative follow-up showed normalisation of androgen levels and gonadotrophin recovery.

Discussion

Leydig cell tumours account for less than 0.1% of ovarian neoplasms and predominantly affect postmenopausal women. (1) They are often small and may not be detectable on imaging. This case highlights the diagnostic challenges posed by co-existing adrenal incidentalomas and underscores the importance of considering ovarian androgen-secreting tumours in post menopausal women with isolated hyperandrogenism. Surgical resection remains the mainstay of treatment, with excellent prognosis.

Conclusion

This case emphasises the need for a high index of suspicion for ovarian Leydig cell tumors in postmenopausal women presenting with severe hyperandrogenism, even in the absence of obvious virilisation or definitive imaging findings.

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A successful case of obesity pharmacotherapy reversing male infertility recovery

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Introduction

Obesity-related functional hypogonadotropic hypogonadism is increasingly recognized as a significant contributor to male subfertility, manifesting impairment in semen parameters and hormonal disruptions. Treatment options remain limited, underscoring an unmet clinical need. We present a case demonstrating significant fertility improvement with targeted obesity pharmacotherapy.

Case

A 42-year-old man presented with a 3-year history of infertility, obesity (BMI 40.6; 123 kg), T2DM, and erectile dysfunction (ED). Evaluation showed hypogonadotropic hypogonadism (FSH 6.9, LH 4.9 IU/l), low testosterone (3.2), low SHBG (19), and normal remaining pituitary function. Semen analysis confirmed azoospermia. He lost 6.3 kg on Semaglutide (Ozempic) over 3 months and further 10 kg on Tirzepatide (Mounjaro), reducing BMI from 40.6 to 32.1 in 8 months. ED symptoms and semen parameters improved.

Parameter	Baseline	Post-weight loss	Normal range
BMI	40.6	32.1	18.5-24.9 kg/m2
Testosterone	3.2	7.4	11.5-54.5 nmol/l
LH	4.9	2	1.5-9.3 iu/l
FSH	6.9	4.9	1.4-18.1 iu/l
SHBG	19	22	11.5-54.5 nmol/l
Inhibin B		111.5	25-325 pg/ml
Semen analysis			
pH	8	8.1	7.2-8.0
Volume	1.5	5.3	1.4 ml
Concentration	0	31	16million/ml
Morphology	0	2%	4%
Motility	0	39%	> 30%
Total sperm number	0	164.3	> 40million

His partner achieved natural conception 8 months after obesity pharmacotherapy, resulting in a healthy baby girl.

Discussion

Reduced fat mass lowers aromatase activity, decreasing androgen-to-oestrogen peripheral conversion and improving the testosterone–oestrogen ratio essential for spermatogenesis. Direct stimulation of testicular receptors by GIP and GLP-1 enhances Leydig cell function, promoting testosterone synthesis and spermatogenesis. We are currently recruiting for a male fertility sub-study investigating the impact of Tirzepatide-induced weight loss on male reproductive health.

Learning points

1. Fat mass reduction & potential direct stimulation of GLP1 & GIP receptors can improve male fertility outcomes in obesity induced hypogonadism.
2. GLP-1 or dual GLP-1/GIP agonists may offer therapeutic option for male infertility.

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Thyroid

P218

Just in case calcium: a novel strategy to reduce emergency department presentation due to hypocalcaemia following thyroidectomy and parathyroidectomy

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Background

Post-operative hypocalcaemia is a frequent complication following thyroid and parathyroid surgery. At Royal United Hospital, Bath, a "just in case" (JIC) calcium protocol was introduced. This provides patients with oral calcium supplements and information on hypocalcaemia symptoms upon discharge. This study evaluates the effectiveness of JIC calcium in reducing emergency department (ED) presentations and hospital admissions due to hypocalcaemia.

Method

A retrospective analysis was conducted on patients who underwent parathyroid ($n = 51$) and thyroid ($n = 81$) surgery between 2022 and 2024. Data were collected from electronic health records, focusing on pre- and post-operative calcium, PTH, and vitamin D levels, JIC calcium prescription, and hypocalcaemia related hospital attendances. The primary outcome was the rate of ED presentations before and after implementation of JIC calcium.

Results

The cost of JIC is £4.97. The average cost of an ED admission is £137 to £445 depending on investigations. Following the introduction of JIC, the number of admissions following parathyroid surgery was reduced by 50%. There was an 83% decrease in admissions for post thyroid surgery patients with the introduction for JIC. Most symptomatic patients had not received pre-operative calcium or vitamin D screening and many had bilateral procedures or vitamin D deficiency.

Conclusion

JIC calcium appears to be an effective, low-cost intervention for reducing hypocalcaemia related ED attendances. Its targeted use in high-risk patients, combined with improved perioperative screening, could further enhance post-surgical outcomes.

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Audit of thyroid U-classification and subsequent fine needle aspiration cytology

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Background

Thyroid nodules are identified in up to 50% of the population, though malignancy risk is 4–7%. The 2014 British Thyroid Association (BTA) guidelines recommend ultrasound U-scoring of nodules to guide fine needle aspiration cytology (FNAC): U1–U2 should not undergo FNAC, whereas U3–U5 should.

Aim

To assess compliance with BTA 2014 guidelines in the reporting and management of thyroid nodules at George Eliot Hospital NHS Trust.

Methods

A retrospective review of 136 thyroid/neck ultrasounds performed over three years was undertaken (2021-2024). Reports were assessed for inclusion of a U-score (or equivalent classification), and cytology outcomes were reviewed to determine whether FNAC was performed appropriately.

Results

The mean patient age was 60.4 years (111 female, 25 male). Thirty-eight had a single nodule and 98 multiple (range 6–60 mm). **U-classification** was recorded in 115 cases (83%): U2 = 48, U3 = 66, TiRADS = 1; and **it was NOT documented in 21 cases (17%)**. **FNAC** was booked or performed in 58 cases: Thy1 = 23, Thy2 = 16, Thy3+ = 12; 6 were non-diagnostic, pending, or not completed. Deviations included: 3 U2 nodules referred for FNAC, and **17 U3+ nodules where FNAC was not performed or patient lost to follow up.**

Conclusion

The audit identified incomplete U-score documentation and deviations in FNAC practice. Interventions introduced include increasing awareness in staff by

departmental and trust based teaching, dissemination of results to relevant department and laminated BTA U-scoring guidance in ultrasound rooms. Re-audit has been planned to evaluate improvement.

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Coexistence of Resistance to Thyroid Hormone and Graves' Disease

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Resistance to thyroid hormone (RTH) is a rare cause of abnormal thyroid biochemistry. Coexistence with autoimmune thyroid disorders such as Graves' disease is exceedingly uncommon. We present a 44-year-old woman with a longstanding history of palpitations, anxiety, increased bowel frequency, and heat intolerance without weight loss, despite a good appetite. History includes rheumatoid arthritis, and family history was notable for autoimmune thyroid disease and type 1 diabetes. Initial evaluation revealed low TSH (0.03 mU/l) and markedly elevated FT4 (75 pmol/l), leading to a presumptive diagnosis of Graves' disease. She was treated with carbimazole but has lost follow-up. Upon re-presentation in 2018, with persistent symptoms, laboratory tests revealed unsuppressed TSH (1.2 mU/l), elevated FT4 (35.4 pmol/l), positive TSH receptor antibodies (1.6 IU/l) and thyroid peroxidase antibodies. Thyroid ultrasound showed diffuse heterogeneity and increased vascularity. Given the paradoxically normal TSH in the context of high FT4, TSH-secreting pituitary adenoma and RTH were considered. Over the years, thyroid function tests continued to demonstrate elevated free thyroid hormones (FT4 38.5) with inappropriately normal TSH levels (TSH 0.89). Part of the workup included Alpha-subunit 0.2 IU/l(Normal 0-1), SHBH 85 nmol/l(Normal 32-128), and Genetic testing ultimately confirmed a heterozygous pathogenic variant in the THRB gene (c.1357C > A; p. Pro453Thr), consistent with RTH. Management included symptomatic control with propranolol. However, subsequent symptoms exacerbation with suppressed TSH levels (< 0.01) and rising FT4(53.6), suggesting relapse of Graves' disease. Antithyroid therapy was reintroduced, aiming to normalise TSH rather than free thyroid hormone to avoid overtreatment and hypothyroidism. This case highlights the diagnostic and therapeutic challenges posed by the rare coexistence of RTH and Graves' disease. It emphasises the need for individualised treatment strategies focused on TSH targets rather than the normalisation of free hormone levels in such complex endocrine disorders.

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P221

The Hyperthyroid Puzzle: Coexisting Graves' Disease and a Toxic Thyroid Adenoma

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Background
Marine-Lenhart Syndrome represents a rare endocrine disorder occurring in 0.8-4.1% of Graves' disease cases, characterized by the coexistence of Graves' disease and autonomously functioning thyroid nodules. Marine and Lenhart in 1911, this syndrome presents unique therapeutic challenges compared to isolated Graves' disease. This syndrome remains frequently underdiagnosed, and warrants increased clinical recognition given its distinct therapeutic implications.
Case Presentation
We report a case of a 44-year-old female presenting with thyroid goitre, diarrhoea, and unintentional weight loss. Laboratory evaluation revealed severe hyperthyroidism with suppressed thyroid-stimulating hormone (< 0.01 μIU/mL), elevated free thyroxine (2.58 ng/dL), elevated free triiodothyronine (8.7 pg/mL), and elevated thyroid-stimulating immunoglobulins (0.72 IU/l). Thyroid ultrasonography demonstrated hypoechoic nodules in the right lobe, showing TR4 features, that measures 10 × 9 × 8 mm (width × height × length). Radioiodine uptake scan revealed asymmetrical in site with the right thyroid gland is functionally larger on the left lobe. There is increased uptake in the expanded interpolar region of the right lobe. There is significantly less uptake in the rest of the thyroid gland. The thyroid uptake at 20 minutes post administration is calculated 57% uptake in the right lobe with contralateral suppression, appearances are in keeping with toxic nodule in the right interpolar region. The combination of elevated thyroid-stimulating immunoglobulins and a hyperfunctioning nodule established the diagnosis of Marine-Lenhart Syndrome. Initial management with carbimazole achieved biochemical remission of the Graves' component.
Conclusion
This case highlights the importance of comprehensive evaluation in hyperthyroid patients, including thyroid-stimulating immunoglobulin assessment and functional imaging, to identify Marine-Lenhart Syndrome and guide appropriate therapeutic decision-making.

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P222

Unmasking pembrolizumab-induced hypothyroidism in a complex multimorbid renal tumour patient: a case report

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Background
Immune checkpoint inhibitors (ICIs), such as pembrolizumab, are increasingly used to treat advanced malignancies, including renal cell carcinoma. Thyroid dysfunction is a well-recognised immune-related adverse event (irAE) of ICIs, commonly presenting as transient thyrotoxicosis followed by hypothyroidism.[1] This case report highlights overt hypothyroidism developing in a patient with previously normal thyroid function following pembrolizumab therapy.
Case Presentation
A 70-year-old man with multiple comorbidities—ischemic heart disease, heart failure with reduced ejection fraction, chronic obstructive pulmonary disease, hypertension, atrial fibrillation, psoriasis, and a history of prostate cancer treated via robotic prostatectomy—was admitted with chest sepsis requiring inotropic support. Incidentally, CT imaging revealed two renal masses with heterogeneous enhancement, regional lymphadenopathy, and a suspected tumour thrombus extending into the renal vein and inferior vena cava. He underwent robotic right nephrectomy with excision of the tumour thrombus. Postoperatively, pembrolizumab therapy was initiated. Baseline thyroid function tests were normal (TSH 0.45mIU/l). Within weeks, he developed overt hypothyroidism, evidenced by a markedly elevated TSH of 49.60 mIU/l and a low free T4 (< 3.2 pmol/l). Levothyroxine treatment was started, and the patient is under close follow-up with regular thyroid function tests and outpatient thyroid ultrasound.
Conclusion
Pembrolizumab-induced thyroid dysfunction is a frequent irAE, with hypothyroidism occurring in up to 10% of patients.[2] The pathophysiology may involve destructive thyroiditis or autoimmune mechanisms, even in patients without prior thyroid disease.This case underscores the importance of routine thyroid function monitoring during ICI therapy. Early recognition and management of endocrine irAEs are essential to safely continue immunotherapy and optimise patient outcomes.[3]
References
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P223

Graves' disease: prospective 10 year outcomes for 100 consecutive individuals at a single centre

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Introduction
The prevalence of Graves' disease is approximately 1%. We undertook an evaluation of outcomes for 100 people diagnosed with Graves' disease over a 10-year period.
Methods
All individuals were seen in the endocrinology outpatient clinic as consecutive presentations at a single UK centre. Individuals were first seen between 2012 and 2014. Individuals were first seen between 2012 and 2014.
Results
Of the 100 consecutive patients, 15 were male and 85 were female. The median age at diagnosis was 39.5 years(Interquartile Range(IQR):31-52) with median 43 years (IQR:31-61) for males and 39 years (IQR:31-51) for females. Eighty-seven

individuals received carbimazole in the first year. 8 people were started on propylthiouracil, 3 did not receive any medical treatment while 2 received both propylthiouracil and carbimazole. Distribution of FT4 at baseline was skewed: median FT4 29.3pmol/l falling to 10-year median 16.2 pmol/l (Gaussian distribution). TSH was suppressed at baseline. TSH levels increased up to 5-year(1.10 mU/l); 10-year follow-up(1.15 mU/l). Over time, 25% continued to exhibit low/-suppressed TSH levels, while 9% had elevated TSH levels. Overall, 37% individuals relapsed, 24% post-radioactive-iodine. For those who relapsed the median age at diagnosis was 34years (IQR:30-53) vs no relapse at 42years (IQR:32-52). At last/10-year follow-up 39% were euthyroid and not on therapy 22% remained on pharmacotherapy alone, 12% had undergone thyroid surgery, radioactive iodine alone 13% with combination treatment for 7%. 7% had died. Thyroid eye disease affected 26.7%males and 24.7%females. Baseline TRAb showed positive correlation with baseline FT4(Spearman's rho=0.284, P = 0.004), with no significant association between baseline TRAb and relapse likelihood

Conclusion

Only about one third of patients remained in remission off anti-thyroid treatment, with a further one third requiring definitive treatment with thyroidectomy or radioactive iodine, demonstrating the potential for immunomodulatory therapy deployment in the future.

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P224

The change in thyroid hormone profile pre- and post- initiation of levothyroxine: an evaluation of longitudinal thyroid hormone profile over time

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Introduction

There continues to be much discussion around optimization of thyroid hormone status in hypothyroid individuals. Over 10 million thyroid function tests (TFTs) are carried out in England each year, most requests coming from primary care. This study aimed to investigate how thyroid hormone levels change in the years pre- and post-initiation of levothyroxine (LT4).

Methods

Using citywide population health records, we analysed TSH/FT4 results during the period 2012-2023(12 years) for patients diagnosed with primary hypothyroidism and whose medication started within the period 2015-2019(5 years). Only patients with more than total of 5-TFTs during the test period were included. Reference ranges relevant to diagnosis were thyroid stimulating hormone(TSH) maximum 4.2miU/l / free thyroxine(FT4) minimum 12.0pmol/l.

Results

In the years prior to medication starting, TSH increased progressively more rapidly. Once on medication TSH fell to levels at or below TSH level even several years before diagnosis (3.1mu/l vs historical 3.5mu/l). Average daily levothyroxine dose continued to increase over the years post-initiation from 49 mg to 69 mg/day at 7-years with a corresponding rise in median FT4 from 13.0 to 16.1pmol/l. Median FT4 was higher than historical values from the end of year11 of treatment. 60% of women by age 50 years had started replacement treatment vs 50% of men, in keeping with younger age of onset. Levels of TSH were higher in individuals aged 60-years or more before LT4 initiation and remained so afterwards.

Conclusion

This population-based study reflects varying responses in different patients, but with overall further evidence for the increasingly unphysiological' TFT profile in treated hypothyroid individuals, in the years post-levothyroxine initiation. Both levothyroxine dose and measured FT4 continuing to increase significantly in the years after levothyroxine started, suggesting that dose adjustments may in some cases be driven by patients' perceived lack of benefit rather than biochemical profile.

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P225

Spontaneous normalisation of thyroid hormones in Graves' hyperthyroidism

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Background

Monitoring thyroid hormones is essential in the management of Graves' hyperthyroidism, but the magnitude of meaningful change of thyroid hormones over a few weeks without treatment remains uncertain. Furthermore, the proportion of patients with hyperthyroidism who normalise thyroid hormones spontaneously without treatment is unknown, potentially leading to unnecessary therapy in some individuals.

Methods

We reviewed FT4 measurements in patients with Graves' hyperthyroidism who had two blood tests performed weeks apart, prior to antithyroid drug therapy. Analytical and biological variation of FT4 was considered to estimate the reference change value (RCV). Changes were classified as significant if FT4 normalised or if the percentage change exceeded the combined expected variability (>20%). Long-term clinical data was analysed to evaluate the significance of these short-term changes. Regression analyses were performed to assess the magnitude of change and its predictors.

Results

Among 233 patients with high baseline FT4 tests, 32 (13.7%) showed spontaneous normalisation of FT4 levels on repeat testing after a median (IQR) of 33 (54-21) days. During longer term follow-up, 18 (56%) of these 32 patients remained euthyroid without treatment, whereas 14 (44%) ultimately required therapy. Baseline FT4 concentration was the only independent predictor of spontaneous normalisation, with lower initial levels associated with a higher likelihood of normalisation (odds ratio 0.86; 95% CI 0.78 – 0.93).

Conclusion

Spontaneous normalisation of FT4 occurs in approximately 1 in 7 patients with Graves' hyperthyroidism, particularly among those with mildly elevated baseline levels. These findings support a cautious approach to immediate initiation of antithyroid therapy in selected patients, emphasising the importance of close biochemical monitoring to identify those who may deteriorate over time. Recognising the potential for spontaneous resolution can help avoid unnecessary treatment and optimise patient management.

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P226

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) in endocrine crisis

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Background

Autoimmune Polyglandular Syndrome Type 3A (APS-3A) comprises autoimmune thyroid disease with type 1 diabetes mellitus (T1DM) in the absence of adrenal involvement. Concurrent metabolic crises are rare and diagnostically challenging.

Case

A 29-year-old woman with no medical comorbidities was admitted following resuscitation from out-of-hospital cardiac arrest with hyperpyrexia, encephalopathy, sinus tachycardia, metabolic acidosis, and ketonaemia (4.0 mmol/l). Investigations showed glucose 20 mmol/l, HbA1c 95 mmol/mol, TSH < 0.01 mIU/l, FT4 37 pmol/l, FT3 16.6 pmol/l, and TRAb 73 U/l (<3.3), consistent with concurrent diabetic ketoacidosis and Graves' thyrotoxicosis. Thyroid storm was the clinical diagnosis and the Burch-Wartofsky score 90, consistent with thyroid storm (clinical diagnosis). Echocardiography revealed severe biventricular failure (LVEF ≈ 30 %). Despite circulatory support, she developed refractory cardiogenic shock requiring veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Treatment included propylthiouracil 250 mg TDS, Lugol's iodine 5 drops TDS, and hydrocortisone 100 mg QDS, alongside insulin infusion and supportive care. Over nine days, thyroid hormones normalised; ECMO was weaned with recovery of LVEF to 50–55 %. Islet autoantibodies (GAD, IA-2, ZnT8 > 2000 U/mL) confirmed autoimmune T1DM, establishing the diagnosis of APS-3A. Therapy was transitioned to carbimazole 15 mg BD with a block-and-replace regimen once biochemically hypothyroid. The patient continues to recover and was discharged for rehabilitation.

Discussion

This case illustrates the rare coexistence of thyroid storm and DKA as simultaneous features of APS-3A, culminating in thyrotoxic cardiomyopathy necessitating temporary mechanical support. The clinical severity may exceed biochemical derangement; aggressive and early support is required in thyroid storm and early ECMO as a bridge to recovery can be lifesaving.

Conclusion

Severe presentations of endocrine emergencies can include simultaneous thyroid storm and DKA (each due to autoimmune disease APS-type 3A). In severe

cardiorespiratory failure ECMO can be successfully employed to allow endocrine management leading to recovery.

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P227

Immune checkpoint inhibitor-induced thyroiditis in a patient on amiodarone

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Introduction
Immune checkpoint inhibitors (ICPis) are increasingly used in the management of advanced malignancies but may cause immune-related endocrine adverse events, including thyroiditis. Differentiating ICPi-induced thyroiditis from other causes of thyrotoxicosis, such as amiodarone-induced thyroiditis or Graves' disease, can be diagnostically challenging.
Case Presentation
We report a 73-year-old male with stage IV melanoma on ipilimumab and nivolumab who developed thyrotoxicosis one month after initiating ICPi therapy. He presented with malaise, fatigue, confusion, and poor oral intake. Laboratory findings revealed suppressed TSH (<0.02 mU/l) and markedly elevated free T4 (>150 pmol/l). Thyroid antibodies were negative, and examination showed a diffusely enlarged, non-tender thyroid gland. The patient was also on long-term amiodarone, raising the possibility of amiodarone-induced thyroiditis. He was managed with corticosteroids, propranolol, carbimazole, intravenous fluids, and antibiotics. His thyroid function gradually improved, and carbimazole was discontinued. At follow-up, thyroid function normalized, and clinical symptoms resolved. In this case, diagnostic complexity arose due to concomitant amiodarone therapy, which itself can precipitate thyrotoxicosis through destructive thyroiditis or excess iodine exposure. Key features supporting ICPi-induced thyroiditis in this patient included: temporal relationship with initiation of ICPi therapy, rapid onset and progression of symptoms, negative thyroid autoantibodies, absence of classical amiodarone-related biochemical or clinical features, improvement with steroids and supportive treatment
Conclusion
This case highlights ICPi-induced thyroiditis as an important differential in oncology patients presenting with thyrotoxicosis. Despite concurrent amiodarone therapy, the timing of onset, clinical course, negative antibody profile, and response to treatment supported ICPi-induced thyroiditis as the final diagnosis. Clinicians should maintain a high index of suspicion to enable prompt recognition and management of endocrine complications in patients receiving immunotherapy

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P228

Retrospective audit on the management of amiodarone-induced thyroid dysfunction

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Objective
To complete a retrospective clinical audit on the management of amiodarone-induced thyroid dysfunction in one centre using the existing *European Thyroid Association 2018* guidelines, and to create a flowchart for clinical practice.
Methods
Patients were identified from thyroid clinic lists at University Hospital of Wales, Cardiff. 30 patients with amiodarone-induced thyroid dysfunction seen between 1st January 2023 and 1st May 2025 were identified. Clinical records were reviewed to study amiodarone use, investigations, diagnosis, and management plans. In addition, information was collected on treatment medications, length of treatment and whether emergency or definitive treatment was completed.
Results
Of the 30 patients, 22 were male and 8 were female. 18 were symptomatic on presentation, while 12 were found on thyroid monitoring. 26 (86.7%) patients were diagnosed with Amiodarone-Induced Thyrotoxicosis (AIT), compared to 4 (13.3%) with Amiodarone-Induced Hypothyroidism (AIH). 11 (42.3%) patients were confirmed to have AIT type 2, using colour-flow doppler sonography of the thyroid. Amiodarone was stopped in 22 (73.3%) of patients. All patients were discussed with cardiology. In general, 16 (61.5%) patients with AIT were treated with carbimazole, followed by 4 (15.4%) treated with carbimazole and steroids. Specifically, 8 patients (72.7%) with AIT type 2 were treated with carbimazole. AIH was managed with levothyroxine in 3 (75.0%) patients. No patients had emergency or definitive treatment.
Conclusions
Diagnosis of AIT into type 1, 2 or mixed was not consistently made prior to initiation of medical treatment. No patients were treated with glucocorticoids only, despite 11 being diagnosed with type 2 AIT. Generally, the department may need to proactively consider the need for emergency treatment in high-risk groups, such as the elderly or patients with reduced left ventricular function.

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P229

From hypothyroidism to thyrotoxicosis: a case of Thyroid peroxidase-related dyshormonogenesis complicated by autoimmune Graves' disease"

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Thyroid dyshormonogenesis (TDH) is an uncommon cause of congenital or persistent goitre, due to defects in thyroid hormone biosynthesis. Mutations in the thyroid peroxidase (TPO) gene are most frequently identified, and may predispose to goitrous enlargement with paradoxical thyroid function tests (TFTs). Coexistence of TDH with autoimmune thyroid disease, especially Graves' disease may lead to complex biochemical and clinical presentations. A 57-year-old man with a 'multinodular goitre' diagnosed in 1994 underwent right hemithyroidectomy in 2013 for compressive symptoms, maintaining euthyroidism on levothyroxine. In 2020, he developed palpitations and was found to be thyrotoxic (FT4 62 pmol/l, suppressed TSH), despite dose reduction and cessation of levothyroxine. TFTs showed disproportionately elevated FT3 compared to FT4 and he was referred to the endocrine team. The remnant left thyroid lobe was soft and 'boggy' to touch, unlike a typical nodular goitre. Thyroid ultrasound revealed thyroiditis, and blood tests showed elevated TPO antibodies (687 IU/mL) and TRAb (73 IU/l), consistent with autoimmune thyroid disease. He was started on block and replace regimen to optimise thyroid function. The combination of an unusual goitre with atypical thyroid function suggested dyshormonogenesis. In 2024, extended genetic testing with R145 panel confirmed compound heterozygosity for a pathogenic nonsense variant in the TPO gene, diagnostic of TDH type 2A. This explained impaired FT4 synthesis with compensatory FT3 excess, complicated by coexistent autoimmune thyrotoxicosis.He is managed with carbimazole 40 mg and levothyroxine 100 μg daily, with consideration for completion thyroidectomy due to residual goitre and malignancy risk. This case underscores the importance of considering dual pathology in paradoxical or refractory TFTs. TPO-related dyshormonogenesis may coexist with autoimmune thyroid disease, resulting in labile biochemistry and therapeutic challenges. Genetic testing clarifies diagnosis, guides management, and informs long-term surveillance.
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P230

Acute neurological presentation of Graves' hyperthyroidism

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Introduction
We report a case of a young man who presented with severe cerebellar dysfunction, widespread choreiform movements and thyrotoxicosis. A rare diagnosis of Encephalopathy Associated with Autoimmune Thyroid disease (EAATD) linked to Graves' disease was made, a condition usually described in association with Hashimoto's thyroiditis
Case
A 26-year-old male presented with acute severe ataxia and dysarthria. Examination revealed widespread signs of cerebellar dysfunction, hyperreflexia, choreiform movements and bilateral saccadic pursuit. Cognition was intact and there were no bulbar or meningeal signs. T3 10.4pmol/l, T4 38.3pmol/l TSH $<$ 0.008mU/l, TSH-receptor antibodies (TRAB) 35.14IU/l and anti-TPO antibodies 790.6kIU/l. MRI brain, EEG, CSF, autoimmune screen and ACE were normal

excluding other relevant differential diagnoses. In view of the temporal association with hyperthyroidism, a diagnosis of EAATD was made, jointly with neurologists. He was treated with 40 mg carbimazole and IV methylprednisolone (1gmx3) followed by 60 mg prednisolone. Over the next 4 weeks, he demonstrated rapid recovery with no neurological sequelae and TRAB down to 17IU/l. Prednisolone was tapered off over 8 weeks and he remains on carbimazole.

Discussion

EAATD is rare, and described in association with Hashimoto's thyroiditis, whereas reports in association with Graves' are even rarer. Diagnosis is made by excluding relevant systemic conditions, and rapid response to steroids along with improvement of thyroid biochemistry. Although several possible mechanisms are described the exact pathogenesis remains unclear. Uncommon features demonstrated by our case were male gender and predominant cerebellar involvement with absence of seizures, abnormalities of cognition and normal CSF, all indicating focal neurological involvement. We also demonstrated post-therapy decline in TRAB in parallel with clinical improvement, not described previously.

Conclusion

EAATD with acute cerebellar syndrome and choreiform movements can be presenting features of Graves' hyperthyroidism and the diagnosis should be considered in patients with this combination especially since early therapy can lead to complete recovery.

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P231

Evaluating the link between thyroid function test (TFT) results and levothyroxine dose in the management of hypothyroidism: can we improve dosing regimes?

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Introduction

Over 10 million thyroid function tests (TFTs) are conducted annually in England, the majority requested from primary care. Previous research found that only 25% of patients treated with Levothyroxine had TSH and FT4 levels within the range encompassing 75% of untreated individuals. This study aimed to further investigate differences in thyroid hormone levels, accounting for diagnostic codes and prescribed doses.

Methods

Using a comprehensive city-wide population dataset, we analysed simultaneous TSH and FT4 results from 47,869 diagnosed hypothyroid patients on Levothyroxine and 393,101 untreated (euthyroid) individuals collected over a 14-year period.

Results

The FT4 distribution in treated individuals closely resembled that of untreated individuals but was consistently shifted toward higher FT4, even at the lowest Levothyroxine dose. This separation increased progressively with dose (F value rising from 1.5 to 4.2). In contrast, TSH distribution differed markedly: while untreated individuals showed a near-normal pattern, those on Levothyroxine displayed a pronounced "hockey stick" distribution, heavily skewed toward low or undetectable TSH, with increasing skewness as dose increased. Among untreated individuals, 90.3% had TSH within the reference range, with only 0.8% exhibiting low FT4. Conversely, just 43.8% of treated patients had TSH within range. Median Levothyroxine doses were higher in men than women across all age groups, peaking at 107 mg/day (men) and 93 mg/day (women) at ages 50–59. With treatment, FT4 rose and TSH fell progressively with age, both effects more pronounced in women. TSH levels in treated and untreated populations aligned only around FT4 = 20 pmol/l—below this, treated individuals had higher TSH, and above it, lower TSH for equivalent FT4.

Conclusion

FT4 and TSH distributions differ substantially between treated and untreated individuals. Only 43.8% of those on Levothyroxine maintained TSH within the reference range, with increasingly unphysiological TSH suppression at higher doses.

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P232

The change in thyroid hormone profile pre- and post- initiation of levothyroxine: an evaluation of longitudinal thyroid hormone profile over time

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Introduction

Optimizing thyroid hormone status in hypothyroid individuals remains a subject of considerable debate. Over 10 million thyroid function tests (TFTs) are performed each year in England, the majority requested in primary care. This study aimed to investigate how thyroid hormone levels evolve in the years preceding and following the initiation of Levothyroxine (LT4) therapy in patients with primary hypothyroidism.

Methods

Using comprehensive city-wide population health records, we analysed TSH and FT4 results from 2012–2023 (12 years) for individuals diagnosed with primary hypothyroidism who commenced LT4 treatment between 2015–2019. Their TFT results were compared across the years before and after LT4 initiation. Only patients with more than five TFTs during the study period were included. Reference ranges relevant to diagnosis were defined as TSH $\leq$4.2 mIU/l and FT4 $\geq$12.0 pmol/l.

Results

In the years prior to starting LT4, TSH increased progressively, indicating declining thyroid function. Following initiation, TSH levels fell rapidly to values equal to or below those observed several years before diagnosis (3.1 vs historical 3.5 mIU/l). The average daily LT4 dose rose steadily from 49 mg at initiation to 69 mg/day after seven years, accompanied by an increase in median FT4 from 13.0 to 16.1 pmol/l. From the end of the first year of treatment, FT4 levels remained consistently higher than pre-treatment values. By age 50, 60% of women and 50% of men had commenced LT4 therapy, reflecting earlier onset in women. Individuals aged $\geq$60 years had higher TSH levels than younger adults, both before and after treatment.

Conclusion

This population-based analysis demonstrates diverse treatment responses and a trend toward increasingly "unphysiological" TFT profiles following LT4 initiation. The continued rise in both FT4 and LT4 dose suggests that ongoing adjustments may often reflect perceived lack of benefit rather than biochemical necessity.

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P233

Toxic thyroid nodule initially misdiagnosed as secondary hypothyroidism

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Introduction

Thyroid disorders are commonly encountered in clinical practice, but their presentations can often be subtle or misleading. Biochemical test results must always be interpreted in conjunction with the patient's clinical picture to avoid misdiagnosis. In particular, differentiating between central hypothyroidism and thyroid hormone abnormalities caused by autonomous thyroid nodules can be challenging.

Case Presentation

We report the case of a 49-year-old lady referred for evaluation of a multinodular goitre. Ultrasound imaging identified benign thyroid nodules, and initial thyroid function tests revealed a slightly suppressed TSH with normal T3 and T4 levels. However, subsequent blood tests showed persistently low TSH and low T4, although T3 was not measured at that time. Based on these findings, she was diagnosed with secondary hypothyroidism and started on Levothyroxine therapy. When the Levothyroxine dose was increased to 100 mg, the patient developed symptoms consistent with thyrotoxicosis. Interestingly, she reported no significant difference in well-being whether on or off treatment and had no prior history of hypothyroid symptoms. Her obstetric history included two uneventful pregnancies. Further endocrine assessment revealed persistently suppressed TSH with elevated or high-normal free T3, and normal free T4

levels. A TRH stimulation test showed a non-responsive TSH, while pituitary MRI and other pituitary hormone levels were normal. Considering the clinical context and biochemical profile, a nuclear medicine thyroid uptake scan was performed, confirming T3 thyrotoxicosis due to a toxic thyroid nodule. Levothyroxine was discontinued to avoid worsening thyrotoxicosis.Following detailed discussion, the patient elected to undergo hemithyroidectomy as definitive treatment for the toxic nodule.

Conclusion

This case highlights the diagnostic challenge in distinguishing central hypothyroidism from TSH suppression caused by autonomous thyroid hormone secretion from a toxic thyroid nodule. Persistent elevation of FT3 combined with suppressed TSH and the absence of pituitary pathology should prompt consideration of toxic nodular disease.

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P234

Thyroid dysfunction is frequently screened for but rarely identified in rapid access cardiology services

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Symptoms of thyroid disease (TD) can overlap with those of cardiac disease. Clinics offering rapid assessment of cardiac symptoms are expanding in Ireland. We sought to determine; (i) the frequency of TFT measurements and (ii) the prevalence of TD in patients presenting to a rapid access cardiology clinic (RACC). A retrospective review was conducted of all patients presenting to the RACC over one week. Seventy-six patients attended, median age 55 years, 53% male. The majority (65%) were GP referrals. Common presenting symptoms were chest pain (50%), palpitations (30%), and dyspnoea (30%). Pre-existing TD, exclusively hypothyroidism, was documented in 4% of patients. TFTs (TSH, FT4, Roche assay) were performed in 95% (72/76). 5% (4/72) were abnormal, as follows; hypothyroidism (n1; TSH 8.68mU/l, FT4 12.6pmol/l), isolated hypothyroxinaemia (n2; TSH 2.52mU/l, FT4 11.6pmol/l; TSH 0.77mU/l, FT4 11.0pmol/l), and isolated hyperthyroxinaemia in 1 (TSH 1.12mU/l, FT4 21.8pmol/l). Reference intervals: TSH 0.27-4.2mU/l, FT4 11.9-21.6. Despite the high rate of TFT testing in this cohort, abnormal results were uncommon. When present, these did not prompt specific follow-up actions. Our findings suggest that routine TFT screening in RACC patients may be unnecessary, and that testing could be reserved for those with known TD or clinical suspicion. Improved communication pathways between endocrinology and cardiology are needed to ensure appropriate follow-up for the small subset of patients who require further endocrine evaluation.

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P235

Self-examination saves lives - the curious case of a theatre nurse

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A 49-year old female scrub nurse was referred to the Thyroid MDT having noted a palpable lump over her neck after opting to examine herself following a thyroidectomy case in theatre. US thyroid revealed several nodules with both lobes of the thyroid, of varying sizes; the largest was in the L lobe, measured 35mm × 27mm and was iso-hyperechoic, with areas of central necrosis, consistent with a U3 classification. She was clinically and biochemically euthyroid. FNA was subsequently performed, with cytology confirming a Thy3F lesion. The case was discussed at MDT and she was offered a hemithyroidectomy, which was later performed and confirmed the diagnosis of follicular carcinoma, staging pT2 N0 R0. Her case was re-discussed at MDT, with a plan agreed for completion right hemithyroidectomy, which showed a 30mm widely invasive follicular carcinoma, staging pT2 N0 R1 (vascular invasion, positive margin). The case was discussed at MDT once more, with a plan agreed for radio-iodine ablation. She remains euthyroid on appropriate thyroid hormone replacement, and will remain under dynamic risk assessment going forwards. Clinical self-examination has proven to be an effective tool in improving early detection of breast and testicular cancers, aided by promotional tools and campaigns which have encouraged uptake of this among the general public. This case highlights the importance of self-examination in other contexts, and extending the application of this in helping improve early detection of head and neck cancers as well.

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Immune checkpoint inhibitor-induced thyroid dysfunction in patients with pre-existing hypothyroidism: a case series

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Background

Immune checkpoint inhibitors (ICIs) significantly improve survival across malignancies but often induce endocrine immune-related adverse events (irAEs). Thyroiditis is the most common endocrine irAE, typically presenting as transient thyrotoxicosis followed by hypothyroidism. However, data in patients with pre-existing hypothyroidism are limited.

Methods

We conducted a retrospective review of six patients with primary hypothyroidism who developed thyroid dysfunction during ICI therapy at a UK tertiary cancer centre. Thyroid function tests (TFTs), levothyroxine (LT4) dosing, symptoms, and outcomes were analysed.

Results

All six patients (aged 42–65) had thyroid dysfunction during ICI therapy (pembrolizumab, nivolumab, ipilimumab, or avelumab).

- Four developed overt thyrotoxicosis (free T4: 25.3–39.7 pmol/l, TSH <0.02 mU/l) ; one had subclinical thyrotoxicosis, and one developed new-onset hypothyroidism (TSH 35.9 mU/l, T4 3.5 pmol/l).
- Symptoms included palpitations ($n = 3$), fatigue ($n = 4$), and atrial fibrillation ($n = 1$).
- LT4 was initially withheld in 2, increased in 2 (up to 150 μg/day), and reduced or adjusted in the remainder. Notably, **4/6 patients required higher LT4 doses post-ICI**, suggesting increased irreversible thyroid damage. Two patients remain stable on LT4; four died due to cancer progression.

Conclusion

ICI-induced thyroiditis can occur in patients with pre-existing hypothyroidism and often follows a **biphasic pattern**, complicating LT4 titration. Higher LT4 needs post-treatment suggest more severe thyroidal destruction than typical autoimmune hypothyroidism. **Close biochemical monitoring and multidisciplinary management** are essential for optimal outcomes.

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Keywords
immune-related adverse events, thyroiditis, hypothyroidism, immunotherapy, levothyroxine

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Carbimazole-induced hepatotoxicity: two cases emphasising early recognition and management

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Introduction

Carbimazole hepatotoxicity occurs in ~0.1–0.2% of patients. A 2024 systematic review of 271 antithyroid-drug–induced liver injury (DILI) cases found carbimazole/methimazole accounted for 55.7%. Among these, 67.4% had a cholestatic pattern, 90.7% achieved complete resolution after drug withdrawal, and mortality was 5.6%.

Case 1

A 63-year-old woman with Graves' disease on carbimazole 40 mg daily presented after two months with pruritus and abnormal liver tests (ALT 218 U/l, ALP 723 U/l, GGT 711 U/l, bilirubin 21 μmol/l). Workup excluded viral, autoimmune, metabolic causes, and imaging showed normal biliary anatomy. After stopping carbimazole, liver function normalized within eight weeks. She underwent total thyroidectomy for definitive therapy.

Case 2
A 71-year-old man with multinodular goitre and intermittent T3 toxicosis began carbimazole 5 mg daily, and routine monitoring revealed elevated ALP, prompting immediate cessation. Rechallenge produced recurrent ALP 221 U/l and GGT 226 U/l (normal ALT, bilirubin), confirming causality. He subsequently received radioiodine therapy.
Discussion
These cases typify carbimazole-induced hepatotoxicity: a primarily cholestatic pattern (67.4%), median onset ~28 days (14–42 days), and an idiosyncratic mechanism—as evidenced by Case 2's reaction to a low dose. Positive rechallenge (though successful in only ~75% of cases) strengthens causality. Both recovered fully, consistent with the 90.7% resolution rate. Early detection, whether by routine monitoring or prompt evaluation of symptoms (e.g. pruritus), is key. Compared to propylthiouracil, carbimazole carries a lower risk of severe outcomes: no reported liver transplants in carbimazole-only cases and lower mortality (5.6% vs ~14.3%). Median recovery is ~58 days post-discontinuation.
Conclusion
Clinicians should maintain vigilance for cholestatic hepatitis within 4–8 weeks of carbimazole initiation. Immediate drug discontinuation and timely transition to definitive therapy (surgery or radioiodine) yield excellent prognosis, with >90% achieving full resolution.

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P238

Cardiac tamponade, abdominal ascites and pleural effusion in newly diagnosed severe hypothyroidism

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Introduction
Pericardial effusion is a well-documented but increasingly uncommon manifestation of hypothyroidism, due to earlier detection through routine thyroid function tests. We present a case of newly diagnosed severe hypothyroidism presenting with cardiac tamponade, abdominal ascites and pleural effusions.
Case Presentation
A woman in her late 30s presented to the Coronary Care Unit with dyspnoea and a large pericardial effusion detected on transthoracic echocardiography. Over the past 6 months, she had developed progressive abdominal bloating, anorexia, constipation and noticeable weight loss. On examination, she was hypothermic (34.8°c, later 32.9°c), with BP 130/106, HR 77/min, RR 15/min, and SpO2 95%. Physical examination revealed abdominal ascites, non-pitting lower limb oedema to the shins, slow motor movements, and an apathetic affect. Laboratory tests revealed severe primary hypothyroidism, with markedly high TSH (>150 mU/l), low FT4 (<0.2 pmol/l) and low T3 (<0.3 pmol/l). Random cortisol levels were within normal range. CT thorax, abdomen and pelvis showed gross circumferential pericardial effusion (maximal depth 54mm) with right ventricular flattening consistent with cardiac tamponade, along with large volume ascites, and bilateral pleural effusions. No solid masses or lesions were identified. Urgent pericardiocentesis yielded sterile, protein-rich fluid (albumin 45 g/l, LDH 246 g/l, glucose 2.6 mmol/l, and total protein 78g/l). The patient was appropriately started on oral levothyroxine therapy, with intramuscular administration considered due to progressing myxedema psychosis and non-compliance.
Discussion
This case highlights an atypical first presentation of hypothyroidism involving multi-serous effusions and paradoxical weight loss. The patient had no previous thyroid function tests so the duration of her hypothyroidism could not be ascertained, however the presence of cardiac tamponade suggests long-standing disease. Progression to cardiac tamponade is rare and requires urgent pericardiocentesis. Pericardial effusions secondary to hypothyroidism that do not cause tamponade typically resolve with thyroid replacement therapy alone.

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P239

A case of thyrotoxicosis and hypercalcemia in a patient with thyroidectomy

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Introduction
I present a case of a young patient that had stable thyroid function tests for years on the same dose of thyroid medications and how losing weight on a GLP-1 agonist led to adverse effects.
Case presentation
A 36 year old female initially presented to her GP with thirst, fatigue, urinary frequency and constipation ongoing for weeks. She has a background of hypothyroidism and hypoparathyroidism secondary to thyroidectomy and radiotherapy (2012 for papillary thyroid cancer); ALL (at age 12 which was cured with sibling allogenic transplant); T2DM in remission and depression. At the time of presentation she was on Liothyronine 5 mg , levothyroxine 1500 mg once weekly, Ozempic 0.25 mg once weekly, Adcal-D3 2 tablets , alfacalcidol 1 mg TDS, Ramipril . blood test by GP showed hypercalcemia, acute kidney injury stage 3 and normocytic anaemia and she was sent to hospital for further management. On arrival to hospital, she was managed with IV fluids, nephrotoxic medications and Adcal-D3 were held and she was referred to endocrine team. Thyroid function test was done because she was tachycardic and it showed hyperthyroidism. The plan from endocrine team was stop liothyronine; recheck thyroid function test in a few days; IV fluids; hold Adcal-D3 until calcium levels normalise. Ultrasound thyroid and whole body CT were unremarkable.
Discussion
The conundrum was patient had been relatively stable on her dose of thyroid medications, calcium and vitamin D replacement so it was puzzling she all of a sudden became thyrotoxic and hypercalcaemic. On careful history taking, we realised she had lost 30 kg in less than 2 years since starting Ozempic for her diabetes. The take home message from this case is with the prevalence of weight loss medications it is important for clinicians to be aware of the need to adjust weight based dosing medications to avoid adverse effects.

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P240

Mind the meal: getting levothyroxine timing right on the wards

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Background
Hypothyroidism is a common endocrine condition, and levothyroxine remains the mainstay of treatment. Despite clear recommendations from the National Institute for Health and Care Excellence (NICE), hospital practice often deviates from best standards. Breakfast timings, polypharmacy, and varying awareness among doctors and nurses can compromise drug absorption and therapeutic efficacy.
Aim
To evaluate adherence to national guidelines on levothyroxine administration in hospitalised patients, identify barriers to compliance, and improve practice through targeted education and visual reinforcement.
Methods
This quality improvement project (QIP) was undertaken at Croydon University Hospital between May and September 2025. A prospective observational audit was conducted across the medical wards. Findings were discussed with clinical teams, followed by face-to-face educational sessions for nursing and prescribing staff. Key messages were displayed on the ward quality boards using eye-catching posters to reinforce correct practice. A re-audit assessed the impact of these interventions.
Results
In the initial audit of 40 patients, only 13% received levothyroxine in accordance with guidelines. Common barriers included simultaneous administration with medications that impair absorption, including proton pump inhibitors (50%), calcium supplements (20%), iron (7.5%), and post-breakfast dosing (60%). Following education and poster dissemination, the re-audit of 45 patients demonstrated a rise in overall compliance to 60%, with 42% achieving complete compliance. Concomitant use of interfering drugs reduced markedly (PPIs 27%, calcium 4%, iron 4%).
Conclusion
This QIP identified a significant gap in awareness regarding levothyroxine administration. The marked improvement following active education and visible reminders illustrates the importance of education driving changes. Efforts to embed these improvements through electronic prescribing adjustments and continued pharmacy collaboration are ongoing. Given its clear clinical implications, this initiative merits wider implementation and national consideration to enhance adherence to levothyroxine administration standards across inpatient settings.

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P241

A patient with persistent thyrotoxicosis; our experience and our hypothesis

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Background
Persistent thyrotoxicosis despite medical therapy remains a major challenge and is widely attributed to suboptimal adherence. We present a case of thyrotoxicosis with severe adverse impact on health, who was successfully cured with thyroidectomy despite persistently raised thyroid hormones. We also propose that impact of thyrotoxicosis on mental health drives noncompliance setting up a vicious cycle.
Case
A 35-year-old woman with Graves' disease (onset 2015, TSH <0.005mIU/l, T4 80.9pmol/l, T3 $>30,7$pmol/l) remained thyrotoxic despite maximum dose of carbimazole and propylthiouracil. Adherence to medication (confirmed by prescription record), investigations and attendance was patchy with long gaps in follow up. By 2024, she had lost >20 kg weight and demonstrated features of apathetic thyrotoxicosis. Despite obvious challenges, radioiodine was discussed but declined by the patient. She agreed to thyroidectomy and was hospitalized for 2 weeks preoperatively for "supervised" Lugol's iodine. Unfortunately, supervision of ingestion of medication proved difficult and after two weeks T4 was 24.3pmol/l and T3 17.9pmol/l. Surgery was high risk, but this was considered to be lower than from ongoing thyrotoxicosis. Invasive monitoring with arterial and femoral venous lines was instituted and remifentanil–esmolol infusions maintained cardiovascular stability. She was transferred to ICU for 24-hours and the remainder of her stay was uneventful. 2 months postoperatively she is euthyroid, compliant with thyroxine with remarkable improvement in physical and mental health
Conclusions
This case demonstrates that if clinical circumstances demand, thyroidectomy can be considered despite suboptimal biochemical control. Multidisciplinary care, pharmacological support and planned ICU care are required to mitigate the risk. We also hypothesize that bidirectional interaction between non-compliance and mental health effects is a major driver for persistent thyrotoxicosis. Altered serotonin and dopamine dynamics lead to low mood, impaired adherence, sustained thyrotoxicosis, and further worsening of mood. Supporting mental health is integral to successful management of severe hyperthyroidism.

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P242

Dual Autoimmunity: Myasthenia Gravis and Graves' Disease

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23-year male presented to Endocrinology OPD with 5 months history of bilateral eye prominence and left-eyelid drooping, evening-worsening of ptosis and ocular fatiguability in the form of intermittent diplopia. Initial consultation with a neurologist revealed diagnosis of ocular myasthenia gravis. Patient's autoimmune markers including anti AChR and anti Musk were negative, although RNST was suggestive of NMJ disorder and CE-MRI Brain was normal. He was started on Pyridostigmine following which mild improvement noticed in ptosis but patient discontinued therapy. Few months later patient reconsulted neurophysician. RNST was repeated which revealed findings consistent with thyrotoxicosis (Graves' disease). Endocrinologist's opinion sought thereafter. On detailed history assessment there were no symptoms suggestive of thyrotoxicosis. Eye examination by exophthalmometer revealed proptosis [22/23 mm (L/R)]. There was moderate left ptosis with palpebral aperture height 8 mm, MRD 1 = 2 mm. Right eye palpebral aperture height was 15 mm with superior / inferior limbus visualized, MRD 1 = 8 mm, MRD 2 = 7 mm. He also had restricted left lateral gaze. Left eye ptosis improved with ice pack application. Rest of the neurological examination was unremarkable. Patient's routine biochemistry was unremarkable. TFT revealed thyrotoxicosis, elevated TRAb antibodies; thyroid nuclear scan revealed hyperthyroidism (Graves' disease). Contrast CT of neck/chest revealed normal thymus morphology. MRI bilateral orbits was unremarkable. He was started on an antithyroid drug - Carbimazole (20 mg twice daily), Pyridostigmine (60 mg q8h followed by q6h) and received a short methylprednisolone pulse (120 mg on day 1 followed by 60 mg once daily on days 2–4). Patient follow up at 2 weeks revealed ptosis improvement with left eye palpebral aperture height of 12mm without diplopia. Proptosis remained stable without new inflammatory signs. Patient was finally diagnosed with ocular myasthenia gravis and Graves' disease with mild inactive TED(EUGOGO).

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P243

A case of Severe Mitral regurgitation caused by Thyrotoxicosis in longstanding uncontrolled Grave's disease, requiring urgent inpatient thyroidectomy

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Introduction
Grave's disease is common, with estimated prevalence between 0.2% and 2%. Sympathetic overdrive secondary to Grave's disease can complicate compliance issues. We present a complex case of severe mitral regurgitation secondary to poorly controlled Grave's disease for 11 years, and the subsequent need for urgent definitive inpatient treatment.
Case Presentation
30-year-old female attended the Emergency Department with palpitations, agitation, headache and abdominal pain. Past medical history includes Grave's disease, Generalized anxiety & depression. Since diagnosis in 2014, she had recurrent missed appointments with Endocrinology and surgical teams for review of pharmacological and non-pharmacological management. Biochemical investigations confirmed thyrotoxicosis (TSH <0.05 mIU/l, free T3 >30.72 pmol/l and free T4 34.7 pmol/l). She admitted long-standing non-compliance to medication and prior allergic reaction to Propylthiouracil. Carbimazole 40 mg once-daily and Propranolol 40 mg three-times-daily were restarted. During admission, she developed worsening dyspnoea and non-productive cough. Investigations confirmed concerns of heart failure with elevated BNP (5357 ng/l) and chest X-ray revealed pulmonary congestion. Echo showed severe mitral regurgitation secondary to anterior mitral valve leaflet prolapse; most likely secondary to poorly controlled thyrotoxicosis. After multidisciplinary discussion involving the patient and her family, it was agreed to proceed with inpatient thyroidectomy. Lugol's iodine 5 drops three-times-daily was commenced, and thyroidectomy (uncomplicated) was conducted four days later, after stabilization of thyroid function tests. She recovered well post-operatively and will have close outpatient follow-up with Endocrinology, Surgical and Cardiology teams.
Discussion
Mitral valve regurgitation is common secondary to Grave's disease, occurring in up to 13% of patients. With aggressive treatment of thyrotoxicosis, it has potential reversibility. Our case highlights a complex situation of non-compliance to medication for eleven years and subsequent severe cardiovascular impairment. We emphasise the need for urgent action and support in these vulnerable patients, to prevent end-stage complications of this significant disease.

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P244

Thyroid eye disease in euthyroid and hypothyroid patients; a single tertiary center experience

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Thyroid eye disease (TED) is an autoimmune inflammatory disorder that affects the orbital retrobulbar tissue, an extrathyroidal manifestation of Graves' disease. Whilst most often associated with hyperthyroidism, TED may manifest in both euthyroid patients and those with a background of chronic autoimmune hypothyroidism, in up to 20% cases [(1)] although data is lacking. This audit aimed to review the non-hyperthyroid cohort of patients presenting to a dedicated thyroid eye disease multidisciplinary clinic in a tertiary hospital.
Method
Retrospective Trust approved audit features of TED from MDT database (2016-2025) to include all non-hyperthyroid patients.
Results
30/323 patients were non-hyperthyroid; 14 patients were biochemically euthyroid, and 16 patients were hypothyroid (overt/subclinical). 7 out of 25 documented patients were smokers. The average age was 50.7 (29-73 years) with

female preponderance (73%). The most common ocular presentation was dry, gritty eyes (n:13/30 = 43.3%) and exophthalmos (n:18/30 = 60%), followed closely by ophthalmalgia and diplopia, with 2/3rd of group presenting with multiple symptoms. Though TED activity was mild (CAS score < 3) in more than half of patients (n:16/30 = 53%) ;12 patients (40%) had moderate-severe TED activity/severity and required systemic treatment with steroids/ immunosuppressants/ immunotherapy. Two patients needed orbital decompression, both of whom were noted to be smokers. TRAB was > 3 IU/l in 6 /12 patients with moderate-severe TED. Subsequent thyroid dysfunction occurred in 11 /14 euthyroid patients, with 9/14 becoming hypothyroid (81%) and none became hyperthyroid. Median time for subsequent thyroid dysfunction was 2 months to 5 years.

Conclusion

These findings challenge the perception that non-hyperthyroid patients have milder TED usually not warranting systemic treatment or surgery[2] and importance of recognition of TED in absence of hyperthyroidism. Subsequent thyroid dysfunction in those with euthyroidism and TED, emphasises the importance of advising patients to continue regular TFT monitoring.

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P245

Evaluation of diagnostic and early management practices in anaplastic thyroid cancer

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Background

Anaplastic thyroid carcinoma (ATC) is a rare but highly aggressive malignancy, accounting for <2% of thyroid cancers but up to 50% of thyroid-related mortality. UK median survival is around 3 months. Timely diagnosis, molecular profiling and multidisciplinary care are critical to optimize outcomes. This audit evaluated diagnostic and early management pathways for ATC at a single trust in reference to 2021 American Thyroid Association (ATA) guidelines.

Methods

A retrospective audit identified all ATC cases between January 2013 and December 2024 using SNOMED codes M8021/3, M8020/3, M8050/3, and M0950/3. Data were collected from electronic and pathology records and MDT minutes. Audit standards were derived from the 2021 ATA guidelines for ATC, focusing on tissue diagnosis, staging, molecular testing and MDT coordination.

Results

16 ATC cases were diagnosed over 11 years (median age 71 years; 11 females). 14 patients (88%) had died at analysis. Median survival was 99 days, with one long-term survivor of approximately 5 years. All patients underwent FNA or core biopsy, with both performed in 6 cases. Surgery was amenable in 4 patients (25%). 5 patients (31%) completed BRAF V600E testing with 1 positive. Broader molecular profiling was done in 2 cases (13%). All underwent radiological staging with CT/MRI +/-PET. Documentation of vocal cord assessment at presentation was inconsistent. All but 2 patients were discussed at MDT (incomplete records).

Conclusion

A revised ATC pathway now recommends mandatory molecular testing, rapid inpatient FNA plus core biopsy and MDT discussion with early palliative input. A re-audit is planned after 12 months.

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P246

Don't forget the 'eye' in thyroid: a multi centre national audit reviewing endocrinologist assessment and management of thyroid eye disease in UK

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Thyroid eye disease (TED), is a frequent extrathyroidal manifestation of Graves' disease, affecting 25-50% of patients, impacting vision and quality of life with delayed recognition resulting in poor clinical outcome. The Thyroid Eye Disease Amsterdam Declaration Implementation Group (Teamed) principles were initiated in 2009 [2] to improve management of patients with TED. The Team ED 5 objectives aimed to promote better care for patients with, or at risk of TED with 5 key recommendations; accurate diagnosis of Graves' disease, screen all patients for TED, alert patients to risk, prevent deterioration and early referral to eye specialist clinic. The aim of national multi-centre retrospective audit was to assess the effectiveness of this approach, with a standardised audit tool developed and applied across 9 centres*. It included patients with new or relapsed GD diagnosis seen in endocrinology clinics for 6 months (July - Dec 2024). There was a cohort of 566 patients with an average age of 46.3 years and female preponderance (80%). It was encouraging to see 93% of patients were accurately diagnosed on basis of TRAB testing. Clinicians recognized TED in 2/3rd of cases though standardized CAS scoring was only done in 13.6 % of patients and the early warning card was offered only in 6.8% of cases. Smoking status was documented in 48.8% of cases, 9.7% of which were active smokers. Smoking cessation advice was documented as given to only 10% of patients. The results suggest that although accurate diagnosis of GD and screening for TED is prevalent in clinics, further work is needed in optimizing care. Endocrinologists can play a key role by increasing patient awareness via TED early warning card, addressing smoking as an important modifiable risk factor, maintaining euthyroid profile and liaison with ophthalmologist in multi-disciplinary clinic for moderate - severe TED.

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P247

A new national rare thyroid disease service enables early diagnosis and management of rare forms of thyroid disease

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Background

Some forms of thyroid disease (TD) pose significant diagnostic difficulties. A national rare thyroid disease service (RTDS) was established in Ireland (population 5.2m) in 2020. Operating quarterly, it accepts nationwide referrals from primary care practitioners and specialists for patients with confirmed/suspected complex/rare TD.

Methodology

Clinical note review of attendances at RTDS in first 4 years (January 2021 - October 2024) to determine referral sources, practice volume, patient demographics, and final diagnoses.

Results

71 patients attended. The average age was 42.6 years, the majority were female (69%). Referrals were from endocrinologists (adult 87%; paediatric 4%) and primary care (9%). Most were from Dublin and surrounding counties (86%). On average 10.8 people attended each clinic; each patient had 2.4 visits on average. 46% of patients were referred with discordant TFTs, 25% with complicated hypothyroidism (abnormal TFTs, reset HPT axis in congenital hypothyroidism, thyroxine malabsorption, etc), 15% with complicated hyperthyroidism (fluctuating TRAb, unknown aetiology, etc), 10% with suspected assay interference and 3% with known Resistance to Thyroid Hormone. Patients received a diagnosis within 2 visits. Most (72%) had specialised testing at a reference laboratory and genetic testing was performed in 45%. A formal diagnosis was established in 97% of patients, investigations are ongoing in 3%. Complicated hypothyroidism (25%), T4 assay interference (20%) and complicated hyperthyroidism (17%) were the most common diagnoses. Cases of RTH Beta (10%), Familial Dysalbuminaemic Hyperthyroxinaemia (6%), TSH assay interference 4%, TTR mutation 4%, drug induced TD (4%), TSHoma (1%) and non-thyroidal illness (1%), were also identified. Less commonly, some individuals were found to have no identifiable TD (4%).

Conclusion
The spectrum of TD diagnosed and managed at the RTDS is highly variable. Access to a specialist clinic linked with appropriate specialist biochemical support and genetic testing facilitates timely diagnosis and appropriate management of complex and rare TD.

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Patient-level drivers of increased levothyroxine (LT4) prescribing: an analysis of greater manchester population health records (2010–2024)

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Introduction
Levothyroxine (LT4) prescriptions in England have increased from 9 million annually in 2000 to 30 million in 2024, outpacing the incidence of overt hypothyroidism. This study used patient-level primary-care-data to quantify increase in LT4-treated patients identify demographic/clinical characteristics associated with this growth.
Methods
Data was available from patients who received LT4 prescriptions in Greater Manchester (population = 2.85million) 2010-2024. Patients were included with diagnosis of hypothyroidism /no recorded diagnosis (other thyroid disorders were excluded). The overall number of new patients recorded over the 14-years was compared as percentage to the 2010-patient baseline to give Average Annual Rate of Increase (AARI) across strata of sex/age at treatment start/average daily dose/BMI. Demographic changes were accounted for using prescribing rates calculated from the 2011England population applied to the 2023population.
Results
Of 990,000 patients with recorded thyroid function tests, 106,000 received LT4. Of the cohort included in the analysis, 41,689 were already on medication and 58,070 patients started treatment post-2010. This gave an overall **9.8% AARI**. Significant, disproportionate growth was observed in specific subgroups: Dose: 4% Patients taking very low doses (0–39 mg/day) showed a **47% AARI**. The 17% on 40-79 mg/day showed a **20% AARI**. Age: The 20-39 age group, 11% of the 2010 cohort, showed a **22% AARI**. The 80+ age group with 3% in 2010, showed **16% AARI**. Sex: Males, with 17% of the 2010 cohort, showed a **13% AARI**. Demographic changes accounted for 4,033 of the increase, together with subgroup growth (low daily doses/age 20–39/80+/males), these collectively accounting for estimated 62% of overall patient increase (with allowance for double-counting). BMI/rate of treatment cessation remained constant.
Conclusion
LT4 use has more than doubled, primarily driven by an expansion of treatment into specific patient groups. These shifts strongly suggest a broadening of treatment criteria, explaining a significant portion of the recent years' growth.

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Thyroid eye disease: implementation of a standardised protocol in an irish tertiary endocrinology unit

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Background
Thyroid Eye Disease (TED) is an autoimmune condition affecting the retro-ocular tissues. It is associated with Graves' disease, and the spectrum of signs and symptoms ranges from mild to sight threatening. Screening, diagnosis, initial management and decision for referral to Ophthalmology are key skills for Endocrinologists in managing patients with Graves' Disease. Modifiable risk factors for the development of TED include uncontrolled Graves', cigarette smoking and the use of radioactive iodine. The Endocrine Society suggests the TEAMeD-5 programme to reduce morbidity associated with TED. This includes: 1) Diagnose Graves' accurately, 2) Screen all patients with Graves' for TED, 3) Provide an early warning card to highlight symptoms of TED, 4) Prevent TED development by modifying risk factors and 5) Early specialist referral. There is abundant material available to implement this programme.
Method
Using a positive TRAB antibody as a method to identify potential patients with Graves' disease, a chart review was undertaken to review screening for TED in patients undergoing treatment for Graves' and to ensure smoking cessation was advised and documented.
Results
Of the 103 charts reviewed, 84 (82%) had documented screening for TED. Methods of screening however were heterogenous, only 3 patients were screened using the validated screening tool the 'Clinical Activity Score' (CAS). 79 (77%) of charts had documentation of the smoking status. 33 patients were active smokers or vapers, of these, 88% had a documented discussion on smoking cessation. No patients were given a warning card for TED.
Discussion
Endocrinologists play an important role in the management of Thyroid Eye Disease. This audit has shown our centre performs moderately well in certain aspects of the TEAMeD-5 programme to reduce morbidity with TED, however several of the aspects are not implemented or are sporadically employed. We aim to implement this program fully and re-audit our adherence.

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TSHoma in hypothyroidism: diagnostic and therapeutic challenges

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Background
TSH-secreting pituitary adenomas (TSHomas) are rare functional pituitary tumours, with an incidence of 1–2 per million. They present diagnostic challenges, particularly in patients with pre-existing hypothyroidism, where abnormal biochemistry may be misattributed to inadequate replacement.
Case Presentation
A 72-year-old man with longstanding hypothyroidism and prostate carcinoma was referred to endocrinology by his GP in 2021 with persistently elevated TSH despite escalating levothyroxine doses. Biochemistry showed raised TSH with inappropriately normal/high free thyroid hormones across multiple laboratories, excluding assay interference. Family studies were normal. A mildly elevated α-subunit and raised SHBG prompted pituitary MRI, which demonstrated an 8 mm left-sided microadenoma. Levothyroxine was discontinued, after which TSH remained elevated with free hormones at the upper reference range. At pituitary MDT in April 2022, advice was to remain off levothyroxine, perform a TRH stimulation test, and continue surveillance. The TRH test demonstrated a blunted TSH response, consistent with autonomous secretion. The patient remained well until 2024, when palpitations and insomnia developed alongside a mild rise in free T3. Repeat MRI showed no progression. A further MDT deferred surgery and recommended somatostatin analogue therapy. In June 2025, Lanreotide was commenced, resulting in biochemical improvement and symptom resolution.
Discussion
This case illustrates the complexity of diagnosing TSHomas in the context of hypothyroidism. Exclusion of assay interference, α-subunit measurement, TRH testing, and pituitary imaging were essential in establishing the diagnosis. MDT input guided management, ensuring careful consideration of biochemical findings, clinical course, and surgical risk. Importantly, the case underlines the need to consider central causes of abnormal thyroid function in patients with discordant biochemistry, even when a background of primary hypothyroidism exists.
Conclusion
TSHomas should be considered in patients with discordant thyroid function tests. MDT-guided somatostatin analogue therapy can provide effective disease control, allowing deferral or avoidance of surgery in selected patients.

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P251

Weekend crisis: a repatriated patient with myxoedema coma

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A 78-year-old Irish male was repatriated from Malawi, where had been an inpatient for a month. His vitals in ED included a T 34.6C, HR 52bpm, GCS of 13/15 (E3V4M6), blood glucose fluctuated (nadir 2.3mmol/l). His weight was 77 kg. His difficult catheterisation yielded a residual volume of 4L. His TSH was 130.23mU/l (0.3–4.2) and fT4 was undetectable. On day two 9AM cortisol was 388nmol/l (160–550). On Saturday (Day3), he deteriorated with a GCS of 10/15 (E3V2M5): he was hypotensive (76/50mmHg), hypoxemic and bradycardic (59bpm), with blood glucose of

4.6mmol/l. His haemoglobin dropped from 90 to 68g/l (130–168), requiring urgent blood transfusion. Prompt treatment also included fluid resuscitation, IV hydrocortisone (100 mg), and IV antibiotics for a suspected HAP/CAUTI. He was transferred to a monitored bed. IV levothyroxine 300 mg was given, followed by IV liothyronine (10 mg twice daily), which was sourced from another hospital. His clinical status rapidly improved following the administration of both thyroid hormones and supportive measures, with his vitals normalising. From Sunday, levothyroxine 100 mg was administered via NG tube. IV liothyronine was continued for three days. Over the weekend IV hydrocortisone was continued at 50 mg four times daily and then reduced to 20 mg thrice daily for two days, then stopped. This case underscores the importance of a high index of suspicion for myxedema coma in patients with unexplained altered mental status, hypothermia and undetectable fT4, serving as a valuable reminder of the challenges in diagnosing and managing this life-threatening endocrine emergency, especially out-of-hours and when a detailed history is unavailable, highlighting the need for both local and national guidelines.

	07/05	10/5	11/5	12/5	15/5	20/5	27/5	02/6	9/6	17/6
TSH 0.3–4.2mU/l	130.23	124.65	80.77	48.79	29.86	54.1	55.56	37.8	18.36	6.47
FT4 9–23pmol/l	<5.4	<5.4	6.6	7.1	7.7	8	8.8	10.6	11.4	13

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Innovation in Teaching and Assessment

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Integrating Endocrinology and Genetics: Reflections from the First Year of a Joint Specialty Clinic at the University Hospitals of Leicester

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Background
Many endocrine disorders have an underlying genetic component, yet clinical management often occurs in isolation between endocrinology and genetics services. To bridge this gap, a Joint Endocrinology and Genetics Clinic was established at the University Hospitals of Leicester in 2024. The aim was to provide an integrated, patient-centred model of care that facilitates timely genetic diagnosis, personalised management, and family counselling, while also promoting genomic literacy among clinicians in training.
Methods
The clinic is jointly led by a Consultant Endocrinologist and a Consultant Clinical Geneticist, supported by with wider MDT including genetic counsellors, specialist nurses and residents. The GeNotes platform is used during consultations to guide genetic testing and consent. Patients are referred from general and specialist endocrine clinics where a hereditary or syndromic cause is suspected. Data were collected on clinic activity, referral indications, genetic investigations, and educational outcomes.
Results
Since its launch, five clinics have been conducted, and 27 patients have been reviewed. Suspected familial cases included those with potential multiple endocrine neoplasia, paraganglioma–pheochromocytoma syndromes, hyperparathyroidism, pituitary adenoma and AVP related polyuria. The presence of an on-site Clinical Geneticist facilitated the discussion regarding appropriate genetic testing and cascade testing for family members. Genetic counselling was provided when indicated, improving patient understanding and reducing the need for additional appointments. Feedback from residents and students highlighted the clinic's educational value, particularly in enhancing awareness of genomic medicine and multidisciplinary working.
Conclusion
The joint Endocrinology and Genetics Clinic has demonstrated the clinical value of a multidisciplinary, genomics-integrated model within secondary care. It streamlines diagnostic pathways, supports holistic patient support and strengthens training in genomic medicine. Expansion of this model could inform the future design of precision-endocrinology services across the NHS.

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Enhancing transition from paediatric to adult endocrine care: a prospective study of patient experience and intervention feasibility

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Objectives
Transition from paediatric to adult endocrine services is a critical period for young people with chronic conditions, who are vulnerable to loss to follow-up, suboptimal disease management, and long-term health consequences. Despite national recognition of the importance of high-quality transition pathways, data evaluating the transition experience remains limited. This study aims to assess the existing transition process and analyse the feasibility of a newly developed structured transition checklist.
Methods
A prospective evaluation was conducted using a standardised questionnaire administered to young people who had transitioned to adult services within the preceding two years. Outcomes included understanding of the transition pathway, preparedness for self-management, perceived support from paediatric and adult teams, and recommendations for improvement. Findings from this initial cycle informed development of a structured transition checklist and patient information leaflet, guided by validated transition frameworks, Ready Steady Go and the Transition Readiness Assessment Questionnaire.
Results
A total of eight patients were included in the study. Most participants (87.5%) transitioned at age 17, with the remainder at age 16. Nearly two thirds of respondents (62.5%) felt that they had been transitioned too early. Understanding of the transition process was limited, with 75% rating this as 3/5. Preparedness for self-management was suboptimal, with 37.5% rating this as 2/5 and 37.5% as 3/5.Perceived support declined between paediatric and adult services (mean scores 3.75/5 and 2.9/5). Notably, no participants received supportive transition materials, despite 87.5% reporting these would have been beneficial. Overall satisfaction with the transition process was moderate (mean 3.4/5).
Conclusions
Significant gaps persist in transition preparedness, perceived support, and availability of patient-centred resources within endocrine transition pathways. Young people demonstrated strong receptiveness to structured written interventions. The newly developed checklist and patient information leaflet appear feasible for wider implementation, with ongoing work evaluating their long-term impact on patient experience and engagement.

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Optimising Nebido® prescribing and documentation in a tertiary endocrine day-unit: a quality improvement project

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Background
Nebido® (testosterone undecanoate) is frequently used for treating primary and secondary hypogonadism. Its safe long-term use requires structured, protocol driven monitoring. At King's College Hospital, the Programmed Investigation Unit (PIU) delivers Nebido® treatment with patients allocated to either "standard" or "enhanced" pathways based on predefined biochemical thresholds as per local guidelines. We observed inconsistencies in pathway allocations and documentation, which prompted a quality improvement project aimed at enhancing clarity, safety, and efficiency.
Methods
A retrospective audit was performed of all Nebido® administrations between January and December 2024. Data were collected from EPIC, CITO and LCR for demographics, indication, pathway allocation, dosing interval, monitoring (FBC, LFTs, PSA, testosterone) and completeness of PIU documentation. Patients who received $\leq$1 injection or were discharged to external providers were excluded. Findings were compared with the local Nebido protocol, which delineates criteria for pathway assignment and recommended monitoring intervals.
Results
Seventy-eight patients met inclusion criteria; 56 (72%) were managed on the standard pathway and 22 (28%) on an enhanced pathway. Approximately 20% of the allocations showed partial deviation from protocol, most commonly escalation to enhanced monitoring for isolated elevated haemoglobin with normal haematocrit. Despite the guidance suggesting annual monitoring once stable, many patients on standard-pathway were monitored frequently with blood tests at nearly every visit. Documentation of pathway, adverse effects, biochemical trends and follow-up plans was lacking in many of PIU entries, limiting clarity.
Conclusions
Rather than reflecting individual practice gaps, the findings did highlight system-level opportunities to standardize monitoring and documentation. A biochemical classification tool, EPIC SmartPhrases (.nebidooverview and .Nebido), and targeted education sessions were introduced to help identify the correct pathways more reliably and reduce unnecessary testing. We are doing a subsequent audit to evaluate improvements in documentation practices, monitoring frequency and adherence to the local protocol.

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Nurses as Health Evangelists: Nurse-led Community diabetes champions Innovation in teaching program first time in Pakistan leading to Nurses' brand value elevation

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Background
There is a plethora of misinformation mixed with myths in social media-led communities about diabetes and an ill-informed image of nurses about knowledge of Diabetes Mellitus (DM) presents a gap for research in this area. The growing burden, incidence, prevalence and complications for the 33% of the population living with Diabetes Mellitus in Pakistan needs an urgent attention.
Aim of the Study
The aim of this research project was to present nurses as knowledgeable DM experts who play a role in training local nurses and community members to become "health evangelists. It will facilitate the graduate nurses to advance the practice with development of Nurse Practitioner (NP) and Advanced Nurse Practitioner Role (ANP) in endocrinology particularly DM Care First time in Pakistan through innovative training.
Methodology
The research project employed the cross-sectional survey data collection. The findings led to First Nurse-Led Diabetes Care Course implemented at Al-Kawthar University, Karachi-Pakistan. The future activities will enhance productivity with producing 30-60 second myth-busting videos on different social media channels and formats to engage the community for a better, health-conscious, and authentic knowledge-based society.
Results
The findings for the brand evangelism scale applied to check and recruit the graduate nurses who fall higher on the brand evangelism scale, who can be recruited for the advocacy for diabetes knowledge in advance roles. Additionally, the Aaker brand equity model applied to check the brand value perception of the community and nurses before and after the feedback of current progressing DM Care Course. The data analyzed by SPSS and Smart PLS software. This project served both academia and practitioners by creating a knowledge base for the nurses, raising awareness about diabetes, elevating nurses' image, creating strategies for the policymakers and healthcare industry.
Keywords
Diabetes Mellitus, Advanced Nurses Roles, Brand Value, Innovation in Teaching, Nurse-Led Diabetes Care
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Late Breaking

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Implementation of a Longitudinal Cohort to Analyse the Health Status of Adults with Congenital Adrenal Hyperplasia (CaHASE2)

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Congenital adrenal hyperplasia (CAH) represents one of the most prevalent forms of primary adrenal insufficiency, affecting an estimated 1 in 15,000 individuals. Suboptimal health status and care provision among adults living with CAH has been described in several countries. The CaHASE2 initiative was launched in 2023 to implement a robust, prospective, longitudinal cohort study aimed at analysing the health status of adults with CAH in the UK and Ireland. Following consensus on a minimal dataset for real-world data acquisition, participating centres commenced systematic data collection utilizing the international I-CAH registry. To date, 488 adults diagnosed with CAH have been successfully recruited, contributing data from 766 clinic visits for analysis. The current cohort predominantly comprises younger to middle-aged adults, although 130 participants are aged 51 years or older, providing valuable future opportunities to investigate health challenges that may emerge later in life. Preliminary analyses of this growing dataset show that a considerable number of recruited patients are classified as overweight or obese. Assessment of 17-hydroxyprogesterone (17OHP) concentrations suggests that a significant proportion of patients may be receiving overtreatment. Androstenedione levels are below 8 nmol/l in most patients. However, a significant fraction still exhibits suboptimal control based on hormonal biomarkers. Interestingly, preliminary findings reveal no discernible correlation between current glucocorticoid dosage and patient weight or body surface area. Presently, 23 centres are actively contributing data to the I-CAH registry, with additional sites pending approval, which is anticipated to further boost patient recruitment and data volume. Over the subsequent 12 months, the project will focus on collaborating with principal investigators to enhance the volume and completeness of longitudinal data entries. This improved data completeness will be crucial for comprehensively investigating variations in healthcare provision, health status, and outcomes, and will facilitate the provision of anonymised benchmarking data to all participating centres.

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Androgen and glucocorticoid receptor activation is co-regulated via tissue-specific metabolism by 11β-hydroxysteroid dehydrogenases

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Steroid receptors play essential roles in physiology and disease, including breast and prostate cancer. The interaction between different steroid receptors has been studied extensively at the level of their physical interaction on chromatin. We hypothesized that androgen receptor (AR) and glucocorticoid receptor (GR) stimulation is co-regulated by tissue-specific metabolism via 11β-hydroxysteroid dehydrogenases that metabolize both glucocorticoids and adrenal-derived 11-oxygenated androgens, but with opposing effects on their bioactivity for their respective receptors. We used breast cancer cell lines with both AR and GR expression as a model to investigate the role of 11β-hydroxysteroid dehydrogenases for the co-regulation of AR and GR activity. Using liquid chromatography-tandem mass spectrometry, we show that breast cancer cells generate active 11-oxygenated androgens from abundant circulating adrenal precursors, while inactivating cortisol to cortisone. CRISPR/Cas editing showed that the oxidative activity of 11β-hydroxysteroid dehydrogenase type 2 (HSD11B2) is required for these metabolic conversions. Using RNA-Seq, we show that loss of HSD11B2 abolishes the induction of AR target genes in response to circulating 11-oxygenated androgen precursors while sustaining the induction of GR target genes in response to cortisol. Overexpression of the reductive 11β-hydroxysteroid dehydrogenase type 1 isoform, which catalyzes reactions opposing HSD11B2 activity, i.e. 11-oxygenated androgen inactivation and the reactivation of cortisol from cortisone, impairs the response of AR targets to 11-oxygenated androgens but promotes the response to glucocorticoids. We conclude that beyond the well-established role of 11β-hydroxysteroid dehydrogenases for the regulation of systemic and local GR activation, 11β-hydroxysteroid dehydrogenases additionally function as metabolic hubs that coordinate AR and GR activity by locally controlling the agonist levels for both receptors. Additionally, our results suggest that 11-oxygenated androgens are functionally distinct from classic androgens, such as testosterone, because they are specifically activated in the absence of glucocorticoid action due to their shared metabolic pathways.

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Modified-release hydrocortisone (Efmody) in congenital adrenal hyperplasia: real-world outcomes from a tertiary endocrine service in the UK

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Introduction
In classic congenital adrenal hyperplasia (CAH), maintaining adequate glucocorticoid replacement to suppress androgen excess while avoiding treatment-related metabolic complications remains a significant clinical challenge. There is limited real world data on the effectiveness of modified release hydrocortisone (Efmody) in CAH in achieving these goals.
Aim
To evaluate biochemical and metabolic outcomes before and after transition to Efmody in adults with classic CAH

Methodology
Retrospective review was conducted from the CAH database of Sheffield Teaching Hospitals NHS Foundation Trust. Data was collected on demographics, anthropometric measurements, pre and post Efmody biochemical parameters including androgens, HbA1c, and lipid profile.
Results
Data of 18 adults were analysed; 83.3% ($n = 14$) had a salt losing phenotype and 10(52.6%) were men. Mean age 47.2 years(20-68 years). Duration of follow up after switching to Efmody ranged from 7-529 weeks(mean 226.8). Before Efmody, 10 patients were taking hydrocortisone and 8 were on prednisolone, with a mean hydrocortisone-equivalent dose of 24.1 mg/day. After transition, mean Efmody dose was 23.1mg/day (SD$\pm$5.2mg; $P = 0.68$). Mean fludrocortisone dose 125microgramsg/day (SD$\pm$87.2micrograms). Among 15 patients with paired biochemical results, significant reductions were observed in 17-hydroxyprogesterone (pre Efmody median 88.1nmol/l (IQR 26.8-209.0nmol/l) vs postEfmody median 51.9nmol/l, (IQR 10.1-81.8nmol/l); $P = 0.03$) and androstenedione (pre Efmody median 14.6nmol/l (IQR 6.4-23.5nmol/l); vs post Efmody median 6.2 nmol/l (IQR 3.1-9.2nmol/l); $P = 0.018$). Weight showed a non significant rise by 2 kg ($P = 0.68$) and HbA1c demonstrated a trend of improvement by 4.5mmol/mol following Efmody ($P = 0.46$). The parameters in the Lipid profile (Total cholesterol, non HDL cholesterol, HDL, Triglycerides) remained largely similar following initiation of Efmody.
Conclusion
Overall, Efmody resulted in significant improvement of disease control particularly for 17 OHP and androstenedione in CAH with stable metabolic parameters. The small sample size is a limitation and further studies are needed to evaluate the effect on metabolic health.

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Single centre experience of managing primary hyperaldosteronism

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Background
Primary aldosteronism (PA) is a leading cause of secondary hypertension but remains underdiagnosed in routine practice. Diagnostic delays often occur due to the complex influence of antihypertensive therapy and hypokalaemia on the renin–angiotensin–aldosterone system. Adrenal vein sampling (AVS) is the gold standard for identifying unilateral disease suitable for adrenalectomy.
Methods
We retrospectively reviewed all patients with confirmed PA who underwent AVS between 2009 and 2025. Clinical history, biochemical data, imaging, and management outcomes were extracted from case notes. Lateralization was assessed using the Lateralization Index (LI), calculated as the aldosterone-to-cortisol ratio of the dominant adrenal divided by the non-dominant adrenal vein (LI $\geq$2 indicating unilateral disease).
Results
Thirty-eight patients were identified (mean age 57 years, range 28–76; 15 female). Baseline blood pressure averaged 153/87 mmHg on 2.3 antihypertensive agents; 58% were hypokalaemic. Mean aldosterone-to-renin ratio (ARR) was $\geq$176, with aldosterone levels averaging 1029 pmol/l. CT revealed adrenal nodules in 76% (10 $>$10 mm). AVS demonstrated unilateral disease in 28 patients; 23 underwent adrenalectomy (18 left, 5 right), with one declining surgery and three awaiting intervention. Eight had bilateral secretion, though three showed marked asymmetry. Three AVS procedures failed to cannulate the right adrenal vein. Postoperatively, ARR normalized in 37/38 surgical patients; 14 discontinued all antihypertensives, and overall medication burden fell from 3.18 to 0.41 agents. Mean BP improved from 154/86 to 127/79 mmHg. Younger patients (mean age 53.4) with higher ARR (245.7) were more likely to achieve complete medication withdrawal compared to conservatively managed patients (mean age 57.4, ARR 85.4). Non-surgical patients also showed BP improvement (147/87 to 129/81 mmHg).
Conclusion
AVS reliably stratifies PA, enabling targeted adrenalectomy with high cure rates in appropriately selected patients. Younger age and higher ARR predict surgical success, reinforcing AVS as an essential tool in PA management

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Romosozumab in routine clinical practice: real-world experience from a single tertiary centre

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Background
Romosozumab, a dual-action anabolic and anti-resorptive therapy, was approved for NHS use in England and Wales in 2022 for the treatment of severe osteoporosis. Despite robust trial data, real-world UK evidence remains limited, particularly regarding patient selection, bone turnover responses, and early fracture outcomes in high-risk postmenopausal women.
Objective
To evaluate 12-month experience of romosozumab in a real-world NHS setting at a large tertiary metabolic bone centre.
Methods
We performed a retrospective analysis of prospectively collected data from postmenopausal women with severe osteoporosis treated at the Queen Elizabeth Hospital Birmingham. Eligibility reflected NICE TA791 criteria: mean baseline T-score –3.58 (spine) and –2.46 (hip), with $\geq$1 fragility fracture within 24 months or very high FRAX risk. Patients with prior myocardial infarction or stroke were excluded. Baseline QRISK scores were recorded (mean 9.0%$\pm$4.42). Changes in bone turnover markers (P1NP, CTX), biochemical parameters, 12-month BMD (DXA), and incident fragility fractures were assessed.
Results
Twenty-seven women (mean age 64$\pm$7 years) completed 12 months of romosozumab. Significant BMD gains were observed at the lumbar spine (mean T-score –2.64; +14%) and total hip (–2.04; +5%). P1NP rose to 62.09 µg/l, while CTX fell to 0.27 pg/mL, demonstrating the expected anabolic-dominant profile. Serum calcium and renal function remained stable. Two new vertebral fractures occurred during treatment; no non-vertebral fractures or treatment-limiting adverse biochemical changes were identified.
Conclusion
In this real-world NHS cohort, romosozumab produced clinically meaningful improvements in spine and hip BMD, with favourable bone turnover responses and low short-term fracture incidence. These data support its effectiveness and tolerability in routine UK practice and contribute to the emerging national evidence base on its early implementation following NICE approval. Larger multicenter datasets are needed to establish long-term outcomes and optimise patient selection pathways.

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The "SALAMA-D": a prospective oman cohort study on vitamin D status

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Background
The 25-hydroxyvitamin D (25OHD) endocrine system acts as an essential nutrient for bone development, maintenance, and many other extra-skeletal activities. However, in RCTs like VITAL, ViDA, D2d, etc. [1, 2, 3]. The causal links were not found. Its deficiency is a global health concern, with growing evidence of its high prevalence in sunshine-rich nations due to cultural and lifestyle factors.
Objective
To determine the status of 25OHD by identifying associated demographic, clinical, and lifestyle risk factors in a large Oman cohort presenting for a routine health check-up from 1stJanuary, 2024, to 31stDecember, 2024.
Methods
This cohort study named The SALAMA-D recruited 1700 consecutive participants aged 12-79 years who underwent a comprehensive health screening at two branches of Al-Salama Medical Center in Muscat, Oman. Serum 25OHD levels were measured among 67 other parameters of blood and urine. Deficiency was defined as 25OHD $<$ 20 ng/mL, insufficiency as 21-29 ng/mL, and sufficiency as $\geq$30 ng/mL. Data on demographics, comorbidities like diabetes, hypertension, dyslipidemia, anaemia, thyroid profile, and lifestyle factors, including sun exposure and diet, were collected via structured questionnaires.
Results
The overall prevalence of vitamin D deficiency and insufficiency was 90.1%. A striking 68% of the cohort were women, who exhibited significantly lower mean

25OHD levels (15.2 ± 6.1 ng/mL) compared to men (21.8 ± 7.5 ng/mL, $P < 0.001$). The age group 30-50 years was most affected. A strong association was found with comorbidities: 72% of deficient / insufficient participants had at least one of diabetes, hypertension, anaemia, or dyslipidemia. The primary self-reported causes were avoidance of sun exposure (90% reported) and inadequate dietary vitamin D intake (82%).
Conclusion
The SALAMA-D study reveals an alarmingly high prevalence of low vitamin D in Oman. A national public health strategy promoting safe sun exposure and food fortification is urgently needed.

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A systematic review and network meta analysis of pharmacological approaches to enhance bone mineral density in functional hypothalamic amenorrhoea

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Background
In Functional Hypothalamic Amenorrhoea (FHA), sustained low oestrogen together with nutritional deficiency leads to significant deterioration in bone health. When psychological and nutritional interventions fail to restore menses within 6-12 months, pharmacological treatment is usually introduced to preserve bone health. Nevertheless, the relative efficacy of available pharmacotherapies remains unclear.
Aim
To compare the efficacy of available pharmacological treatments for bone mineral density (BMD) in women with FHA using network meta-analysis (NMA) for the first time.
Methods
Medline/Embase/Emcare/Cochrane/CENTRAL/ISRCTN/ClinicalTrials.gov were searched until 20-September-2025. Eligible randomised-controlled trials (RCTs) examining pharmacotherapies for lumbar spine (LS), femoral neck (FN), or total hip (TH) BMD were considered and synthesised according to PRISMA-NMA recommendations. Outcomes were reported as standardised mean differences (SMDs) with 95% confidence intervals (CIs).
Results
Thirteen RCTs were included (LS-BMD: $n = 897$; FN-BMD: $n = 370$; TH-BMD: $n = 750$). *Transdermal* hormone replacement therapy (HRT) was better than control (placebo or no intervention) in increasing LS-BMD with SMD 0.34 (95% CI 0.03, 0.64) and FN-BMD with SMD 0.57 (0.04, 1.10) over 12-18 months. By comparison, *oral* HRT and the combined oral contraceptive pill (COCP) did not increase BMD at any skeletal site over 12-24 months. Finally, teriparatide was superior to *transdermal* HRT, *oral* HRT and COCP for LS-BMD with SMDs 1.48 (0.38, 2.59), 1.69 (0.48, 2.91) and 1.75 (0.66, 2.83), but not FN or TH-BMD.
Conclusions
Transdermal HRT and teriparatide both produce significant LS-BMD improvements in women with FHA, while *transdermal* HRT also increases FN-BMD. By contrast, *oral* HRT and COCP show no benefit at any skeletal site.The difference in the effect of *transderma*l vs *oral* oestrogens may be partly explained by differential effects on IGF-1. This is the first NMA comparing all pharmacological treatments for bone health in FHA, offering key new evidence to shape clinical guidelines.
Study registration
PROSPERO (CRD42024576872).

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P263

A rare case of hypercalcaemia in pregnancy not related to primary hyperparathyroidism: the importance of a carefully orchestrated multidisciplinary approach

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Background
Hypercalcaemia in pregnancy is rare, with potential adverse obstetric and perinatal outcomes. It is often difficult to detect as patients can be relatively asymptomatic, and serum calcium is infrequently measured routinely during pregnancy. Diagnosing the cause is made more complex by changes in calcium metabolism during pregnancy. We present a rare case of hypercalcaemia in pregnancy not related to primary hyperparathyroidism and how an orchestrated multidisciplinary approach ensured the optimal care for mother and baby.
Case Presentation
A 38-year old lady, G1P0, 27 weeks pregnant, and with background of gestational diabetes, was referred to Endocrinology with serum calcium of 2.79 mmol/l, was performed in view of painful wrist. Serial serum calcium levels remained elevated, and parathyroid hormone levels were at low normal limit. Other investigations revealed adequate vitamin D, normal phosphate, thyroid, renal and liver functions. A 24-h urine calcium was normal at 5.3 mmol/24h (range 2.5 – 7.5). To complicate things, she had a palpable axillary lymph node but ultrasound/FNA came back reassuringly benign. The hypercalcaemia was felt to be placental-driven and a multidisciplinary care plan was set up. She was encouraged to have adequate daily hydration and avoid any calcium-containing agents. She had close monitoring of serum calcium. She was seen by maternal medicine team in addition to her Obstetricians. Neonatal team was pre-informed and involved for the delivery. She was thoroughly educated of the condition, potential risks and care plan. She had an uneventful delivery with the support of multidisciplinary team, and both mother and baby had normal calcium levels on monitoring.
Learning Point
This case highlights the importance of a well-planned multidisciplinary approach to ensure safety of mother and baby in rare cases of hypercalcaemia in pregnancy. It is also important to ensure mother is well-supported and educated of the condition and potential risk.

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P264

Management of florid primary hyperparathyroidism: a rare case of life-threatening hypercalcemia with a palpable parathyroid adenoma and bilateral nephrocalcinosis, requiring urgent inpatient parathyroidectomy

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Background
Primary hyperparathyroidism (PHPT) is usually a mild or asymptomatic condition; however, severe or "florid" cases can lead to life-threatening metabolic disturbances and multi-organ dysfunction. We present a rare instance of extreme PHPT characterised by profound hypercalcemia that was resistant to maximal medical treatment, complicated by bilateral nephrocalcinosis and acute kidney injury (AKI).
Case
A healthy woman in her 30s presented with nausea, vomiting, and general weakness, prompting biochemical analyses that revealed critical hypercalcemia (corrected calcium level of 4.99 mmol/l), significantly elevated parathyroid hormone (PTH) at 107 pmol/l, hypomagnesemia, hypophosphatemia, and acute kidney injury (creatinine level of 179 µmol/l). Imaging studies, including neck ultrasound and MIBI scan, identified a 3.5-cm mixed solid-cystic vascular lesion posterior to the left thyroid lobe, suggestive of a parathyroid adenoma, in addition to a smaller nodule on the right. Renal ultrasound indicated bilateral nephrocalcinosis with cortical calcifications. Despite comprehensive medical management—including intravenous fluids, pamidronate, cinacalcet, magnesium and phosphate supplementation, and vitamin D repletion—persistent hypercalcemia above 3.7 mmol/l led to signs of end-organ damage. Consequently, an urgent inpatient parathyroidectomy was performed, during which a well-defined vascular mass was excised. Histopathological examination confirmed a benign parathyroid adenoma with no evidence of capsular or vascular invasion.
Outcome
Postoperatively, calcium levels were normalised within 48 hs. Transient hypocalcaemia was effectively managed with oral calcium and vitamin D supplementation. Renal function showed improvement, and the patient was discharged with a plan for outpatient endocrine follow-up.
Conclusion
This case underscores the severe complications associated with florid primary hyperparathyroidism (PHPT) in a young adult, the limitations of medical therapy in cases of profound hypercalcemia, and the critical importance of early surgical

intervention. A multidisciplinary approach is essential to prevent irreversible renal damage and optimise patient outcomes.

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P265

Severe hypomagnesaemia and hypocalcaemia with secondary hypoparathyroidism induced by long-term proton pump inhibitor use

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Background
Proton pump inhibitors (PPIs) are widely prescribed for gastroesophageal reflux disease (GORD) but have been associated with hypomagnesaemia. Chronic hypomagnesaemia can lead to hypocalcaemia and secondary hypoparathyroidism, which may present with neuromuscular symptoms. Recognition of this adverse effect is critical to avoid unnecessary investigations and ensure appropriate management.
Clinical Case
A 59-year-old female presented to A&E with a three-year history of intermittent paraesthesia affecting her hands, feet, and mouth. Her past medical history included hypertension, GORD, and previous myocardial infarction. She was prescribed long-term high dose lansoprazole therapy (30mg BD). Initial laboratory investigations revealed severe hypocalcaemia (1.50 mmol/l; normal range: 2.20–2.60) and hypomagnesaemia (0.24 mmol/l; normal range: 0.70–1.00) , low vitamin D (26 nmol/l; normal >50) and inappropriately low parathyroid hormone (PTH) (29 ng/l; normal: 12–88), consistent with secondary hypoparathyroidism. Her symptoms resolved with intravenous magnesium and calcium replacement. She was discharged on oral supplementation with follow up in endocrinology clinic. Despite treatment adherence, she re-presented with recurrent symptoms and persistently low magnesium (0.25mmol/l) and calcium (1.80mmol/l), again requiring intravenous replacement. In endocrinology clinic, chronic PPI use was identified as a potential cause and lansoprazole discontinued. She required further intravenous replacement followed by oral magnesium, calcium and high dose vitamin D supplementation. Subsequent blood tests demonstrated normalisation of calcium (2.46mmol/l), magnesium (0.84mmol/l), and PTH (38 pg/mL) within 3 weeks.
Conclusion
This case highlights PPI-induced hypomagnesaemia as an under-recognised cause of secondary hypoparathyroidism and hypocalcaemia. Long-term PPI use should be considered as a potential cause in patients with unexplained neuromuscular symptoms or electrolyte disturbances, particularly when refractory to treatment. Regular monitoring of serum magnesium and calcium levels should be considered in long-term PPI users, particularly those at higher risk, such as older adults and those on concurrent diuretic therapy.

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P266

"It must be normocalcaemic hyperparathyroidism!" Diagnostic pitfalls of the PTH assay

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Introduction
High parathyroid hormone (PTH) usually associated with parathyroid disorder, but sometimes the elevation is false due to assay interference, such as macro-PTH or heterophile antibodies. In macro-PTH, PTH binds to immunoglobulins, slowing its clearance from the blood. Although these complexes are typically biologically inactive, they can produce misleading laboratory results, complicating both diagnosis and clinical management.
Case presentation
A 35-year-old woman was referred for evaluation of markedly elevated PTH, ranging from 20.2 to 25.6 pmol/l, despite mostly normal serum calcium, which was mildly elevated only once at 2.61 mmol/l. Vitamin D was 69 nmol/l, and eGFR was 85 mL/min/1.73m^2. She reported non-specific symptoms including episodic weakness, tremors, muscle and bone pain, polydipsia, neck swelling and intermittent hoarseness. Renal ultrasound revealed no calculi, while thyroid ultrasound identified a benign U2 nodule. Twenty-four-hour urinary calcium excretion was 7.32 mmol/24h (reference 2.5–7.5), and DEXA scanning demonstrated osteopenia. Given the discordance between PTH and calcium levels, assay interference was suspected. Polyethylene glycol (PEG) precipitation was performed, revealing a monomeric PTH of 2.97 pmol/l with a low recovery of 24%. To confirm test specificity, a parallel PEG assay was performed on a patient with elevated PTH due to confirmed parathyroid pathology, yielding 76% recovery. Subsequent testing using an alternative assay produced a normal PTH of 22.4 ng/l (reference 15–68).
Results
The initial elevated PTH readings were found to be falsely raised due to immunoassay interference. PEG precipitation and confirmatory testing with an alternative assay demonstrated normal PTH levels, consistent with the presence of macro-PTH and effectively excluding hyperparathyroidism.
Conclusion
Discordantly elevated PTH with normal biochemical and imaging findings should prompt evaluation for assay interference, including macro-PTH. PEG precipitation offers a useful confirmatory approach. Integrating clinical and laboratory input is essential to prevent diagnostic error and unnecessary investigations.

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P267

Accelerated multidisciplinary management of primary hyperparathyroidism in pregnancy through a one stop specialist pathway

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Background
Primary hyperparathyroidism (PHPT) in pregnancy is rare and associated with substantial maternal–fetal risk, including miscarriage, nephrolithiasis, acute kidney injury, fetal growth restriction, and neonatal hypocalcaemia. Diagnostic imaging options are restricted, and the second trimester represents the safest window for parathyroidectomy. The UK's first One Stop PHPT Clinic at Queen Elizabeth Hospital Birmingham was developed to enable accelerated identification and coordinated consultant-led multidisciplinary management of high-risk cases.
Case Summary
A 35-year-old woman, gravida five with four previous miscarriages, was referred with recurrent nephrolithiasis and symptomatic hypercalcaemia. Biochemistry confirmed PHPT, with deterioration over four months, including corrected calcium rising to 3.06 mmol/l and parathyroid hormone (PTH) to 14.4 pmol/l, alongside worsening symptoms. Early pregnancy at six weeks' gestation was concurrently identified, significantly intensifying maternal–fetal risk and narrowing the window for definitive treatment, which triggered immediate consultant-led review, bypassing routine nurse-led triage. As pregnancy contraindicates nuclear scintigraphy, urgent radiology–endocrine collaboration enabled rapid localisation using neck ultrasound and low-dose 4D CT, identifying a right inferior parathyroid adenoma. At $17+6$ weeks' gestation, the case was reviewed at a combined Parathyroid–Gynaecology–Obstetric multidisciplinary team (MDT) meeting, where second-trimester parathyroidectomy was unanimously recommended. Parathyroidectomy was performed at 22 weeks' gestation, achieving an intra-operative PTH reduction from 16.1 to 4.06 pmol/l. Postoperative calcium normalised without hypocalcaemia, recovery was uncomplicated, and fetal monitoring remained reassuring. The pregnancy is ongoing and progressing normally.
Learning Outcomes
- To recognise PHPT as a rare but high-risk condition in pregnancy requiring early senior involvement
- To understand imaging limitations in pregnancy and the role of radiology–endocrine collaboration
- To demonstrate how a One Stop PHPT service model and MDT consensus can enable timely localisation and definitive management

Conclusion
A structured One Stop PHPT pathway enables accelerated, consultant-led multidisciplinary care for complex PHPT presentations in pregnancy, supporting favourable maternal and fetal outcomes.

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P268

Adalimumab-induced hypophosphataemia: an unknown adverse effect

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We report a case of recurrent, treatment-resistant hypophosphataemia associated with Adalimumab, resolving after drug cessation. A 59-year-old woman with rheumatoid arthritis, type 2 diabetes, chronic kidney disease, cirrhosis and hypertension was admitted in May 2025 with severe hypophosphataemia (0.26mmol/l) and hypomagnesaemia (0.46mmol/l). She had multiple similar admissions since 2023. She denied gastrointestinal losses, alcohol use, or antacid intake. Her medications included adalimumab, hydroxychloroquine, insulin, metformin, amlodipine and omeprazole (subsequently changed to famotidine). Despite treatment with intravenous phosphate, magnesium and high dose Vitamin D, hypophosphataemia persisted. Investigations:

	Normal range	Jul-24	May-25
Phosphate(mmol/l	*0.8-1.5*	0.23↓	<0.2↓
Calcium(mmol/l)	*2.2-2.6*	2.87↑	2.41
Magnesium(mmol/l)	*0.7-1*	0.57↓	0.46↓
PTH(pmol/l)	*2.2-14*	0.8↓	4
Vitamin D(nmol/l)	*> 50*	58.8	30↓

- **eGFR:** 30ml/min *(> 90)*
- **FGF-23:** 112RU/mL *(< 100)*
- **1,25 Vit D:** 144pmol/l *(55–139)*
- **24-hr urine phosphate:** <2.13mmol/day (*13-42*)
- **24-hr urine calcium:** 5.27mmol/day (*2.5-7.5*)
- **Urinary protein:** 13g/l
- **PET CT 2024:** breast and pulmonary nodule (intraductal breast papilloma and necrotising granulomatous inflammatory pulmonary nodule resected via video-assisted thoracoscopic surgery)
- **DEXA 2024:** normal bone density

Although FGF-23 was mildly elevated, low urinary phosphate and normal acid-base status made tumour-induced osteomalacia and renal tubular disorders unlikely. Notably, the onset of hypophosphataemia coincided with the initiation of Adalimumab for rheumatoid arthritis. As her rheumatoid arthritis was stable, Adalimumab was withheld following Rheumatology discussion. This resulted in a normalisation of her biochemistry and symptoms, which remain stable four months following Adalimumab discontinuation. Although the underlying mechanism remains unclear, TNF-α inhibition may influence renal phosphate handling. Additionally, cirrhosis may exacerbate hypophosphataemia, as chronic liver disease can impair gluconeogenesis and ATP turnover, promoting an intracellular phosphate shift. This case describes an unusual case of recurrent hypophosphataemia in an Adalimumab-treated patient. With the rising use of biologic therapies, clinicians should remain alert for unknown adverse effects.

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P269

Navigating the diagnostic dilemmas of hypercalcemia in pregnancy

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Introduction
Hypercalcemia in pregnancy is rare with limited treatment options, causing serious consequences to mother and foetus. Changes in calcium homeostasis in pregnancy can delay Primary hyperparathyroidism (PHPT) diagnosis.
Case Presentation
A 35-year-old pregnant woman was detected with hypercalcemia (3.06 mmol/l) at 14 + 1 weeks. Calcium was 2.83 mmol/l in March 2025, following a miscarriage. She was otherwise asymptomatic. She was commenced on intravenous fluids. Biochemistry revealed: PTH 14.5 (1.6-6.9 pmol/l), phosphate 0.88 (0.8-1.5 mmol/l) and Vit-D 75 (> 50 nmol/l). Thyroid and renal function tests normal. 24-h urinary calcium excretion was 22.08 (2.50-7.50 mmol/24hs) whereas, urine calcium creatinine ratio (UCCR) was 0.023, diagnostic of PHPT. Imaging was limited to Ultrasound Neck and KUB. No parathyroid adenoma or renal calculi. She was referred to the regional tertiary centre where she underwent parathyroid exploration with left superior parathyroidectomy at 16 + 4 weeks, in view of severe hypercalcemia. Intraoperatively PTH dropped (310 to 22 pmol/l) with Calcium returning to normal (2.3mmol/l) post-operatively indicating cured PHPT. Histopathology revealed parathyroid lipoadenoma.
Discussion
Normal changes to Calcium homeostasis in pregnancy such as reduction PTH may render PHPT diagnosis challenging. The high transplacental transfer of calcium (mediated by PTH-rP), although may confer some protection against hypercalcemia, can cause diagnostic delays by masking hypercalcemia. Hypercalcemia increases risks of miscarriage, preeclampsia, and neonatal hypocalcaemia. Definitive management is surgical, ideally in second trimester to minimize risks of miscarriage and preterm labour. Conservative measures may be considered in mild cases (Calcium <2.85 mmol/l). Multidisciplinary coordination between endocrinology, endocrine surgeons and obstetrics is essential for optimal outcomes.
Conclusion
UCCR is not reliable in distinguishing PHPT from FHH, and where FHH is a strong possibility, genetic testing should be arranged. In pregnancy, PHPT is a biochemical diagnosis. Imaging is for guiding surgical approach and not for diagnostic purposes.

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P270

Beyond primary hyperparathyroidism: exploring physiologic PTH dynamics

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Introduction
Hypercalcaemia is a metabolic disorder with multiple aetiologies including granulomatous diseases like sarcoidosis. This is a patient with renal sarcoidosis with fluctuating PTH levels following treatment with steroids, illustrating the interplay between steroid therapy and calcium homeostasis.
Case Presentation
A 61-year-old female with background of CKD presented with AKI secondary to severe hypercalcemia (3.8 mmol/l) with PTH of 4.2 (1.6-6.9 pmol/l) and Vit.D of 55(> 50 nmol/l). Phosphate was 2.08mmol/l. After IV fluids and Pamidronate, she was referred to Nephrology and Endocrinology. ACE levels were elevated: 247 (20-70 IU/l). Imaging revealed bilateral axillary and inguinal lymphadenopathy with splenomegaly, but lymph node biopsy excluded lymphoproliferative malignancy. Urinary calcium excretion was elevated (17.44 mmol), with UCCR of 0.12, likely influenced by CKD. USS Neck and SESTAMIBI ruled out parathyroid adenoma. Possibility of renal sarcoidosis considered. As patient was not amenable to renal biopsy, high-dose corticosteroid therapy was initiated following which calcium, ACE levels and renal function normalized. Although the PTH was initially low normal, post glucocorticoids, a fluctuating pattern was seen and showed direct temporal association with dosing adjustments. Whenever the glucocorticoids were increased, the PTH trended up to reach levels as high as 17.2, with low normal calcium, with PTH dropping to normal with down titration of glucocorticoids.
Discussion
Hypercalcaemia in sarcoidosis is primarily driven by extrarenal synthesis of calcitriol by activated macrophages within granulomas, enhancing intestinal calcium absorption. Corticosteroid-induced suppression of calcitriol creates transient functional Vit-D deficiency, lowering calcium. Parathyroids respond physiologically by increasing PTH. This secondary hyperparathyroidism is not pathological but adaptive. This mechanism explains the fluctuations in PTH with steroid treatment.
Conclusion
Corticosteroid-associated suppression of calcitriol can trigger a physiological rise in PTH, leading to secondary hyperparathyroidism. Recognizing this adaptive response is crucial to avoid misdiagnosis of primary parathyroid disease and unnecessary interventions.

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P271

Immune check point inhibitors induced autoimmune diabetes

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Background
Immune-Checkpoint-Inhibitors (ICIs) are novel, ground-breaking cancer agents that mediate T-cell activation via targeting surface "check-point" proteins. An undesirable side-effect is autoimmunity against native tissues, with endocrine organs being affected in 10% of patients receiving this treatment. ICIs can trigger abrupt-onset autoimmune diabetes, typically within 6–25 weeks of treatment initiation, although this remains uncommon ($\leq$1%). Many patients present with Diabetic Ketoacidosis (DKA) (59–86%) and pancreatic autoantibodies may be absent (50%). Early recognition is important due to the severity of the metabolic disturbance.
Case
A 41-year-old man with renal-cell carcinoma received adjuvant pembrolizumab following a left nephrectomy. Within weeks, he presented with osmotic symptoms and hyperglycaemia, leading to a diagnosis of severe DKA and

immune-mediated diabetes secondary to pembrolizumab. There was no previous history of diabetes. Standard diabetes autoantibodies, commonly present in Type-1 Diabetes (T1DM), were negative. He was managed as per standard DKA treatment protocol and was established on a basal-bolus insulin regimen.

Discussion

ICIs utilise the innate immune system to identify and attack cancer cells by activating CD8+ T-cells. Endocrine organs can be involved, with the thyroid and pituitary being the commonest and the adrenals and pancreas the least common. PD-1 inhibitors are the most prevalent in reported cases of ICI-induced diabetes. PD-1 is expressed on effector T-cells in peripheral tissues and dampens their activation against self-antigens. PD-L1 is expressed in islet cells and PD-1 expression is reduced in T-cells of patients with T1DM. HLA-DR4 is the commonest genotype in ICI-induced diabetes. Approximately 50% of patients are positive for ≥ 1 autoantibody, and most have a raised HbA1c on presentation with acute hyperglycaemia. Guidelines (ESMO 2022) suggest random glucose monitoring before each immunotherapy cycle, but real-world data indicate this is not always implemented, highlighting the need to maintain a high index of suspicion for new hyperglycaemia during immunotherapy.

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P272

The effect of Semaglutide (Wegovy) in patients with genetic variants linked to obesity

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Introduction

It is estimated that around 5% of patients with severe (BMI $>40 kg/m^2$) and early onset obesity will have a monogenic cause, commonly within the leptin-melanocortin pathway. Treatment with Setmelanotide is available for POMC or LEPR deficiency only, whereas NHS testing for severe early onset obesity comprises a panel of 33 genes. Society for Endocrinology Guidelines recommend patients with "proven genetic cause of obesity and not eligible for Setmelanotide" should be prioritised for GLP-1 treatment.

Methods

We retrospectively analysed patients within the Somerset Weight management service, with a proven genetic cause of obesity treated with Semaglutide between January 2024 and August 2025.

Results

181 patients were treated with Semaglutide, 12 with a genetic variant (GV) known to cause obesity and 169 with no genetic variant or weren't tested (NGV). Baseline characteristics for the GV and NGV respectively were: 63.6%, 66.8% female, mean age: 35.5 (SD 11.4), 52.5 (SD 14.3), mean weight: 146.4kg (SD 39.3kg), 142.0kg (SD 34.7kg) and mean BMI: $50.3 kg/m^2$ (SD 11), $50.2 kg/m^2$ (SD $10.5 kg/m^2$). Within the GV group 11 and 9 patients had 6 month and 12 data, with mean weight loss of 9.1% (SD 3.9%) and 12.2% (SD 4.6%) respectively. In the NGV group 104/169 had 6 month data and 54/169 12 months data with mean weight loss of 9.5% (SD5.5%) and 13.7% (SD 6.6%) respectively. No patients in the GV group stopped due to side effects and 8.3% stopped within the first 6 months in the NGV group.

Discussion

We have shown that individuals with a genetic variation that is associated with obesity achieve similar weight loss with semaglutide to those without a known genetic variant and is extremely well tolerated. Genetic testing is unlikely to be necessary if an individual meets other criteria for prescribing GLP-1 medication on the NHS.

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P273

High-resolution HPLC–ESI–MS profiling of bile acids and key precursors in human plasma and faeces: a translational tool for endocrine–metabolic phenotyping

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Background

Bile acids are cholesterol metabolites that influence glucose and energy homeostasis via receptors including FXR and TGR5. Translational endocrinology needs robust, isomer-resolving bile acid quantification in clinically relevant matrices.

Aim

To develop and validate a high-resolution HPLC–ESI–MS assay for major bile acids and key precursors, and to demonstrate utility across human and mouse samples.

Methods

An HPLC–ESI–Orbitrap method (negative ion mode) was optimised to quantify 17 bile acids (unconjugated, glycine- and taurine-conjugated) plus two precursors (dihydroxycholestanoic acid and trihydroxycholestanoic acid) using three deuterated internal standards. Sensitivity, linearity and within-/between-day precision and accuracy were evaluated using pooled plasma spiked at four QC levels. The assay was applied to healthy human plasma and faeces and to mouse plasma and tissues. For biological validation, Swiss mice received cephalothin (2 mg/mL) and neomycin (2 mg/mL) in drinking water for 17 days ($n = 10$/group).

Results

Limits of detection (LOD) were 0.05–0.30 nmol/mL and lower limits of quantification 0.1–2.0 nmol/mL, with chromatographic separation of key isomer groups. Precision/accuracy met predefined criteria for 15 analytes across the analytical range. We quantified 11 bile acids in human plasma and faeces; human plasma profiles were dominated by glycochenodeoxycholic acid, chenodeoxycholic acid and cholic acid (~65% of total quantified bile acids). Cross-species profiling showed expected differences: in mouse plasma, taurine conjugates comprised >95% of total bile acids, with taurocholic acid and tauro-β-muricholic acid representing >80%. Antibiotic treatment decreased most unconjugated bile acids (often below LOD) and increased most tauro-conjugated bile acids up to 10-fold in colon and caecal content.

Conclusion

This validated platform enables sensitive bile acid and precursor profiling in human plasma/faeces with complementary mouse data, supporting endocrine–metabolic phenotyping and biomarker work involving dihydroxycholestanoic acid and trihydroxycholestanoic acid in disorders of cholesterol–bile acid metabolism.

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P274

Improving the assessment and recording of body mass index (BMI) in adult inpatients to improve identification of obesity: *a quality improvement project*

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Background

Obesity is a major determinant of inpatient morbidity, length of stay and treatment complexity, with over 1.2 million obesity-related hospital admissions in England each year. Accurate BMI documentation is the gateway to identifying obesity in hospitalised patients. Four medical wards were identified as having the lowest BMI-recording rates in a London hospital, representing a priority area for targeted improvement.

Aim

To improve BMI recording by at least 10 percentage points across four medical wards within 12 weeks.

Methods

EPIC's SlicerDicer enabled automated extraction of BMI completion and classification across baseline, PDSA-1 and PDSA-2 measurement periods. A multidisciplinary root-cause analysis identified alert fatigue, workflow fragmentation and low situational awareness of missing BMI data as key barriers. PDSA-1 implemented passive prompts (posters, computer-station reminder cards). PDSA-2 introduced an active behavioural intervention: a nurse-led five-minute weekly huddle embedded into morning handover, incorporating rapid teaching, role allocation and peer reinforcement. Outcomes were BMI-recording proportion and inpatient obesity prevalence (BMI $\geq 30 kg/m^2$). Proportions were compared using chi-square testing.

Results

Period	Total patients	BMI recorded *n* (%)	Obesity (BMI ≥30) *n* (%)
Baseline	575	358 (62.23%)	89 (17.2%)
PDSA-1	551	343 (62.3%)	92 (26.8%)
PDSA-2	497	391 (78.67%)	114 (22.9%)

PDSA-1 learning directly shaped an improved PDSA-2. BMI recording rose from **62.23% to 78.67%**, a **+16.4-point absolute** and **26% relative improvement** ($\chi^2 = 18.24$; $\mathbf{p = 0.000019}$). The increase in obesity prevalence during PDSA-1 (**17.2% → 26.8%**) reflected case-mix variation, as recording rates were unchanged. Prevalence increased to **22.9%** in PDSA-2 once BMI capture improved, indicating enhanced case-finding. Weekly run charts demonstrated clear special-cause variation emerging only after PDSA-2.

Conclusion
A workflow-integrated, co-designed huddle was markedly more effective than passive prompts, resulting in significant improvements in BMI documentation and obesity identification. This low-cost, staff-owned model provides a scalable approach for embedding obesity recognition within routine inpatient care.

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Metabolic and diabetic phenotype of patients admitted with diabetic foot attack in the West of Scotland

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Introduction
With increased incidence of diabetes, more patients with poor glycaemic control risk diabetic foot attack (DFA) - an acute presentation of diabetic foot disease. DFAs are commonly aggravated by an underlying infection on poorly perfused limb, potentially leading to major limb amputations (MLA). Although a surgical issue, early recognition by allied healthcare may reduce incidence and adverse outcomes. This research aims to understand the diabetic and metabolic profile of a DFA cohort.
Methods
Our retrospective cohort of 94 patients admitted to tertiary care at the Queen Elizabeth University Hospital, Glasgow. Biochemical and clinical data were collected using online patient records. Statistical analysis was performed using R.
Results
94 patients (89.4% male, mean 63.8 years old), 92.6% had type 2 diabetes (T2DM), mean 13 years since diagnosis. 81% had prior documented input from specialist services, podiatry was most common compared to vascular and diabetes. 34.5% of T2DM patients were on oral multi-therapy exclusively, 36.7% on insulin and 14.3% without prior therapy. Average HbA1c was 81.6mmol/mol and admission capillary blood glucose 13.4mmol/l. Mean albumin was 24.9g/l, CRP 142.5mg/l and 27.7% had CKD. 58% had overweight or obese BMI. MLA rate was 35.1% and 30-day mortality 4.1%. Statistical significance for association with MLA was found for albumin (OR 0.81, CI 95% 0.93-1.01) and CRP (OR 1.01, CI 95% 1.00-1.01) at $P < 0.05$, with near significance for CKD (OR 0.42, CI 95% 0.16-1.06) on a univariate level with only albumin standing at a multivariate level.
Conclusions
Our data highlights acute and chronic metabolic influences on DFA, with albumin as a key indicator. Chronically poor glycaemic control with high insulin dependence is characteristic, and although poor patient compliance remains an issue, the real-world applications of our data illustrate the urgency of identifying high-risk individuals, early tertiary referral, and patient education.

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P276

Impact of three edible green leafy vegetables on serum lipid profile and reproductive hormones in hyperlipidemic wistar rats

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Hyperlipidemia refers to a group of inherited and acquired illnesses in which the body's lipid levels are abnormally high. Obesity is a public health concern with its prevalence being significantly greater among women. Being a medical disorder, obesity is associated with metabolic dysfunction. Overweight people tend to develop a resistance to insulin – a hormone that regulates blood sugar levels. This study was therefore aimed at evaluating the ameliorative effect of diets formulated with three different leafy vegetables (*Telfairia occidentalis, Celosia argentia and Amaranthus hybridus*) on hyperlipidemia, a metabolic dysfunction associated with induced obesity in female wistar rats. The phytoconstituents of the vegetables were quantified and the active compounds were identified with Gas chromatography- mass spectroscopy (GC-MS). Thirty-five female wistar rats were completely randomized into 7 groups. Effect of continued feeding with high-fat-diet was observed. All the vegetable-based formulated diets significantly reduced body weight, with *Telfairia* occidentalis producing the most pronounced effect. Serum triglycerides ranged from 0.90–4.48 mmol/l; the HFD + *Telfairia* occidentalis group significantly ($P < 0.05$) lowered triacylglycerol levels, whereas HFD alone elevated them. Serum HDL ranged from 0.08–0.85 mmol/l, with HFD + formulated with three different leafy vegetables (*Telfairia occidentalis, Celosia argentia and Amaranthus* hybridus showing increased levels. In the heart lipid profile, untreated HFD-induced rats showed markedly elevated LDL (0.95–8.43 mmol/l) compared to vegetable-treated and orlistat-treated rats. The HFD + formulated with three different leafy vegetables (*Telfairia occidentalis, Celosia argentia and Amaranthus hybridus* group produced a significant increase in serum insulin ($P < 0.05$). The vegetable diets showed divergent effects on reproductive hormones, with T. occidentalis significantly reducing testosterone and progesterone levels. In conclusion, the formulated feeds had an ameliorative effect on metabolic dysfunctions associated with hyperlipidemia in rats and can therefore be explored in the management of obesity and other diseases related to it.

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P277

Improving safe insulin use and management of hypoglycaemia in diabetic patients- an endocrinology-led quality improvement project

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Background
Hypoglycaemia is a common and potentially life-threatening complication in hospitalised patients with diabetes with increased risk of neurological injury, cardiac arrhythmias, prolonged hospital stay and increased mortality. Initial audit identified failure to comply with trust guidelines, inconsistent documentation and inappropriate aftercare in patients who experienced inpatient hypoglycaemia.
Aims
This quality improvement project aimed to improve compliance with hospital hypoglycaemia guidelines to 70% in 3 months with the secondary objective of increasing adherence to electronic hypoglycaemia proforma created as an intervention to 50%.
Methodology
A baseline audit was conducted with 31 inpatients with hypoglycaemia across medical wards in the County Hospital, Stafford. Key standards assessed included appropriate treatment according to consciousness level, documentation, repeat glucose monitoring and approriate aftercare. Interventions were implemented using Plan–Do–Study–Act (PDSA) cycles, including introduction of an electronic hypoglycaemia management proforma, educational video on the trust intranet, targeted teaching sessions of reminder posters in clinical areas. A re-audit was performed with 37 patients 3 months after implementation to assess impact.
Results
The baseline audit demonstrated suboptimal compliance with trust guidelines, e.g. IV glucose bolus given in 50% patients in unresolved hypoglycaemia in conscious/semiconscious patients who are able to swallow and omitting the next due dose of insuline in 51% of the cases. The overall compliance with the trust guidelines was 33%. Following the interventions, compliance improved significantly to 86% where the new electronic proforma was used and 44% where it was not used. Statistical analysis using Fisher's exact test demonstrated a significant improvement in guideline adherence ($P = 0.016$, 95% confidence interval).
Conclusion
This project demonstrated that simple, low-cost interventions can significantly improve the management of hypoglycaemia in the hospital setting. Sustaining these improvements will require continued education, incorporation of guidelines into staff induction, and ongoing audit cycles to ensure patient safety and high-quality care.

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P278

HDAC5 overexpression induces skeletal muscle atrophy via autophagy-lysosome pathway activation, despite enhanced protein synthesis in mice

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Insulin resistance, type 2 diabetes, and obesity accelerate muscle protein degradation (MPD) via the ubiquitin-proteasome (UPS) and autophagy-lysosome pathways (ALP). Although associations exist between ubiquitin E3 ligases and class IIa histone deacetylases (HDACs), and between elevated HDAC4/5 levels and impaired oxidative metabolism, the precise link between HDAC5 and muscle atrophy remains unknown. In a previous unpublished *in vivo* study, our group showed HDAC5 overexpression for 3 months reduced skeletal muscle mass by ~20%; however, contrary to the hypothesis that atrophy is caused by reduced protein synthesis, these atrophied muscles displayed increased protein synthesis. To better understand these unexpected results and the underlying mechanism of wasting, we investigated the time-dependent effects of AAV-mediated HDAC5 overexpression in mouse skeletal muscle. In this time-course study, HDAC5 overexpression induced muscle atrophy, with significant mass reduction at 4 and 8 weeks and a trend at 2 weeks. Mechanistically, we confirmed a counterintuitive increase in absolute newly synthesized protein at 8 weeks, ruling out protein synthesis inhibition as the primary cause. We found a distinct temporal pattern in the proteolytic pathways: UPS activation was delayed (E3 ligases and protein ubiquitinylation increased only at 8 weeks), failing to account for the early 2-week muscle loss. Crucially, ALP activation was early and dominant: key autophagy markers LC3B-II and p62 were significantly elevated at 2, 4, and 8 weeks post-AAV, strongly correlating with initial muscle mass reduction. Furthermore, increased levels of phospho-AMPKα (Thr172) at 4 and 8 weeks suggest a potential role for AMPK signalling in the HDAC5-induced ALP activation. In conclusion, HDAC5 overexpression induces rapid skeletal muscle atrophy through the early and sustained activation of the ALP. This suggests ALP activation is the initial and dominant mechanism responsible for HDAC5-induced muscle atrophy. Further investigation is needed to define the precise regulation between HDAC5 and the AMPKα/ALP axis.

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P279

Prevalence of fatty liver among diabetes vs non diabetes population with obesity awaiting bariatric surgery- a tertiary care center experience in Sri Lanka

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Type 2 diabetes mellitus and obesity are well-known risk factors for non-alcoholic fatty liver disease (NAFLD). The purpose of our study was to compare the prevalence of NAFLD in obese patients awaiting bariatric surgery between those with and without diabetes. 245 people who underwent Bariatric surgery from 2013 to 2022 at Colombo South Teaching Hospital, Sri-Lanka, were retrospectively analyzed for the presence or absence of diabetes and hepatic parameters indicating FL, including liver transaminases and ultrasonography evidence. 109 (44.4%) had diabetes, of them 31% were males, 69% were females, mean age was 40.6±10.2, mean weight was 115.8 kg ±24.4(range 75-204), mean BMI was 45.4kg/m2 ±7.4 (range 31.2-68.1), mean fasting plasma glucose (FPG) was 140mg/dl, and mean HbA1c was 8.5%. 84 were on oral hypoglycemics and 24 were on insulin. 136 (55.6%) of pre-bariatric surgery population had no diabetes. Mean age was 34.3years±9.9 (range of 15-57). Majority (73%) were females. Mean weight and mean BMI were 121kg+/-45.3 and 45.6kg/m-2, respectively. Mean FPG was 95mg/dl and mean HbA1c was 5.5%. Diabetes group had mean AST of 35u/l±20.7 among females and 39.1u/l±18.4 among males, mean ALT was 45±27.3u/l in females and 48.8±21.4 u/l in males. Non diabetes group had AST of 22±13.1 u/l among females and 29.3±13.2u/l among males with a mean ALT of 32±22.8 u/l for females and 37.6±21.2u/l for males. 88% of diabetes group had FL on ultrasonography, (grade 1 in 34%, grade 2 in 60% and grade 3 in 6.2%). Non-diabetes group had FL among 57% (grade 1 in 54%, grade 2 in 42% and grade 3 in 4%). Results indicate, obese pre-operative bariatric surgery population with T2DM has high prevalence of NAFLD compared to non-diabetes population as evident by both raised liver transaminases and ultrasonography.

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P280

Metabolic threat, obesity identification, and diabetes perception gaps among nurses: first national research survey in Pakistan

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Background
Metabolic diseases/non-communicable diseases (NCDs) particularly obesity & diabetes producing grave burden for the country's healthcare with 33% of population living with diabetes in Pakistan. Nurses' perception, understanding, and recognition of metabolic risks including diabetes and obesity may be enormously inadequate. No national-level evaluation has thoroughly examined these differences in nurses' perceptions in Pakistan.
Objective
The purpose of this study was to evaluate the knowledge, perception, and identification practices of nurses in Pakistan about obesity and diabetes to identify important professional and demographic aspects linked to perception gaps.
Methods
A nationwide cross-sectional survey design recruiting graduate nurses using a validated self-administered questionnaire to gather data of perceptions regarding obesity, diabetes, and lifestyle modification. After ethical approval & consent obtained, data was assessed using descriptive statistics, SPSS & inferential methods.
Results
A total 0f 1% graduate nurses across country from 62 cities responded. The significant gaps in the understanding of diabetes risk markers, the acknowledgment of obesity as a metabolic danger, and the perception of lifestyle-related preventative methods were identified. Perception gap scores were found to be significantly correlated with clinical experience, qualification level, employment environment, and previous exposure to metabolic health training ($P < 0.05$).
Conclusion
The first nationwide survey of its kind in Pakistan revealed marked gaps in nurses' perceptions and knowledge of metabolic risks, obesity detection, and diabetes risk awareness. In clinical practice these gaps make it more difficult to effectively prevent and manage NCDs. The results highlighted the critical need for organized training programs, improved curriculum integration, and national awareness campaign which led to implementation of First Nurse-Led 8-week Diabetes Care Course. As a fundamental aspect of nursing competencies in Pakistan, metabolic health should be given top priority in future policies and practice guidelines.

Keywords
Metabolic threats, Obesity identification, Diabetes perception, Nurses, National survey, Pakistan, Non-communicable diseases.

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P281

A case report illustrating the limited sensitivity of the oral glucose tolerance test (OGTT) in pregnancies following bariatric surgery

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The current NICE guidelines outline testing for Gestational Diabetes Mellitus (GDM) via two different pathways: self monitoring glucose and two 75g 2-h OGTTs in women identified as high risk for GDM. The first of these takes place immediately after their first booking and the second between 24 - 28 weeks. Pregnant women who have undergone bariatric surgery often have delayed gastric emptying and absorption which will interfere with the traditional OGTT and the testing values of glucose. We present a case of a late diagnosis of GDM in a 33 year old Caucasian female who underwent sleeve gastrectomy a decade ago. Her booking BMI was 39 kg/m2. Based on this BMI she would be a GDM risk. The booking HbA1c was 32 mmol/mol. She successfully passed the recommended OGTT at 24-28 weeks. However, on further investigation via blood glucose monitoring at home, she was found to have unusually high fasted glucose >9 mmol/l and 1 h post-prandial blood glucose levels >8 mmol/l, indicating GDM. Her fetal scans did not indicate any evidence of macrosomia or placental insufficiency. She was started on metformin 500mg BD and glucose monitoring at home became within pregnancy target range. This case highlights the lack of sensitivity of OGTT in post bariatric surgery pregnancies and therefore increases risks associated with untreated GDM on maternal/fetal health and pregnancy outcomes. The NICE recommended OGTT had not been successful in identifying this patient's gestational diabetes mellitus. The implications of this late diagnosis suggest that current guidelines are not adequate at diagnosing GDM in post-bariatric surgical patients. This results in under diagnosis and subsequent lack of treatment, which may ultimately result in poorer patient health outcomes. We propose post bariatric surgery pregnancies to be tested with regular glucose monitoring and to base treatment on home monitoring results.

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P282

When enough may not be enough: a case of hyperhomocysteinemia

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Introduction
Hyperhomocysteinemia (HHcy) is a metabolic disorder with cardiovascular, thromboembolic, and ocular complications. Nutritional deficiencies and renal impairment are common causes. HHcy without these should prompt investigation for re-methylation disorders/cystathionine β-synthase (CBS) deficiency.
Case Presentation
A 42-year-old male detected with HHcy during evaluation for CRVO. Plasma homocysteine was 62.2 (0–15 μmol/l). Vit.B12 was normal, but serum folate (3.8 μg/l) although within reference range, was below therapeutic target (>6 μg/l) recommended for HHcy. LDL was 4.1 with HDL 0.9 mmol/l. Liver, thyroid and renal function normal. He was given folic acid to meet therapeutic target. Repeat homocysteine was 27.3 μmol/l post folate supplementation with normalization of homocysteine and resolution of biochemical abnormalities. Genetic testing was planned.
Discussion
Homocysteine metabolism intersects with one carbon metabolism, methylation pathways, and amino acid homeostasis through re-methylation (requiring folate and vit.B12 and trans-sulphuration to cysteine, catalysed by CBS and requiring vit.B6. Hypothyroidism and insulin resistance can interfere with hepatic methylation leading to HHcy. Even biochemically euthyroid individuals with impaired thyroxine sensitivity can develop HHcy due to impaired re-methylation. Thyroxine replacement reduces homocysteine levels and in combination with folate offers superior therapeutic benefits. The most common genetic cause of HHcy is homozygosity for *MTHFR* 677C→T variant. Homozygotes develop raised homocysteine when serum folate is low. Even folate levels within normal range may be insufficient for optimal re-methylation in patients with MTHFR polymorphisms. Hence therapeutic folate targets (>6.8 μg/l) are recommended. In our case, folate supplementation led to a marked reduction in homocysteine from 62.2 to 27.3 μmol/l, confirming the critical role of optimized folate status.
Conclusion
This highlights the importance of considering genetic causes in adults with HHcy. Systematic evaluation, genetic testing, and coordinated metabolic follow-up are key to optimizing outcomes in these rare but treatable disorders.

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P283

Virtual follow-ups: are these impacting the quality-of-care patients with diabetes mellitus receive? an audit

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Introduction
All patients 12-years-old and above with diabetes mellitus should receive the 9 care processes recommended by National Institute for Health and Care Excellence (NICE) annually. This is because it can reduce risks of complications or detect them earlier. The 9 parameters include HbA1c, blood pressure, cholesterol, retinal screening, feet examination, urine albumin creatinine ratio, creatinine, weight and smoking status. Since the Covid-19 pandemic, many consultations were moved to telephone/video calls. This begged the question of whether patients were still receiving all the care processes despite not having face-to-face consultations. Hence, an audit was done in a district general hospital to determine if all appropriate patients with diabetes were receiving the care processes.
Methods
Data was collected retrospectively from December 2022 till January 2023 over a 6-weeks period involving 3 consultants' clinics using letters from the trust's electronic health records. Sample size was 108 – 60 patients had type 1 diabetes, 43 type 2, and 5 had diabetes due to miscellaneous causes.
Results
Amongst the 108 patients, 7 patients only had telephone consultations in the previous 18-24 months; the rest had mixtures. Only 14 out of 108 patients had all parameters checked; 44 had eight out of nine checked (42 did not have smoking history documented, 2 did not have retinal screening mentioned).
Discussions
Majority of the patients did not receive all nine care processes. Virtual consultations could have contributed as it could be harder for clinicians to address some of the parameters during such consultations, for example, feet examination. There is also a possibility that doctors in hospitals are assuming Primary Care is addressing them and therefore prioritise less on these parameters during the virtual consultations. Hence, there is also a need to create awareness of addressing all these care processes annually, irrespective of virtual or face-to-face consultations.

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P284

Diagnostic delay: pulmonary cryptococcus masking an ACTH-secreting pulmonary carcinoid

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Background
Ectopic ACTH secretion leading to Cushing's syndrome poses major diagnostic challenges, particularly when the source is obscured by co-existing pathology. Pulmonary cryptococcosis though uncommon, is an important infectious mimic of malignancy in immunocompromised states. Distinguishing infection-related nodules from an ACTH secreting lesion is essential, yet often delayed due to overlapping features.
Case report
A 47-year-old man with type 2 diabetes, hypertension and progressive Cushingoid features was found to have ACTH-dependent hypercortisolism (cortisol 700-800nmol/l, ACTH 632-156ng/l) with failure to suppress on overnight dexamethasone testing. Inferior petrosal sinus sampling confirmed ectopic ACTH secretion and metyrapone was commenced. Ga^{68}DOTATATE PET/CT demonstrated a cluster of left lower lobe nodules with low-level uptake. FDG-PET/CT prompted by neuroendocrine MDT, revealed 3-4 cavitating FDG-avid nodules. Biopsy showed dense inflammatory change consistent with fungal infection, and serology supported pulmonary cryptococcosis. Fluconazole was initiated, but subsequently symptomatic hypocortisolism occurred, likely due to a synergistic drug interaction, requiring block-and-replace therapy. Over subsequent months, lung parenchymal changes regressed and cryptococcal antigen titres fell from 1:32 to negative. However, interval CT revealed new soft tissue foci in the anterior mediastinum, prompting further MDT review. Follow-up imaging identified a distinct basal left lower lobe nodule that had enlarged with moderate DOTATATE uptake, in contrast to the regressing infection-related nodules. CT-guided biopsy confirmed a typical pulmonary carcinoid tumour (synaptophysin+, chromogranin+, CD56+), establishing the ACTH-secreting primary. Surgical resection planned.
Discussion
This case highlights diagnostic complexity of ectopic Cushing's syndrome. Pulmonary cryptococcosis may obscure or mimic the radiological appearance and metabolic activity of an underlying neuroendocrine tumour. A coordinated multidisciplinary approach, supported by serial imaging and targeted histopathology was essential in establishing a pulmonary carcinoid tumour. Clinicians should retain a high index of suspicion for dual pathology in ectopic Cushing's syndrome, as overlapping processes can substantially delay accurate localization and timely management.

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P285

Safety and tolerability of SGLT2 inhibitor in patients with arginine-vasopressin deficiency

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Sodium-glucose co-transporter-2 inhibitors (SGLT2i) are used therapeutically in type 2 diabetes (T2DM), cardiovascular and renal disease. SGLT2i reduce the risk of cardiovascular events, kidney disease progression and hospitalisation for heart failure. A transient osmotic diuresis is expected on initiation. The safety of initiating SGLT2i in patients with arginine-vasopressin deficiency (AVP-D) remains unexplored. Few case reports have cautioned against its use due to risk of hypernatraemia and dehydration. We report a case series of eight patients with AVP-D initiated on SGLT2i under close supervision and their medium-term outcome. All patients (M:F,1:1) were established on desmopressin therapy

(DDAVP) for AVP-D due to sellar($n = 3$), suprasellar($n = 3$) or intracranial($n = 2$) tumours. Indications for SGLT2i therapy were: T2DM($n = 7$) and heart failure($n = 1$). On initiation with oral dapagliflozin 10mg daily, patients monitored their daily weights for a week and reported any osmotic symptom or dehydration (>5% weight loss). Serum biochemistry was checked before and a week after initiation. Data is expressed as median(range). There was no change in weight, serum sodium and urea after a week: 93(72-108) vs. 93(72-110)kg, 138(126-143) vs. 138(132-145)mmol/l and 4.7(2.1-10.7) vs. 4.7(2.6-8.6)mmol/l, respectively. One patient with adipsic AVP-D required an increase in obligate daily fluid intake from 1L to 1.2L due to acute weight loss. 3/8 patients experienced polyuria. Two were managed with uptitration of DDAVP. One patient chose to stop SGLT2i due to developing concurrent vaginal thrush. For the seven patients who were stabilised on SGLT2i there was no incidence of electrolyte imbalance, diabetic ketoacidosis or hospital admission due to osmotic decompensation over a median 13(6-36) months. HbA1c, serum sodium and creatinine remained stable during follow-up. Our data supports the use of SGLT2i in patients with AVP-D under close supervision on initiation. Medium-term data is reassuring.

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P286

Effectiveness of new generation incretin-based therapies in hypothalamic obesity: a single centre real-world experience

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Hypothalamic obesity (HO) is usually caused by hypothalamic damage from treatment of sellar/suprasellar tumours. Therapeutic options have been limited. Emerging evidence on the efficacy of new generation glucagon-like peptide-1 receptor agonists or dual agonist (GLP1RAs) is promising. We report our experience of GLP1RAs in patients with HO. 15 patients were offered GLP1RAs but only 13 were included in this retrospective analysis (two excluded due to medication non-adherence and side effect requiring cessation). Of 13 patients (M:F=7:6), over 60% were established on at least four pituitary hormonal replacements and 11 out of 13 patients had type 2 diabetes. GLP1RAs used were: Mounjaro®(6), Rybelsus®(5), Ozempic®(1) and Trulicity®(1). Doses were uptitrated based on tolerability and patient preference. Data is expressed as median(range). Paired student's t-test was used for statistical analyses between continuous variables. At start of GLP1RAs, median age was 44(17-67) years and BMI 44(27-70) kg/m^2. Over a median follow-up of 18(6-40) months, baseline weight, BMI and HbA1c dropped by 22(6-67) kg, 7(2-29) kg/m^2 and 16(1-70) mmol/mol respectively ($P < 0.05$). Most patients were on less than maximal licensed dose of Mounjaro® or equivalent dose of Ozempic®. There was a 17(8-41) % weight loss from baseline ($P < 0.05$). For the eight patients with medium-term data beyond 12 months, a plateau in weight loss was observed. Unfasted untimed total serum cholesterol, non-HDL cholesterol and triglycerides dropped by 23(2-47) % from 5.1(3.7-9.2) mmol/l, 38(3-66) % from 4.1(2.9-8.2) mmol/l and 39(50-78) % from 2.7(1.1-8.1) mmol/l respectively ($P < 0.05$). There was no significant change serum HDL cholesterol. GLPRAs at submaximal doses induce durable clinically significant weight loss in patients with HO and offers a promising treatment strategy.

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P287

Clinical outcomes following supply-driven transition from intranasal to oral desmopressin in AVP-deficiency- a single centre experience

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Introduction
Arginine vasopressin deficiency (AVP-D) requires lifelong desmopressin replacement. In March 2025, the national suspension of intranasal desmopressin necessitated urgent transition to oral alternatives. However, optimal conversion ratios and clinical response remain undefined. We evaluated clinical outcomes following this supply-driven transition.

Methods
A retrospective review at a tertiary UK centre (01/01/2025 – 01/07/2025) identified patients with confirmed AVP-D switched from intranasal to oral desmopressin. Demographic and clinical data were collected. Conversion ratios (intranasal: oral) were calculated before and after titration.
Results
2 patients were included (mean age 52.6±2.3; 31% male). 15/42 (35.7%) isolated AVP-D; 11/42 (26.2%) partial hypopituitarism; 16/42 (38.1%) panhypopituitarism. Median intranasal desmopressin dose pre-switch was 10 mg/day (IQR 10 – 20). Initial median oral dose before titration was 200 mg/day (IQR 100 – 200); final median oral dose of 200 mg/day (IQR 162.5 – 300) after titration. 23/42 (54.8%) were switched initially using 1:10 ratio (10 mg intranasal desmopressin to 100mg oral tablet). 13/23 (56.5%) reported symptomatic recurrence, warranting further titration. The remaining 19/42 (45.2%) were switched initially using a median ratio of 1:20 (IQR 1:11.8 – 1:20). 10/19 (52.6%) reported symptomatic recurrence. Overall, switching from intranasal to oral desmopressin resulted in 16 patient calls, 79 additional blood tests and one hospitalisation.
The Pituitary Foundation's Desmopressin Shortage Impact Report:
A national survey ($n = 224$) by The Pituitary Foundation found that most patients (75.2%) previously using intranasal desmopressin experienced poorer symptom control post-switch and nearly half (47.2%) required additional endocrine input, highlighting substantial patient and healthcare burden due to this shortage.
Conclusion
Only 45% (19/42) of patients achieved adequate symptom control post-switch, suggesting insufficient initial conversion ratios. A ratio closer to **1:15** may reduce symptomatic recurrence and subsequent dose titrations, although inter-patient variability necessitates tailored titration. This supply-driven switch increased clinical burden, highlighting the need for standardised guidance and prospective studies.

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P288

Silent corticotroph adenomas – experience at a single pituitary centre

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Introduction
Silent corticotroph adenoma (SCA) is a subtype of clinically non-functioning adenoma (NFA) that shows immunohistochemistry characteristics of an adrenocorticotropic hormone secreting adenoma without biochemical or clinical manifestation of hypercortisolism. Some reports suggest a more aggressive clinical course in comparison to NFA. We analysed our experience with SCA between 2016 and 2025.
Results
There were 24 patients in the study: 12 men and 12 women. Mean age at presentation was 44 years, range 22-76. Majority presented to acute/emergency services or ophthalmology ($n = 15$; 62.5%). Most patients presented with visual disturbances ($n = 17$; 70.1%). 16 had evidence of visual field loss at presentation (66.7%) and 3 (12.5%) had cranial nerve involvement. 10 had hypopituitarism at presentation (41.7%), and post-operatively 12 (50%) were hypopituitary. All had macroadenoma, maximum dimension 10 mm or more; mean 25.2 mm (range 10 to 50 mm). All had suprasellar extension. Optic chiasm compression was evident in 17 (70.1%), a further 3 had chiasm elevation without compression (12.5%). In all, 20 (83.3%) had chiasm involvement of some description. 3 had complications – 1 each had post-operative CSF leak, bleeding and meningitis. Of the 17 with visual disturbance, 12 (70.1%) recovered vision partially or fully. Histology was consistent with SCA; all cases staining for ACTH and in more recent reports T-Pit, synaptophysin, cytokeratin and Ki-67 index were available. 4 patients had Ki-67 index between 5-8%, and of these 2 required radiotherapy due to rapid re-growth.
Conclusion and discussion
In our series, 70% of cases presented with acute visual disturbance and 41% had evidence of hypopituitarism at presentation. 83% of cases had optic chiasm involvement. 70% of patients recovered vision post-surgery. This data adds to the existing evidence base of this distinct subtype and underscores the need for prospective studies looking at their long-term clinical course and prognosis.

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P289

Sheehan's syndrome without massive haemorrhage: importance of recognising subtle postpartum hypopituitarism

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Introduction
Sheehan's syndrome results from postpartum pituitary infarction and is typically associated with major obstetric haemorrhage. However, pituitary injury may also occur with moderate blood loss or perioperative hypotension, leading to subtle postpartum presentations that may delay diagnosis.
Case Presentation
A 42-year-old woman presented eight weeks postpartum following an emergency caesarean delivery of twins at 32+3 weeks. The estimated blood loss during the surgery was 1.5L. She experienced one episode of intraoperative hypotension (SBP 60) which resolved with intravenous fluids; no transfusion or vasopressors were required. She first presented to her GP with lethargy, cold intolerance, reduced appetite and blurred vision and was found to have a cortisol of 56 nmol/l. On admission, she had a blunted response on Short Synacthen test (baseline cortisol 52 →155 → 218 nmol/l) with suppressed ACTH (<1.5 ng/l). Thyroid function demonstrated secondary hypothyroidism [FT4 (7.6 pmol/l) and TSH (0.05 mU/l)]. Gonadotropins were low (FSH 2 IU/l, LH <1 IU/l) with oestradiol <90 pmol/l. Her IGF1 was low (2.6nmol/l). Prolactin and electrolytes were normal. Initially pituitary MRI was reported as normal, but a second review by specialist neuroradiologist identified uniform increased T2 signal and non-enhancing central pituitary tissue with peripheral rim enhancement, consistent with non-haemorrhagic adenohypophyseal infarction in keeping with Sheehan's syndrome. She was treated with hydrocortisone (100 mg IV loading, then 50 mg QDS, stepped down to maintenance 10–10–5 mg daily), followed by levothyroxine 50 μg daily. Outpatient endocrine follow-up was arranged at discharge.
Discussion
This case highlights early Sheehan's syndrome in the absence of massive postpartum haemorrhage. Transient hypotension may have contributed to pituitary hypoperfusion, with biochemical and MRI findings confirming evolving hypopituitarism.
Conclusion
Sheehan's syndrome should be considered in postpartum women with non-specific symptoms and central hormone deficits, even in relatively uncomplicated parturition.

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P290

An atypical presentation of a giant prolactinoma with temporal lobe oedema and seizure: a case report

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Background
Giant prolactinomas are rare pituitary adenomas with markedly elevated prolactin levels that can present with diverse neurological and endocrine manifestations. This case highlights an atypical presentation with acute neurological symptoms.
Case
A 52-year-old male presented with an episode of LOC and a generalised seizure, followed by post-ictal confusion with amnesia. An MRI of the head and pituitary demonstrated a large sellar fossa and left middle cranial fossa mass measuring 5.3 × 3.8 × 3.1 cm, causing chiasmal compression and extending into the left cavernous sinus and involving the cavernous segment of the ICA, with associated left temporal lobe oedema. He was commenced on levetiracetam and dexamethasone. Further history revealed reduced libido, and examination showed left temporal visual field loss. His pituitary profile demonstrated marked hyperprolactinaemia (prolactin 177,390 mU/l) and hypopituitarism: testosterone 1.1nmol/l, free testosterone 44pmol/l, LH 2.3 U/l, FSH 4.6 U/l, SHBG 8 nmol/l, free T4 7.2pmol/l, TSH 0.36 mU/l, IGF-1 35.3 nmol/l, OGTT showed a nadir GH of 0.1μg/l and cortisol 16 nmol/l (while on dexamethasone). He was switched to hydrocortisone and commenced on cabergoline 500 mg twice weekly, increased to 500 mg OD, as well as testosterone and levothyroxine. After six weeks, his prolactin level reduced substantially to 1,055 mU/l, and MRI of the pituitary showed a decrease in tumour size.
Discussion
The patient's acute neurological presentation was attributed to mass effect from the macroadenoma, with temporal lobe oedema. The unilateral visual field defect reflects asymmetric tumour extension. Cabergoline is a first-line medical therapy with high rates of prolactin reduction and tumour shrinkage.
Conclusion
This case highlights the importance of considering pituitary pathology in patients presenting with seizures and visual field defects. Although rare, giant prolactinomas are highly responsive to dopamine agonist therapy, and early recognition leads to excellent outcomes.

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P291

Evolving multisystem immune-related adverse events after pembrolizumab

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Background
Anti-PD-1 immune checkpoint inhibitor, Pembrolizumab, boosts T-cell activity against cancer cells and treats various solid tumours[2]. It can cause immune-related side-effects including multiple endocrinopathies (thyroid dysfunction, hypophysitis, adrenal insufficiency, and immune-mediated type-1-diabetes)[1]. The case below demonstrated multiple endocrinological toxicities, with transient gonadal axis dysfunction.
Case
A 57-year-old man, known type-2-diabetes and metastatic renal cell carcinoma developed diabetic ketoacidosis (DKA) two weeks after pembrolizumab. His diabetes has been reclassified as immune-mediated type-1 evidenced by impaired β-cell function: insulinpenia (<7μIU/mL), suppressed C-peptide(<50pmol/l), and positive anti-GAD antibodies. Endocrinology evaluation showed hypogonadotropic hypogonadism, but other anterior pituitary hormones were normal. MRI(Pituitary) showed mild stalk thickening. DKA resolved on insulin therapy. Spontaneous recovery of the gonadal axis was observed in two weeks. Four weeks later, he developed severe diarrhoea with elevated faecal calprotectin (> 2000μg/g), endoscopic evidence of immune-mediated mild colitis, prompted pembrolizumab. discontinuation. His symptoms resolved without treatment. Over next two months, he presented with recurrent hypoglycaemia despite reducing insulin doses, and hyponatraemia (Na125mmol/l). His endocrinology evaluation revealed low cortisol (76nmol/l), high TSH (47mIU/l) with undetectable free T4 (<3 .2pmol/l). He was diagnosed as adrenal insufficiency with primary hypothyroidism. Hypoglycaemia resolved with steroid replacement followed by levothyroxine. However, he developed moderate pericardial effusion which also resolved with thyroid hormone optimisation. Repeat tests showed ACTH deficiency (ACTH 3ng/l, cortisol 59nmol/l). He showed good clinical response on Hydrocortisone, levothyroxine, and insulin therapy.
Conclusion
This case illustrates complex and evolving pattern of multisystem immune-related adverse events following pembrolizumab, including new-onset type1 diabetes, immune-mediated colitis, delayed isolated ACTH deficiency, and severe primary hypothyroidism. Despite breadth of toxicity, he achieved good clinical stabilisation with appropriate immunotherapy cessation and targeted hormonal replacement.
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P292

Insulinoma arising from ectopic pancreatic tissue: a rare hepatic presentation of functional metastatic NET causing hypoglycaemia

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Background
Insulinomas are rare pancreatic neuroendocrine tumours (pNETs), with over 99% arising within the pancreas. Ectopic insulinomas account for ~1% of cases and are diagnostically challenging due to atypical anatomical locations. Hepatic ectopic insulinomas are exceptionally uncommon, with only isolated cases reported.
Case Presentation
A 77-year-old woman presented with recurrent fasting-related hypoglycaemia, characterised by confusion, sweating, and loss of consciousness, all resolving with

glucose (Whipple's triad). A supervised 72-h fast confirmed endogenous hyperinsulinemia with markedly elevated insulin, C-peptide, and proinsulin levels and suppressed beta-hydroxybutyrate. Sulfonylurea screening was negative. CT and MRI revealed multiple bilobar hepatic lesions but no definite pancreatic mass. Ga-68 DOTATATE PET-CT demonstrated an intensely avid right mesenteric mass with multiple liver metastases and no further SSTR-positive disease. MRI pancreas showed chronic pancreatitis with coarse calcifications but no discrete tumour. Liver biopsy confirmed a well-differentiated Grade 2 neuroendocrine tumour (Ki-67 4%), positive for synaptophysin, chromogranin, and CD56. Diazoxide and dexamethasone were initially used for hypoglycaemia control but were discontinued due to hyponatraemia and progressive oedema. Octreotide was commenced, initially subcutaneously three times daily, then transitioned to Octreotide LAR 30 mg monthly. Following this, hypoglycaemic episodes completely resolved, with significant functional improvement and gradual weight regain. She remained independent with support and exhibited no symptoms of carcinoid syndrome. The HPB multidisciplinary team deemed the disease inoperable.

Discussion

Ectopic insulinomas most commonly arise from duodenal or gastric ectopic pancreatic tissue; hepatic origin is extremely rare. Advanced molecular imaging—including DOTATATE and GLP-1R–targeted Exendin PET—is invaluable in localising functional NETs when pancreatic imaging is inconclusive.

Conclusion

This case highlights the complexity of diagnosing ectopic insulinoma and the essential role of multimodal molecular imaging in guiding management.

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P293

Predicting the long-term outcome of pituitary tumours revisiting the histopathology

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Case 1

A 27-year-old female presented with blurry vision and was diagnosed with a non-functioning pituitary adenoma. She underwent transsphenoidal resection in 2017 with null cell adenoma histology. She developed post-operative hypopituitarism requiring Hydrocortisone, Levothyroxine and HRT. In 2019 she had another surgery for tumour regrowth and histology revealed a sparsely granulated somatotroph adenoma. The genetic test showed AIP-related familial isolated pituitary adenoma. Her residual tumour has since remained stable, and she is well-controlled on Somatostatin analogue

Case 2

A 76-year-old female underwent two pituitary surgeries (1998, 2007) followed by radiotherapy for a non-functioning pituitary adenoma. A thyroidectomy was also performed for hyperthyroidism many years ago. During a follow up, MRI scan showed interval enlargement of residual pituitary tissue. Progressive bilateral superior temporal visual field defects led to a third surgery for resection of a supradiaphragmatic sellar mass resulting in significant visual improvement. Histology showed thyrotroph adenoma.

Case 3

A 72-year-old female had surgery for a non-functioning pituitary adenoma in 1989, followed by radiotherapy for progression. She developed hypopituitarism, that was managed with Hydrocortisone and Levothyroxine. In 2021, a new left temporal hemianopia led to MRI scan. This confirmed tumour regrowth that was followed by a repeat endoscopic resection. Histology showed sparsely granulated growth hormone adenoma with focally high Ki-67. Patient was commenced on Lanreotide and has achieved an excellent control.

Conclusion

These cases highlight the prognostic value of histopathology in predicting disease recurrence and progression. Sparsely granulated somatotroph adenomas and other Pit-1 lineage tumours are associated with more aggressive clinical behaviour.

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P294

Central diabetes insipidus in association with SARS-CoV-2 infection: a rare postinfectious pituitary complication

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COVID-19 is an acute respiratory viral illness with associated long-term, multisystem effects. Known pituitary complications include hypopituitarism, pituitary apoplexy, and SIADH. Central diabetes insipidus (CDI), however, remains a rarely described consequence. A 44-year-old woman presented with typical CDI symptoms developing two weeks following symptomatic COVID-19 infection, including polydipsia, nocturia, and polyuria of 9.1L per day. Initial investigations demonstrated a normal serum sodium (142mmol/l), but a raised serum osmolality (300mmol/kg) and low urine osmolality (113mmol/kg) consistent with CDI. A water deprivation test confirmed the diagnosis, with normal serum osmolality (291mmol/kg), high urine output (470mL/hr), and low urine osmolality (120mmol/kg) at baseline progressing to a raised serum osmolality (304mmol/kg) with submaximal urine osmolality (373mmol/kg) and urine output (135mL/hr). A 2.3kg weight decrement was also observed. 2µg of intravenous desmopressin was administered, which achieved an increase in urine osmolality (604mmol/kg) and sodium (96mmol/l), reduction in urine output (30mL/hr), and normalisation of serum osmolality (284mmol/kg). MRI pituitary was unremarkable, with no focal lesions or pituitary stalk thickening identified. Desmopressin was commenced at 100µg orally twice daily, but later uptitrated to three times per day due to persistent interdose polyuria. This demonstrates the importance of awareness of potential pituitary complications following COVID-19 infection, including CDI. Given the association with other pituitary pathology, a full pituitary profile should be performed in these patients. Desmopressin appears to be an efficacious treatment in COVID-19 associated CDI, but requires titration based on clinical response.

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P295

Idiopathic lymphocytic hypophysitis presenting with isolated AVP deficiency in a woman of non-reproductive age group

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Background

Lymphocytic hypophysitis (LyH) is a rare autoimmune endocrinopathy. It is more common in peripartum women classically presenting with mass effect symptoms, hyperprolactinemia and symptoms of adenohypophyseal/neurohypophyseal involvement characteristically sparing the posterior pituitary. It is uncommon in the elderly, in whom it can present differently causing diagnostic dilemmas.

Clinical Case

A 68 year-old-woman presented with polydipsia, polyuria, xerostomia and weight loss since 3 weeks and had no headache or visual symptoms. She appeared dehydrated and hypernatremic with a serum Sodium level of 152 mmol/l (133 -146 mmol/l). Other routine blood tests were normal.Further biochemistry showed Serum Osmolality of 313(275-295 mosmol/kg) and Urine osmolality of 92(50-1200). Water deprivation test under close supervision, confirmed AVP-D. She responded well to Desmopressin. Prolactin was 810(109-557 mu/l). The rest of the pituitary hormones were normal. MRI pituitary fossa revealed 11 mm enhancing sellar lesion with thickened enhancing infundibulum suggestive of LyH. There was no history of malignancy, autoimmune/infiltrative/inflammatory disorders or immunotherapy which could have triggered LyH. Connective tissue screen, ACE levels, and tumor markers were negative. She awaits Respiratory input as her CT showed mediastinal lymphadenopathy with lung changes. Pituitary MDT outcome was that of hypophysitis rather than a mass lesion. Interval scan in 3 months' time showed resolving hypophysitis.

Discussion

This is an atypical presentation of LyH and reinforces the importance of a multidisciplinary approach when dealing with a vaguely understood entity like LyH in order to avoid unnecessary diagnostic dilemmas and overzealous treatment. LyH is often self-limiting, but can lead to permanent endocrine deficiencies. Careful observation is warranted with hormonal replacement where indicated.

Conclusion

This is a rare and atypical presentation of LyH in a woman of non-reproductive age group with no pre-existing autoimmune or infiltrative pathology, presenting with isolated AVP deficiency.

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P296

Atezolizumab-associated isolated ACTH deficiency with concomitant primary hypothyroidism

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Immune checkpoint inhibitors (ICIs) are now integral to modern oncology treatments but could be associated with a spectrum of immune-mediated endocrine toxicities. Isolated ACTH deficiency is a recognised yet infrequent complication of PD-L1 inhibitors such as atezolizumab and may emerge following completion of treatment, highlighting the need for ongoing endocrine surveillance. Primary hypothyroidism is another ICI-related toxicity and may occur independently or alongside pituitary dysfunction. A 67-year-old man with advanced squamous cell carcinoma of the lung received atezolizumab between July 2020-July 2022. Four months after completing treatment, he presented with profound fatigue. Biochemical evaluation demonstrated secondary cortisol deficiency, with cortisol 59 nmol/l (normal 140–690) and ACTH 15 ng/l (normal 10–50). Thyroid tests revealed primary hypothyroidism: TSH 32.3 mU/l (normal 0.4–4.0) and free T4 6.5 pmol/l (normal 10–22). Anti-TPO and adrenal cortex antibodies were negative. Gonadal testing showed FSH 1.7 IU/l (normal 1.5–12), LH 1.5 IU/l (normal 1.8–9) and testosterone 7.8 nmol/l (normal 8–30), with normal prolactin and IGF-1. He failed his Short Synacthen Test with a low ACTH level, confirming secondary hypocortisolism. Pituitary MRI showed no structural abnormality, and CT imaging confirmed normal adrenal glands. Hydrocortisone and levothyroxine were commenced, with marked symptomatic improvement. After hormone optimisation, FSH, LH and testosterone normalised. His clinical condition stabilised with ongoing endocrine follow-up. Repeated Short Synacthen Tests and thyroid function tests up to three years after the initial diagnosis showed no recovery of either axis. This case illustrates that dual endocrine toxicity could be associated with PD-L1 inhibition, presenting as isolated ACTH deficiency consistent with immune-related hypophysitis together with concomitant primary hypothyroidism. These findings highlight the importance of long-term endocrine monitoring during and after ICI therapy to support timely diagnosis, appropriate hormone replacement and prevention of serious complications.

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P297

Gonadotroph pituitary adenoma presenting with pituitary apoplexy and cranial nerve palsies: a case report

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Background
Pituitary apoplexy is a rare endocrine emergency caused by haemorrhage or infarction of a pituitary adenoma. It typically presents with sudden headache, visual changes, and cranial nerve (CN) deficits. We report a case of a young male with a gonadotroph pituitary neuroendocrine tumor (PitNET) presenting with apoplexy and requiring serial neurological assessment and urgent multi-disciplinary management.
Clinical Case
A 24-year-old male presented with sudden severe headache, vomiting, and diplopia. Examination revealed left eye exotropia with nystagmus and an isolated right CN VI palsy; visual fields were grossly intact. Non-contrast CT demonstrated a 42mm sellar mass. Over the following 72 hs, he developed right ptosis with mydriasis and near-complete ophthalmoplegia except for downward gaze, indicating additional CN III and IV involvement. Pituitary MRI confirmed an irregular 3cm sellar mass with heterogenous contrast enhancement and suprasellar extension exerting mass effect on the optic chiasm. Laboratory assessment showed low random cortisol (128 nmol/l), low testosterone (3.6 nmol/l; normal 8.4–27.4), and normal prolactin (64 mIU/l; normal 56–278). He was started on intravenous hydrocortisone and transferred to tertiary care centre for urgent transsphenoidal surgery. Postoperatively, he developed transient diabetes insipidus, managed with desmopressin. CN III and IV function improved substantially, with resolution of ptosis and partial recovery of eye movements, while CN VI palsy persisted. Histopathology confirmed a gonadotroph PitNET with extensive haemorrhagic necrosis. Follow-up shows that he has sufficient cortisol reserve, but has growth hormone deficiency. Testosterone was 8.2mmmol/l.
Conclusion
This case illustrates several clinically important features of pituitary apoplexy relevant to both district general and tertiary endocrine practice. Cranial nerve deficits may evolve over several days and recover variably, requiring careful serial neurological assessment. Timely multidisciplinary intervention enabled substantial functional recovery.

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P298

From palpitations to phaeochromocytoma: a case report

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Background
Phaeochromocytomas are rare neuroendocrine tumours, and diagnosis can often be delayed due to their non-specific and varied clinical presentation.
Clinical Case
57 year old lady with a background of hypertension and hypothyroidism presented with palpitations and sweating, with nausea in the mornings since 6 years ago. She visited her GP last year and was found to have elevated BP up to 240/78 mmHg, heart rate of 145 bpm, despite being on anti-hypertensives. Ultrasound showed benign nodules throughout the thyroid and a right supraclavicular mass, histology from ultrasound-guided biopsy showed no evidence of neoplasia. CT TAP showed a large right axillary node measuring 7.73 cm, and a lesion measuring 5.5 cm in the left upper quadrant of the abdomen, which displaced the left kidney. MRI Adrenals confirmed a stable indeterminate left adrenal nodule. MRI of Cervical Spine showed right C6-7 foraminal neurogenic tumour extending along the C7 nerve, felt to represent nerve sheath tumours in her neck and axilla. 24-h urinary Metadrenalines were elevated at >13 µmol/24h, with 24-h urine Normetadrenaline output of 52.49 µmol/24h, 24-h urine 3-Methoxytyramine output of 4.99 µmol/24h. During clinic review, she reported that her father had multiple cutaneous lumps. On examination, she appeared cachexic, and cutaneous lumps were seen over her arms and back. Overnight dexamethasone suppression test was normal. A provisional diagnosis of type 1 neurofibromatosis and phaeochromocytoma was made. She was started on phenoxybenzamine 10mg BD for 12 weeks, which improved her blood pressure to 114/70. 68Ga-DOTATATE PET scan showed soft tissue density mass in the left adrenal with moderate heterogenous DOTATATE avidity and neurofibromas, differentials include phaeochromocytoma or paraganglioma. She was referred to the endocrine surgeons for left adrenalectomy.
Conclusion
This case highlights the importance of history-taking and clinical examination in detecting this uncommon condition.

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P299

Personalised Sick-Day Care Plan in Addison's Disease: Improving Self-Management in a Patient with Functional Dissociative Seizures

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Background
Addison's disease necessitates lifelong glucocorticoid replacement and proactive stress-dose management to prevent adrenal crises. Self-management becomes challenging when comorbid functional neurological disorders mimic crisis symptoms such as loss of consciousness, nausea and light headedness and weakness, leading to diagnostic confusion, frequent hospitalisations and diminished patient confidence.
Case
A 34-year-old male with Addison's disease, postural orthostatic tachycardia syndrome, autism spectrum disorder, and learning difficulties, experienced recurrent functional dissociative seizures confirmed by video electroencephalography. Despite optimised hydrocortisone replacement (Hydrocortisone 10mg in AM, 5mg midday, 5mg PM and Fludrocortisone 100 mg BD) with reassuring day curves and biochemistry, he had recurrent admissions (7/month over one year), receiving parenteral hydrocortisone each time. Episodes featured light-headedness, weakness and collapse lasting up to 45 minutes. Recurrent episodes generated profound anxiety about distinguishing seizures from true adrenal crises.
Intervention
The endocrine team developed a personalised "traffic-light" sick-day protocol:- Green: episodes <10 minutes, feeling well — no hydrocortisone adjustment. Amber: episodes >10 minutes or mild systemic symptoms (nausea, lethargy, hypotension) - take 10 mg oral hydrocortisone, increase fluids, monitor. Red: seizures >10 minutes or definite crisis features (persistent vomiting, systolic blood pressure (BP) <90 mmHg or diastolic BP $<$ 50 mmHg) — 100 mg intramuscular

hydrocortisone and seek emergency care. Implementation was supported by regular nurse-led follow-ups to reinforce education and protocol adherence.
Outcomes
Acute admissions decreased from ~84 to one annually. The patient demonstrated improved discrimination between dissociative seizures and adrenal crises, with reduced anxiety, enhanced symptom recognition, and increased confidence in self-management.
Conclusion
Personalised 'sick-day' protocols effectively enhance self-management in Addison's disease complicated by overlapping functional comorbidities. This structured approach, supported by continuous education, substantially reduces unnecessary emergency care utilisation while empowering patients and improving overall quality of life. This model may benefit similar complex cases.

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P300

Revolutionizing nurse education: a national reforming model for teaching metabolic and diabetes literacy through evidence-based nurse-led diabetes care curriculum first time in Pakistan

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Background
The increasing burden of diabetes mellitus in Pakistan requires a paradigm shift in the training of health professionals. This paper describes the design and implementation of a nationally introduced, evidence-based curriculum reform aimed at increasing the metabolic and diabetes literacy of nurses and establishing a pathway leading to formalized specialized care provision first time in Pakistan being the First Nurse-Led, training model for the 33% of population with diabetes in the country.
Aim
The aim of this study was to transform nursing practice by advancing nurses' professional roles first time in Pakistan through the development and implementation of a comprehensive diabetes care curriculum, systematically designed and refined over several years.
Methods
A mixed-methods approach was used to design and pilot a comprehensive, competency-based curriculum of both theoretical and supervised clinical placement. The findings of First National Nursing Survey of 1% of graduate nurses (1220 respondents) across Pakistan form 62 cities recognised the curriculum. The outcome of the study established a scalable, nationally recognized framework for specialized diabetes nurse practitioners.
Results
Preliminary results show significant enhancements in participants' clinical competence and diagnostic interpretation skills. The effective integration of evidence-informed theoretical teaching with extended clinical practicum provided an immensely engaging and relevant learning environment. The model validated a feasible, scalable, and reproducible pathway to develop Diabetes Nurse Practitioners, addressing a crucial workforce gap.
Conclusion
This national model will transform existing nurse education by embedding a competency-based diabetes literacy into advanced training. Establishment of this nurse-led advanced course is crucial for the national diabetes care infrastructure, enhancing adherence to global treatment guidelines and promoting metabolic health outcomes throughout Pakistan. The study resulted into a National Reforming Model for Teaching Metabolic and Diabetes Literacy.
Keywords
Nurses Advanced Roles, Diabetes Care Curriculum, Nurse-Led interventions, Clinical Competencies, Transforming Nursing Practices

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P301

A rare case of normosmic hypogonadotropic hypogonadism secondary to a genetic loss-of-function variant in TBX3

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Ulnar-mammary syndrome (UMS) is a rare autosomal dominant disorder characterised by apocrine dysfunction, upper limb abnormalities, and hypoplastic mammary glands due to variants in *TBX3*, a transcription factor that plays a role in pituitary tissue development. Associations with delayed puberty are observed, but *TBX3* has only recently emerged as a candidate gene for hypogonadotropic hypogonadism (HH). A 14-year-old male presented with short stature associated with upper limb symphalangism and camptodactyly. He denied an altered sense of smell. His family history was significant for delayed puberty: in his father who required gonadotropin therapy at 17 years, his paternal grandfather, and his paternal aunt who had late menarche requiring hormonal treatment. Examination revealed small testes bilaterally at 3ml, stretched penis length 4.5cm, Tanner staging P1G1A1. Height was 155.1cm (predicted adult height -3.1 SD). Serum biochemistry showed undetectable luteinizing hormone (LH), follicle stimulating hormone (FSH), and testosterone concentrations, inhibin B 121pg/mL (ref. 74 - 470pg/mL), antimullerian hormone 866.5pmol/l (ref. 84.25 - 1109.52pmol/l). Peak growth hormone on insulin tolerance test was suboptimal at 5.63ug/l. MRI pituitary was declined by the patient's mother. Whole exome sequencing demonstrated a heterozygous missense variant in *TBX3* Chr12:114,674,631; c.1244C>G; p.S415*. Paternal DNA samples are awaited. Growth hormone replacement was commenced, followed by recombinant FSH and human chroionic gonadotropin. After 12 months of gonadotropin treatment, testicular volumes reached 15ml bilaterally, SPL 9cm, Tanner staging P2G3A1. Height after 18 months of growth hormone treatment had increased by 7.7cm, and 13.1cm after 30 months. *TBX3* variants associated with UMS can result in congenital, normosmic HH and an associated hypoplastic pituitary gland. In mouse models, *Tbx3* defines a specific progenitor domain during hypothalamic development, thus establishing and maintaining the identity of kisspeptin-neurokinin-dynorphin (KNDy) neurons, vital for pubertal commencement. *TBX3* loss-of-function should be considered in patients presenting with normosmic HH with phenotypic features of UMS.

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P302

"A clearer view?" TED improvements after total thyroidectomy despite unhelpful TRAb clues

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Introduction
Thyroidectomy leads to reduction in thyroid-stimulating hormone receptor antibody (TRAb) in patients with thyroid eye disease (TED), however the association between TRAb decline and clinical improvement remains unclear.
Methods
Retrospective cohort study of patients undergoing total thyroidectomy for Graves' disease with concurrent thyroid eye disease (TED) between 2020 and 2025 at a tertiary institution. Clinical data, orbital symptoms improvement and post-operative outcomes were analyzed to corelate the impact of TRAb on TED.
Results
Nearly167 patients (139F:38M) with a mean age of 44.7 ($\pm$14.7) years underwent thyroidectomy for Grave's disease. Of these, 75 (45%) patients had concomitant TED, with severity as follows: mild – 36(48%); moderate 28 (37%) and severe in 11 (15%). Patients with TED had significantly higher mean TRAb levels compared to those without TED (23.5 ± 10.3 vs. 18.1 ± 12.5; $p = 0.001$), which dropped following surgery. Higher TRAb showed no significant correlation with the various parameters evaluated such as age, gender, race, TED severity, or the need for orbital decompression. However when patients were evaluated for symptoms improvement, 53 of 75patients (71%) experienced clinical improvement in TED symptoms, 13 of 75 (17%) showing no change in symptoms. A total of 9 patients (12%) required subsequent orbital decompression to improve their eye symptoms during the study period. The complications of thyroidectomy included the following: recurrent laryngeal nerve palsy - temporary in 4 (2.3%); permanent in 1 (0.5%); hypoparathyroidism – temporary in 39 (23.3%) and permanent in 13 (7.7%); and haematoma in 1 (0.5%).
Conclusion
Subjective improvements are seen in patients with TED undergoing thyroidectomy. The TRAb levels however do not appear to correlate with the clinical course of disease or severity though the TRAb levels were lowered with surgery. The efficacy of surgery in improving eye symptoms however require comparative studies with patients on medical therapy alone.

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P303

When the spine speaks first: a rare case of thyroid cancer presenting with cord compression

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Introduction
Spinal metastasis is a common complication of many cancers, but it is rare for asymptomatic thyroid malignancies to present as paraplegia. Follicular thyroid carcinoma (FTC) metastasizes to bone in 7% to 28% of cases. While distant metastases often indicate poor prognosis, differentiated thyroid cancer (DTC) can sometimes lead to favourable outcomes.
Case Report
A 71-year-old man presented with a six-week history of thoracic back pain that progressed to bilateral leg weakness, without sensory loss or bowel/bladder dysfunction. He had no history of trauma or known thyroid disease. Examination revealed reduced lower limb power, particularly on the right, with hyperreflexia Blood tests, including Vitamin B12 and folate, were normal. An elevated paraprotein led to a myeloma evaluation, which was ruled out by a bone marrow biopsy. MRI showed a malignant compression fracture at the T9 vertebra with canal stenosis and spinal cord compression. High-dose corticosteroids were initiated, followed by immediate neurosurgical decompression. Histopathology confirmed infiltration by an epithelioid neoplasm positive for TTF1 and thyroglobulin, confirming metastatic carcinoma of thyroid origin. Although thyroid examination and tests were normal, ultrasound revealed a 17-mm nodule in the right lobe with calcification and a hypoechoic area (U4). Fine-needle aspiration revealed a follicular-patterned lesion (Thy3F), positive for TTF-1 and PAX8, which correlated with spinal metastasis histology. After discussion in the multidisciplinary meeting, a plan was made for a total thyroidectomy followed by adjuvant radioactive iodine (RAI) treatment.
Conclusion
It is highly uncommon for differentiated thyroid cancer to manifest as spinal cord compression as initial presentation. This case underscores the importance of including thyroid carcinoma in the differential diagnosis for patients presenting with unexplained spinal lesion. Quick identification and a comprehensive treatment approach involving various specialists are crucial for achieving the best results for the patient and ensuring positive outcomes.

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P304

An audit of the follow-up and management of hypothyroidism in patients with benign thyroid disease treated with radioactive iodine – a trust experience

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Background
Over two-thirds of patients treated with radioactive iodine (RAI) for benign thyroid disease develop hypothyroidism within one year[1] and timely detection and treatment is essential to prevent morbidity[2]. NICE[3] and British Thyroid Foundation (BTF) guidelines[1] therefore recommend thyroid function testing (TFTs) 4-6 weeks post-RAI. We wanted to assess the average time to hypothyroidism in our population and whether thyroid pathology and type and dose of antithyroid drug (ATD) treatment pre-RAI influences time to hypothyroidism.
Aims
Primary – Analyse the timeframe to hypothyroidism and assess our trust's compliance with post-RAI follow-up guidelines. Secondary – Assess correlation between thyroid pathology and type and dose of ATD treatment pre-RAI with time to hypothyroidism.
Methods
A retrospective analysis was undertaken of adults aged > 16 years who received fixed-dose (555 MBq) RAI for benign thyroid disease at London Northwest Healthcare NHS Trust between 2021-2024. Patients with incomplete/inaccessible records and those lost to follow-up were excluded. Data was collected from electronic patient records and analysed with Microsoft Excel and SciPy software.
Results
127 patients were included in the study (67 patients excluded). 62.3% ($n = 79$) became hypothyroid, 11.8% ($n = 15$) became euthyroid and 25.9% ($n = 33$) remained hyperthyroid (17.3%, $n = 22$ had recent RAI <1 year). The median time to hypothyroidism and levothyroxine initiation was 97 and 104 days respectively. There was no difference in time to hypothyroidism between different thyroid pathologies and type and dose of ATD. Only 20.3% of patients had follow-up 4-6 weeks post-RAI as recommended, whilst the majority (67.1%) had delayed follow-up (median 48 days).
Conclusions
Our trust was not compliant with follow-up guidelines post-RAI and this study prompted a trust-wide change in clinical practice; all patients now have TFTs and follow-up booked 6 weeks post-RAI with our endocrine nurse, with a departmental target for a second follow-up to be arranged within 97 days post-RAI.

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P305

Apparent androgen excess in a hyperthyroid male: the role of sex hormone–binding globulin (SHBG) mediated hypertestosteronaemia

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Introduction
Thyroid hormones can cause sex hormone–binding globulin (SHBG) mediated elevation of total testosterone without true androgen excess. We present a case illustrating this paradox.
Case report
A 35-year-old man was referred with abnormal thyroid function tests and unexpectedly high testosterone levels, raising concern for dual endocrine pathology. Although he had symptoms of thyrotoxicosis, he had no clinical features of androgen excess. On examination, he had a diffuse goitre, exophthalmos, and hand tremors, with no gynaecomastia. Biochemical investigations showed thyroid-stimulating hormone (TSH) <0.05 mIU/l (0.2–4.2), free thyroxine (FT4) 110 pmol/l (11–23), free triiodothyronine (FT3) >50 pmol/l (3.1–6.8), total testosterone >52 nmol/l (11–28), SHBG 332 nmol/l (18–54), follicle-stimulating hormone (FSH) 9.2 IU/l (1.4–18.1), luteinising hormone (LH) 13.8 IU/l (1.5–9.3) and positive thyrotropin receptor antibodies, confirming Graves' disease.Free testosterone could not be calculated as levels exceeded the assay limit and were suspected to be low due to profound SHBG elevation. The raised LH was therefore attributed to reduced androgen feedback. After starting carbimazole, testosterone became measurable within two months, allowing calculation of low free testosterone (6.61 nmol/l), supporting the proposed mechanism for the elevated LH. Within eight months of treatment, all biochemical parameters normalised, confirming a thyroid-driven and reversible process.
Conclusion
Hyperthyroidism causes SHBG-mediated hypertestosteronaemia rather than true hyperandrogenism (1,2). Androgen abnormalities in Graves' disease should therefore be interpreted cautiously to avoid unnecessary investigations.
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P306

An Unusual Presentation of Graves' Disease: Thyrotoxic Myopathy

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Introduction
Graves' disease is one of the leading causes for hyperthyroidism, worldwide. Complications include arrhythmias, osteoporosis and ophthalmopathy. Graves' myopathy is not frequently encountered and sometimes overlooked.
Case Presentation
A 73-year-old female presented with leg swelling, difficulty getting up and mobilising. She had severe myalgia in proximal muscles and history consistent with proximal myopathy. Examination revealed mild bilateral exophthalmos and features of chronic venous insufficiency over legs. Power was reduced in proximal muscles. Blood tests revealed: TSH <0.01mU/l, FT4 39 pmol/l. Both TPO and TRAb were raised: >600IU/mL and 17.40 U/l, respectively. NT-pro BNP and CK normal. Notably, her potassium was normal. Venous doppler revealed DVT of the right leg. EMG showed proximal myopathic changes with early recruitment

pattern, supportive of mild non-muscle irritable myopathy, keeping with thyrotoxic myopathy. After commencing Carbimazole, her symptoms improved. She was able to mobilise with ongoing physiotherapy. Neurology agreed with "thyrotoxic myopathy". She received DOAC for DVT. She is back to her baseline mobility, with TSH <0.01, FT4 14.4 and FT3 6.73.
Discussion
While some patients with Graves's disease treated with thionamides may manifest myalgia and rhabdomyolysis (usually associated with rapid thyroid hormone reduction), thyrotoxic myopathy rarely is associated with elevated CK and occurs due to accelerated muscle protein catabolism. Thyrotoxic myopathy is a distinct entity that presents with weakness and muscle wasting, unlike Thyrotoxic Periodic Paralysis (episodes of temporary paralysis and hypokalaemia). Symptoms usually resolve with treatment of underlying hyperthyroidism. Furthermore, hyperthyroidism also promotes a pro-coagulant state by enhancing activity of FVIII and vWF and autoantibody mediated platelet activation.
Conclusion
This case represents an atypical presentation of Graves disease where the patient did not have any of the classical symptoms of hyperthyroidism. When a patient presents with proximal myopathy, a thyroid myopathy should be considered as a differential.

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P307

Type 2 amiodarone-induced thyrotoxicosis in a patient with atrial fibrillation: a case report

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Background
Amiodarone is a class-III antiarrhythmic agent used in chemical cardioversion for patients with atrial fibrillation. Due to its high iodine content, Amiodarone can cause thyroid dysfunction in patients with or without thyroid disease.
Clinical Case
64-year-old lady presented with nausea, vomiting for a few weeks after starting Mounjaro, with tremors, heat intolerance, sweating, and lethargy. She has primary hyperparathyroidism, persistent atrial fibrillation refractory to electrical cardioversion/rate control, and was started on amiodarone 3 years ago. Bloods showed adjusted calcium of 2.97mmol/l, TSH <0.01mU/l, Free T4 >100pmol/l, negative TSH-stimulating immunoglobulins. She was treated for type 2 amiodarone-induced thyrotoxicosis (AIT), hypercalcaemia. Amiodarone and Colecalciferol were stopped, and she was started on Bisoprolol 2.5mg OD, Carbimazole 20mg BD. She had multiple re-admissions to hospital within a month with similar symptoms and shortness of breath with no improvement in her thyroid function tests. Echocardiogram showed normal biventricular systolic function. Neck ultrasound showed a diffusely bulky thyroid with multiple small hypoechoic nodules and normal vascularity, suggestive of thyroiditis. Carbimazole was stopped, and she was started on propylthiouracil 200mg TDS, prednisolone 30mg OD, cholestyramine 4grams ON, and lithium 400mg OD. Radioiodine was deemed inappropriate in her case due to previous use of amiodarone. In view of possible treatment resistance, she was referred to a tertiary centre for consideration of Iopanoic acid. Her symptoms and thyroid function have fortunately improved, with TSH <0.01 and free T4 of 27.8pmol/l after 2 months of quadruple therapy whilst waiting for Iopanoic acid. She was referred to the endocrine surgeons for thyroidectomy and parathyroidectomy.
Conclusion
Classification of AIT can be challenging in the acute setting due to the lack of clinical information. Colour flow Doppler ultrasonography is a useful tool to distinguish between type 1 and 2 AIT.

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P308

Respiratory-led presentation of a retrosternal multinodular goitre with exophthalmos and negative TRAb: an atypical diagnostic challenge

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Retrosternal goitres usually present with long-standing compressive symptoms or overt thyroid dysfunction. This case describes an unusual dual presentation: a respiratory-led pathway to diagnosis (CATCH protocol) and the unexpected presence of bilateral exophthalmos with negative TSH receptor antibodies. These features prompted further diagnostic evaluation and highlight the need for early multidisciplinary team (MDT) involvement. A 74-year-old male was referred to respiratory services with a persistent dry cough. Chest radiography demonstrated mediastinal widening, and CT imaging revealed a large multinodular goitre with retrosternal extension causing critical upper tracheal narrowing. He was initially clinically euthyroid then early thyroid function tests (TFT's) showed biochemical evidence of thyrotoxicosis. Symptoms progressed to exertional dyspnoea, reduced voice volume, facial congestion, and a positive Pemberton's sign. Examination revealed bilateral exophthalmos. Repeat TFT's every 6 weeks demonstrated biochemical thyrotoxicosis (TSH 0.02, FT4 28.9, T3 10.3) with negative TRAb, raising the possibility of euthyroid Graves' orbitopathy or atypical thyroid-associated orbitopathy. Subsequently, carbimazole was initiated but discontinued due to adverse effects. With progressive airway compromise (tracheal lumen 7 mm), antithyroid therapy was re-introduced to optimise thyroid status ahead of surgical intervention. Lung function tests were carried out by the respiratory team to demonstrate the clinical impact of airway compromise. To further complicate this, he had a history of previous sternotomy for cardiac surgery requiring the cardiothoracic team to evaluate the risks of re-sternotomy for goitre excision. This case highlights the importance of recognising thyroid pathology in patients presenting through respiratory pathways and demonstrates how exophthalmos with negative TRAb can complicate diagnostic interpretation. It also underscores the complexity of managing retrosternal goitres in patients with previous sternotomy, where early multidisciplinary involvement is essential. This case provides valuable learning from initial detection in a primary care setting to an MDT involving various medical specialties.

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P309

Double Discordance: A case of double assay interference complicating the management of Grave's Disease

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Graves' disease is a leading cause of hyperthyroidism, typically confirmed by a concordant biochemical and clinical profile. This case demonstrates the diagnostic complexity created by double assay interference affecting both TSH and free T4 measurements. A 38-year-old woman presented with anxiety, tremor and sweating. Examination revealed a small goitre; her identical twin had isolated ACTH deficiency. Initial thyroid function tests on a Roche platform were discordant, showing markedly elevated free T4 (63 pmol/l) with a normal TSH (1.04 mIU/l). Repeat results remained inconsistent. Given the strong clinical suspicion of hyperthyroidism, samples were reanalysed using an Abbott assay, confirming a hyperthyroid state (free T4 37.5 pmol/l, TSH <0.01 mIU/l). TSH receptor antibodies were strongly positive (22.6 IU/l), confirming Graves' disease. Dynamic pituitary testing identified isolated ACTH deficiency, likely secondary to longstanding inhaled corticosteroid therapy for asthma. Hydrocortisone was commenced but discontinued after significant weight gain; she now uses hydrocortisone only during intercurrent illness. Therapeutic management was further complicated by delayed turnaround of Abbott assay results (3–4 weeks), necessitating a 'block and replace' regimen guided by clinical rather than biochemical assessment. Nineteen months after diagnosis, she underwent radioactive iodine ablation, subsequently developing hypothyroidism requiring levothyroxine therapy. Post-radioiodine testing showed complete resolution of the Roche assay interference. This case highlights the impact of dual assay interference on the diagnosis and management of Graves' disease, and the need to consider assay artefact when biochemical data conflict with clinical findings.

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ePoster Presentations

Adrenal and Cardiovascular

EP1

Steroid induced hypertensive crisis- a rare presentation of pheochromocytoma

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Introduction
Pheochromocytoma is a rare tumour of the adrenal glands. Pheochromocytomas clinical manifestations result from production of excessive catecholamines levels. Catecholamines are chemical messengers crucial for various psychological processes including stress regulation and cardiovascular function. The incidence of pheochromocytoma is at 0.2-0.8 per 100 000 persons.
Case presentation
We present a case of 42-year-old female from our centre under investigation for left adrenal incidentaloma consisting of Over Night Dexamethasone Suppression Test (ODST), Renin-Aldosterone Ratio and Plasma Metanephrines. Thirty minutes before admission she experienced sudden onset of cold sweats, occipital headache, dizziness and palpitation. On presentation, her blood pressure was 191/101mmHg, heart rate 71bpm. Patient was transferred to Emergency Department where cardiac events were excluded. Plasma metanephrines levels were significantly elevated, with Plasma Normetadrenaline at 16720pmol/l (reference range 0 -1180pmol/l) and Plasma Metadrenaline 11110pmol/l (reference range 0-510pmol/l). An MIBG scan confirmed suspicion of pheochromocytoma. The patient was counselled extensively on the necessity of preoperative alpha- and beta-adrenergic blockade in the context of suspected/-confirmed catecholamine-secreting tumour(pheochromocytoma).
Conclusion
Pheochromocytoma crisis is a rare, life-threatening emergency. The administration of corticosteroids such as dexamethasone may trigger a catecholaminergic crisis and is contraindicated in patients with a presence of a conclusive diagnosis. While there are a few case reports of such crises triggered by the Low Dose Dexamethasone Suppression Test (LDDST) and High Dose Dexamethasone Suppression Test (HDDST), no cases have been reported following ODST. In such cases, alternative diagnostic modalities like 24-hour urinary free cortisol or late-night salivary cortisol test.

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EP2

Steroid Weaning and Adrenal Recovery in different causes of Cushing's Syndrome

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Background
Adrenal suppression following prolonged steroid exposure presents significant clinical challenges. The optimal strategy for steroid weaning and adrenal recovery remains uncertain. Supporting patients through withdrawal is important to reduce complications including osteoporosis and diabetes.
Case series
Four patients were referred with adrenal insufficiency. **Patient 1:** Had used topical clobetasol for 20 years and was referred with an undetectable cortisol. Following a rapid wean, an initial short synacthen test (SST) demonstrated a peak cortisol of 248nmol/l and ACTH 217ng/l. Four months later a repeat peaked at 368nmol/l and ACTH 23.2ng/l. **Patient 2:** Post adrenalectomy following a four-year history of Cushing's. They were treated with metyrapone for four months pre-surgery. Initial SST demonstrated peak cortisol of 53nmol/l and ACTH 5.3ng/l. Following a prednisolone wean over five months, a repeat SST showed a peak cortisol of 120nmol/l, ACTH 24.8ng/l. She remains well and continues to be monitored in clinic. **Patient 3:** Following surgery for ectopic Cushing's, a baseline cortisol was $<$28nmol/l and ACTH $<$5.0nmol/l with no response on SST. A slower prednisolone wean was required due to glucocorticoid withdrawal symptoms. Repeat SSTs during prednisolone weaning demonstrated HPA axis recovery (peak cortisols at seven and fourteen months were 147nmol/l and 483nmol/l respectively). **Patient 4:** Following pituitary surgery for Cushing's, a slow wean from 4 mg prednisolone was started at 11 months post-surgery. The baseline cortisol was 77nmol/l and ACTH 21.6ng/l. Following a 24-week weaning protocol, she recovered her HPA axis. A repeat SST demonstrated a peak cortisol of 429nmol/l and ACTH 16.6ng/l.
Conclusion
This case series highlights the variability in adrenal recovery following steroid withdrawal, influenced by underlying pathology, duration of exposure, and weaning speed. Close monitoring with serial SSTs and ACTH, individualised weaning plans, and patient education, are critical to support recovery and reduce the risk of adrenal insufficiency.

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EP3

The silent burn-out: opioid-induced adrenal insufficiency in a middle-aged male

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Background
Long-term opioid medication can cause opioid-induced adrenal insufficiency (OIAI), which is an underdiagnosed side effect that arises from the hypothalamic–pituitary–adrenal (HPA) axis being suppressed. Delays in diagnosis and treatment might result from clinical symptoms that are frequently ambiguous and may overlap with other chronic illnesses.
Case
A 54-year-old man was referred for an endocrine evaluation of progressive symptoms of fatigue, low mood, and recurrent falls over six months and abnormal hormonal tests. He had a medical history of testicular cancer, seizures, asthma. He had been treating his chronic cancer pain with tramadol and morphine for a long time. Upon examination, there were no obvious neurological abnormalities, but there was fatigue, proximal limb weakness, and an unusual stride.
Investigations
Serum testosterone was low (0.6 nmol/l) and morning cortisol was borderline (62 nmol/l) according to the first GP blood tests. Later testing revealed low ACTH levels ($<$4 ng/l) and a poor cortisol response to the Short Syn-acthen test (baseline 62 nmol/l, 30 min 381 nmol/l, 60 min 495 nmol/l), which is consistent with secondary adrenal insufficiency. The pituitary and brain MRIs showed no structural abnormalities. Renal and liver function, and electrolytes were within normal limits.
Results
The results were in line with opioid-induced secondary hypogonadism and adrenal insufficiency in the setting of long-term opioid medication. The patient was sent to endocrinology for further care, which included reviewing the opioid dosage and replacing the steroids.
Conclusion
This particular case illustrates **the significance of considering OIAI when patients on long-term opioid treatment** experience unexplained fatigue, weakness, and mood changes. It is essential to understand how opioids depress the HPA axis in order to ensure early diagnosis and appropriate management to prevent avoidable morbidity.
Keywords
opioid-induced adrenal insufficiency, secondary adrenal suppression, morphine, hypogonadism, chronic opioid therapy.

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Bone and Calcium

EP4

Not just a biochemical oddity: asymptomatic hypocalcaemia with a genetic basis

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Autosomal dominant hypocalcemia (ADH) is a rare cause of hypocalcemia that should be considered when no other cause is evident. We describe two patients in whom a diagnosis of ADH was made following appropriate biochemical and genetic investigation. P1 was referred with known, asymptomatic, hypocalcaemia (calcium 2.03mmol/l, RI 2.2-2.6; PTH 3.8pmol/l, RI 1.6-6.9; vitamin D 42nmol/l). She had been investigated elsewhere, where it was deemed idiopathic.

24 hr calcium excretion 3.1mmol. Genetic testing: heterozygous mutation in *CASR* (Ala785Vals), confirming ADH Type 1 (ADH1). Her son (12 years old), was later confirmed to have the mutation. P2 was referred for investigation of asymptomatic hypocalcaemia (calcium 2.03mmol/l, RI 2.2-2.6; PTH 1.8pmol/l, RI 1.6-6.9; vitamin D 70nmol/l). 24 hr calcium excretion 6.1mmol. Genetic testing: heterozygous mutation in *GNA11* (Arg60Cys), confirming ADH Type 2 (ADH2). Neither patient experienced renal calculi, fractures, or dental abnormalities; however, P1 has a small (4mm) intracalyceal calcification on ultrasound. The ADH Type 1 phenotype is better described than that of ADH Type 2; levels of calcium probably remain stable over time. However, nephrolithiasis and nephrocalcinosis can develop at any stage, so periodic renal imaging is recommended. Seizures and basal ganglia calcification can also occur. Long-term monitoring is recommended. The ADH Type 2 phenotype is not fully elucidated, but in the absence of formal recommendations, follow-up for ADH Type 2 is similar to that for ADH Type 1. Our cases add to the literature on ADH Types 1 and 2 and reinforce the need to perform further investigation, even in asymptomatic individuals, if the biochemical profile cannot be explained. Genetic diagnoses allow appropriate follow-up and cascade testing, where desired.

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EP5

Persistent Alkaline Phosphatase (ALP) Elevation as a Marker of Vertebral Paget's Disease

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Introduction
Paget's disease of bone is a chronic disorder of abnormal bone remodelling, often asymptomatic but occasionally presenting with pain, deformity, or reduced function. We describe a case of vertebral involvement diagnosed following isolated and persistently elevated alkaline phosphatase (ALP).
Case presentation
A man in his 60s was referred for investigation of longstanding ALP elevation, most recently 325 IU/l (reference range 35–129). Isoenzyme analysis confirmed a bone origin. Calcium, phosphate, parathyroid hormone, and vitamin D levels were normal. A 2017 skeletal survey showed only mild lumbar degenerative changes. In 2023, CT of the temporal bones revealed a retracted tympanic membrane. Whole-body bone scintigraphy in 2024 demonstrated increased uptake in the entire L4 vertebra and less marked uptake at T7, with cortical thickening and coarse trabeculation—findings consistent with Paget's disease. The patient reported chronic back and leg pain with functional impairment and a history of musculoskeletal trauma. He also noted intermittent tinnitus and unilateral hearing changes, though no skull involvement was seen on imaging. There was no family history of metabolic bone disease. Based on biochemical and scintigraphic findings, a diagnosis of vertebral Paget's disease was made. Intravenous zoledronic acid (5 mg) was recommended as first-line therapy, with counselling on possible side effects, including acute-phase reaction and the rare risk of osteonecrosis of the jaw. Adjunctive measures included analgesia, physiotherapy, and pre-treatment dental assessment.
Conclusion
This case highlights the importance of investigating isolated ALP elevation and the role of bone scintigraphy in detecting metabolically active disease. Timely diagnosis enabled appropriate management of a condition that may otherwise remain undetected until complications arise.
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Endocrine Cancer and Late Effects

EP6

Anaplastic thyroid carcinoma masquerading as subacute thyroiditis: A diagnostic challenge with rapidly fatal outcome"

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Background
Anaplastic thyroid carcinoma (ATC) is a rare, highly aggressive thyroid malignancy characterized by rapid progression and poor prognosis. Early diagnosis remains challenging as ATC can mimic benign thyroid conditions. This case describes an aggressive course of ATC in a young woman with painful neck swelling and an initial diagnosis of Papillary thyroid cancer (PTC).
Case
A 41-year-old woman presented with a 4-day history of painful anterior neck swelling. She was clinically and biochemically euthyroid, with no retrosternal or compressive symptoms. Examination revealed a tender, multinodular 45g thyroid mass without regional lymphadenopathy. An initial impression of subacute thyroiditis was made, and she was scheduled for thyroid ultrasound and fine needle aspiration cytology (FNAC). At one-week review, she had worsening neck swelling with severe headache. Neck ultrasound revealed thyroid malignancy with nodal involvement, FNAC was malignant, suggestive of PTC (Bethesda category III). Chest and abdominal CT scans excluded distant metastases. She underwent a difficult thyroidectomy due to tumor friability. Ten days post-operatively, histology confirmed anaplastic thyroid carcinoma with local invasion. A follow-up chest CT scan revealed pulmonary and bony metastases. She was scheduled for emergency radiotherapy but developed acute respiratory distress, required ICU admission, and died within four weeks of presentation.
Conclusion
This case highlights the diagnostic challenges of ATC, its aggressive progression, and tendency to mimic benign or differentiated thyroid lesions. Early recognition, prompt diagnostic workup, and multidisciplinary management are critical, though prognosis often remains poor despite intervention.

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Metabolism, Obesity and Diabetes

EP7

Intensive vs standard blood pressure control in type 2 diabetes: cardiovascular and microvascular outcomes

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Introduction
Optimal blood pressure (BP) targets in type 2 diabetes mellitus (T2DM) remain uncertain. This study aimed to update the evidence on intensive vs standard BP control in T2DM by incorporating recent large-scale trial BPROAD and reassessing cardiovascular and microvascular outcomes across diverse trials.
Methods
This meta-analysis included eight randomized controlled trials (ABCD, Mehler 2003, ABCD-2V, SANDS, INVEST, ACCORD-BP, J-DOIT3, and BPROAD), comprising a total of 25,686 participants. Intensive arms consistently achieved ~120/70 mmHg regardless of specific trial targets. Follow-up ranged 1.9–8.5 years. The primary end-point was a composite of fatal/non-fatal cardiovascular events; secondary endpoints were diabetic retinopathy, neuropathy and urine albumin excretion (UAE). Pooled odds ratios (ORs) with 95 % confidence intervals (CIs) were calculated with a random-effects model; heterogeneity was expressed as I^2.
Results
Compared to standard BP control, intensive BP lowering reduced composite cardiovascular events (OR 0.88, 95 % CI 0.79–0.97; $I^2 = 17$ %). Retinopathy likewise fell (OR 0.84, 95 % CI 0.71–0.98; $I^2 = 0$ %). UAE risk declined (OR 0.82, 95 % CI 0.71–0.94; $I^2 = 62$ %). The analysis showed an OR of 1.48 (95% CI 1.05–2.10; $P = 0.03$; $I^2 = 0$%) for neuropathy, but the small sample size and wide confidence interval limit confidence in this result.
Conclusion
Lowering BP to approximately 120/70 mmHg, representing a more stringent target than standard control (~135/80 mmHg) is associated with modest reductions in cardiovascular events and improvements in microvascular outcomes including retinopathy and albuminuria in type 2 diabetes. While these benefits are modest and neuropathy data remain limited, the findings support consideration of lower BP targets in this population, applied thoughtfully and tailored to individual risk and tolerability.

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EP8

Proinsulin secretion as a rare cause of hypoglycaemia in a 65-year-old man

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Background
Hypoglycaemia in adults without diabetes requires systematic evaluation to determine its aetiology. Although insulinoma is the most frequent cause of endogenous hyperinsulinaemic hypoglycaemia, proinsulin-secreting tumours are rare and diagnostically challenging.
Case Description
A 65-year-old man presented with recurrent episodes of sweating, confusion, and dizziness that improved promptly with oral glucose intake. On hospital admission, symptomatic hypoglycaemia was confirmed with a plasma glucose of [insert actual value], thus fulfilling Whipple's triad. The patient had no history of diabetes, did not take insulin or oral hypoglycaemic agents, and denied alcohol excess. His past medical history included multiple comorbidity, with no relevant family history.
Clinical Hypothesis
Proinsulinomas are characterised by disproportionate secretion of proinsulin, with suppressed or inappropriately normal insulin and C-peptide levels during hypoglycaemic episodes.
Diagnostic Pathway
During symptomatic hypoglycaemia, his plasma glucose was 2.0-3.0, insulin and C Peptide as inappropriately low/normal but proinsulin was markedly elevated. These findings indicated endogenous hyperinsulinaemic hypoglycaemia driven predominantly by proinsulin secretion.
Discussion and Learning Points
This case highlights the importance of recognising the biochemical pattern of disproportionately elevated proinsulin in the absence of raised insulin and C-peptide. Proinsulin-secreting tumours represent a rare but important cause of recurrent hypoglycaemia in adults. This case highlights the need to consider proinsulin measurement when insulin and C-peptide levels are not diagnostic, despite clear fulfilment of Whipple's triad. Early recognition of this biochemical profile facilitates timely localisation and surgical management, which remains the definitive treatment. Increased awareness of proinsulinomas can prevent diagnostic delay and improve patient outcomes.

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EP9

Monogenic Obesity in a Familial Cluster: Insights into Laurence-Moon-Bardet-Biedl Syndrome (LMBBS) & Lectin Deficiency associated with Genetic Variantsin BBS12 and LEPR Gene

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Monogenic obesity is a rare but clinically significant condition characterized by excessive weight gain due to genetic mutations that affect appetite regulation and energy balance. This case series explores the clinical presentation and genetic underpinnings of monogenic obesity in a familial cluster, focusing on Laurence-Moon-Bardet-Biedl Syndrome (LMBBS) and lectin deficiency associated with genetic variants in the BBS1 and LEPR genes. The index patient, an 11-year-old female, presented with progressive weight gain since infancy, accompanied by acanthosis nigricans on the neck and axillary region. Genetic testing revealed mutations in both the BBS1 and LEPR genes, confirming a monogenic etiology of obesity. Remarkably, her two siblings and a cousin from the paternal side exhibited similar clinical profiles and shared the same genetic variants. This report shows the significance of genetic testing in diagnosing monogenic obesity disorders and highlights the familial clustering observed in such cases. The findings emphasize the need for heightened awareness and consideration of genetic factors in the evaluation of obesity, particularly in pediatric patients with a family history suggestive of monogenic obesity. By elucidating the genetic basis of these conditions, this case series aims to contribute to better clinical management and potential therapeutic interventions for individuals affected by monogenic obesity

Keywords
Monogenic Obesity, BBS-12, LEPR, LMBBS
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EP10

Prevalence and associated risk factors of retinopathy of prematurity in preterm infants

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Objective
To determine the prevalence of retinopathy of prematurity (ROP) and identify associated risk factors among preterm infants admitted to the National Institute of Child Health (NICH), Karachi, Pakistan.
Methods
This cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU) of NICH, Karachi, from October 2020 to March 2021. Preterm infants with gestational age below 32 weeks were included. Diagnosis of ROP was made by indirect ophthalmoscopy after pupillary dilation, performed by an experienced ophthalmologist. Potential risk factors assessed included gestational age, gender, maternal education, socioeconomic status, sepsis, respiratory distress syndrome (RDS), anemia, oxygen dependency duration, and mechanical ventilation.
Results
Among 310 preterm infants (mean age 5.73 $\pm$ 1.49 days), 184 (59.3%) were male and 126 (40.6%) were female. ROP was diagnosed in 139 (44.8%) infants. Multivariate logistic regression analysis demonstrated a significantly higher risk of ROP in infants of illiterate mothers (aOR 3.31; 95% CI 1.08–10.17; $P = 0.036$) and in those with family income $\leq$ 45,000 PKR (aOR 3.70; 95% CI 1.40–9.76; $P = 0.008$). Female gender (aOR 0.12; 95% CI 0.04–0.31; $P < 0.001$), oxygen therapy $\leq$ 4 days (aOR 0.04; 95% CI 0.01–0.12; $P < 0.001$), and NICU stay $\leq$ 12 days (aOR 0.02; 95% CI 0.01–0.08; $P < 0.001$) were associated with significantly lower risk.
Conclusion
Nearly half of the preterm neonates developed ROP. Key contributing factors included maternal illiteracy, low socioeconomic status, prolonged oxygen dependency, and extended NICU stay. Early screening and preventive strategies targeting these factors may reduce the burden of ROP in preterm infants.

Keywords
Retinopathy of prematurity, Preterm infants, Risk factors, Neonatal intensive care, Socioeconomic status
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EP11

Assessment of the antidiabetic potential of portulaca oleracea extract in a cadmium chloride–induced rat model: targeting insulin sensitivity, dyslipidemia, and oxidative stress pathways

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Environmental toxins like cadmium chloride ($CdCl_2$) are implicated in T2D pathogenesis by promoting oxidative stress and impairing insulin signaling. *Portulaca oleracea* (Purslane), a traditional medicinal plant, is rich in antioxidants and omega-3 fatty acids, suggesting potential antidiabetic properties. However, its efficacy against heavy metal-induced T2D and the comparative potency of its different extracts remain poorly elucidated. This study aimed to investigate and compare the therapeutic effects of purslane aqueous extract (PAE) and purslane hydroalcoholic extract (PHE) on a $CdCl_2$-induced rat model of T2D, focusing on glycemic control, insulin sensitivity, lipid metabolism, and antioxidant activity.Thirty-five male Sprague-Dawley rats were divided into five groups: a normal control, a $CdCl_2$-induced diabetic control (1 mg/kg/i.p., daily), a positive control treated with metformin, and two treatment groups receiving either PAE or PHE (400 mg/kg/p.o. each) for four weeks alongside $CdCl_2$. Fasting blood glucose (FBG) and body weight were monitored weekly. An oral glucose tolerance test (OGTT) was conducted at the end of the study. Serum was analyzed for insulin, adiponectin, leptin, alpha-amylase, alpha-glucosidase, and lipid profile. Homeostatic model assessment for insulin resistance (HOMA-IR) was calculated. Oxidative stress markers were measured in hepatic and pancreatic tissues, followed by histopathological examination.Thirty-five male Sprague-Dawley rats were divided into five groups: a normal control, a $CdCl_2$-induced diabetic control, a positive control treated with metformin, and two treatment groups receiving either PAE or PHE (400 mg/kg/p.o. each) for four weeks alongside $CdCl_2$. Fasting blood glucose (FBG) and body weight were monitored weekly. An oral glucose tolerance test (OGTT) was conducted at the end of the study. Serum was analyzed for insulin, adiponectin, leptin, alpha-amylase, alpha-glucosidase, and lipid profile. Homeostatic model assessment for insulin resistance (HOMA-IR) was calculated. Oxidative stress markers were measured in hepatic and pancreatic tissues, followed by histopathological examination.

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Neuroendocrinology and Pituitary

EP12

When hormones tell a deeper story: neurosarcoidosis revealed by central hypogonadism and diabetes insipidus

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We present the case of a 37-year-old male who initially attended the endocrine clinic with a 12 month history of progressive weight gain, erectile dysfunction and occasional headaches. He had no significant past medical history and reported preserved sense of smell, making diagnosis of Kallmann syndrome unlikely. Clinical examination revealed BMI of 40 with abdominal and flank striae, but otherwise normal secondary sexual characteristics including normal beard growth and peripheral body hair. Initial biochemistry showed suppressed gonadotropins with low serum testosterone (0.9 nmol/l), low-normal free T4 (11 pmol/l) with normal TSH (1.1 mU/l), and a normal prolactin level (345 mU/l), raising suspicion of hypopituitarism. While awaiting further iinvestigations, he developed polyuria and polydipsia and was subsequently diagnosed with central diabetes insipidus. He was commenced on desmopressin, testosterone replacement, and thyroxine. CSF analysis, PET-CT, and rheumatological investigations (ANA, ANCA) were undertaken; autoimmune screens were negative. MRI of the pituitary revealed extensive nodular extra-axial enhancement involving the hypothalamic-pituitary axis, third ventricular floor, and extending posteriorly to involve the brainstem and upper spinal cord. The radiological differential included neurosarcoidosis, other granulomatous conditions (e.g., IgG4 disease), lymphoma, or metastases. Further systemic imaging (CT chest/abdomen/pelvis) showed bilateral hilar and mediastinal lymphadenopathy, with parenchymal lung changes and mild retroperitoneal lymphadenopathy. These findings were consistent with a granulomatous process, most likely sarcoidosis. He was referred to the respiratory team who confirmed the diagnosis of sarcoidosis and systemic corticosteroid and immunosuppressive therapy was initiated. This case highlights the diagnostic complexity of infiltrative hypothalamic-pituitary disease and the importance of a multidisciplinary approach. Neurosarcoidosis, though rare, should be considered in patients presenting with partial hypopituitarism and diabetes insipidus with characteristic imaging findings.

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EP13

Carcinoid heart disease; current trends and controversies: a systematic review

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Carcinoid heart disease (CaHD) is a progressively debilitating condition in patients with carcinoid syndrome resulting from chronic exposure to tumour-secreted circulating amines, especially serotonin (with associated valvular plaque deposition and fibrosis), leading to valvular dysfunction and right-sided heart failure. The last decade has witnessed an increase in the incidence of this complex clinical condition, likely due to advancements in imaging techniques and the development of more reliable biomarkers. The natural history of this disease entity remains to be fully elucidated; however, based on results from various clinical trials, different therapeutic options, such as valvular replacement, somatostatin analogues, telotristat, and other molecular-targeted therapies, have emerged. It remains a significant cause of morbidity and mortality in individuals with Carcinoid syndrome. This systematic review examined the evolution and natural history of CaHD, investigated current diagnostic and treatment modalities with a particular focus on morbidity and mortality, and critically appraised the available evidence to recommend further future powered studies. A qualitative review was conducted using Google Scholar and MEDLINE, and the accruing results were illustrated in a narrative format using tables and figures. The diagnosis and management of CaHD remained complex due to systemic malignant disease and cardiac involvement in affected individuals. The last decade, however, has witnessed a remarkable improvement in the overall survival of these patients, largely due to advancements in therapeutics. Nevertheless, the criteria for defining these treatment modalities, particularly with regard to timing, sequence, and priority of use, remain much debated. Early diagnosis and timely surgical intervention are of utmost importance, and the importance of a multidisciplinary approach in the care of these patients cannot be overemphasised. This study critically explores issues surrounding existing controversies in the diagnosis and treatment of CaHD and recommends potential areas for research to improve the overall survival of patients in the near future.

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Reproductive Endocrinology

EP14

Is there a role for testosterone replacement post-gonadectomy in patients with Complete Androgen Insensitivity Syndrome (CAIS)?

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Background
CAIS is an X-linked recessive disorder that renders the androgen receptors non-functional. Hormone replacement therapy is required for maintenance of secondary sexual characteristics, symptom relief, cardiovascular and bone health. However, the role of androgen supplementation in CAIS remains uncertain.
Case presentation
A 45-year-old female with CAIS presents to the menopause clinic complaining of fatigue, hair loss and low libido. She had her testes removed 13 years ago, whereby the Urologist advised her to seek GP advice if she began to experience menopause symptoms. At the menopause clinic, the Gynecologist advised the patient to start estrogen replacement to alleviate her symptoms, explaining the benefits and risks. As well as counseling the patient on smoking cessation, weight loss and exercise. A DEXA scan was also ordered. In view of the patient's low libido, the potential role of testosterone replacement was considered, though evidence for benefit in CAIS is limited. However, a randomized, double-blind crossover trial designed by *Birnbaum et al*, compared the effectiveness of testosterone and estrogen replacement for women with CAIS [1]. The study found that testosterone was well-tolerated and had few adverse effects, but more specifically, that testosterone was superior to estrogen in improving sexual desire. However, it is unknown whether testosterone replacement has the same beneficial effects on cardiovascular and bone health as estrogen replacement, in these women.
Discussion
The patient was started on Oestrogel (0.06%)- 2 pumps/day. At her follow-up appointment, she reported alleviation of her symptoms and normalised libido, so she decided against commencing testosterone. However, the role of testosterone replacement in CAIS remains uncertain and warrants further research.
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EP15

XXY/XX mosaicism with female phenotype a rare entity

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Klinefelter syndrome is most commonly reported sex chromosome abnormality Most patients with klinefilter syndrome have 47XXY genotype. Klinefilter mosaicism is a rare phenomenon with only 34 cases of 47XXY/46XX reported in literature of these only 2 were with female phenotype.47XXY/46XX have heterogeneity in presentation with some presenting with ambiguous genitalia some with ovatestes and few cases reported as female phenotype Our patient is a 18 year old female presented with short stature as her primary complaint since 2 year of age her growth parameters height (-6.77 SDS) and weight (-8.10 SDS) which were significantly below 5th centile physical examination reveals no dysmorphic features no systemic anomalies and sexual maturity corresponding to tanner staging B4T2 investigation include hormonal panel bone age assessment karyotyping and imaging studies conducted Notably karyotyping and FISH analysis revealed mosaic pattern 47XXY/46XX final diagnosis established Mosaicism (47 XXY PREDOMINANT CELL LINE) with co-existing with growth hormone deficiency

Keywords
47XXY/46XX mosaicism ,klinfelter syndrome

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EP16

Down-Klinefelter syndrome (48,XXY,+21); a case report

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Chromosomal disorders are caused by variations in the number of chromosomes and these can be related to either autosomal or sex chromosomes. Among those, trisomy is most prevalent among live births. Down syndrome and Klinefelter syndrome both leads to aneuploidies due to nondisjunction of autosomal and sex chromosomes, respectively. Nonetheless, the global occurrence of a single person having double chromosomal aneuploidy is relatively rare. Here, we report a case of Down-Klinefelter syndrome, a double aneuploidy, in a two-year-old boy who presented to us with ambiguous genitalia and characteristic features of Down syndrome such as epicanthus, bilateral squint, cataract, flat nasal bridge, and simian crease. Double aneuploidy (48, XXY, +21) has been identified by karyotypic analysis, which is suggestive of Down-klinefelter syndrome. Early diagnosis is crucial for counselling and planning for future pregnancies. Chromosomal analysis is strongly suggested for children with a typical Down syndrome phenotype. Early diagnosis of Down-Klinefelter syndrome can impact both short and long-term outcome for these children.

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Late Breaking

EP17

When the aorta was innocent: a CT aortogram unveiling an adrenal pheochromocytoma in a hypertensive crisis

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Pheochromocytomas are rare adrenomedullary tumours producing one or more catecholamines. Initial presentation in crisis due to catecholamine induced haemodynamic instability can mimic other more common causes of hypertensive emergency. We report a young person presenting with hypertensive crisis with a CT aortogram unveiling a pheochromocytoma. A 23-year-old trans female presented to the emergency department with sudden onset palpitations, clamminess and severe chest discomfort. She had a blood pressure of 224/140 mmHg, and a heart rate of 121 bpm. Electrocardiogram demonstrated right-bundle-branch-block with widespread T-wave inversions. Troponin I was elevated at 700ng/l. She was immediately transferred to the intensive care unit for management of hypertensive crisis. Blood pressure spontaneously dropped to 95/70 mmHg demonstrating marked haemodynamic instability. CT aortogram excluded aortic dissection but revealed right adrenal mass measuring 74x68x60mm with central cystic change and necrosis highly suggestive of phaeochromocytoma. She was initiated on cautious intravenous fluids along with alpha blockade with phenoxybenzamine due to unavailability of phentolamine. This was supplemented with intravenous magnesium sulphate providing both vasodilatory and alpha-blocking effect. Phenoxybenzamine 30mg twice daily maintained her blood pressure at target of below 130/80mmHg. Beta blockade in the form of bisoprolol was added once she was adequately alpha blocked. Subsequent results confirmed the diagnosis with elevated plasma normetadrenaline 3210 ng/l (0–200) with plasma metadrenaline 29.5 ng/l (0–100). As she had already been commenced on alpha-blockade, an MIBG scan could not be performed. Following multidisciplinary team discussion, an elective adrenalectomy is planned within 2-3 weeks. She is currently awaiting FDG- PET CT with plasma calcitonin and genetics test results pending. Pheochromocytoma can closely mimic acute cardiac events, particularly in young patients. In our case, the discovery of an adrenal mass during imaging for suspected aortic dissection helped to divert the management in the correct direction in a timely manner.

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EP18

Catecholamine storm: beyond endocrine origins

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Introduction
This is a case of fulminant adrenergic myocarditis (FAM) in a young gentleman with catecholamine storm.
Case presentation
A 24-year-old gentleman with cannabis misuse, otherwise fit, presented with nausea and abdominal pain. Although his observations and glucose levels were normal on admission, shortly thereafter, he exhibited an acute onset of hypertension (180/130 mmHg), tachycardia (160/min), hyperglycaemia (CBG >27.8mmol/l), and ketonaemia (2.6mmol/l). Within hs, he developed cardiovascular collapse (BP 65/40mmHg) with acute heart failure and cardiogenic pulmonary oedema, requiring ITU support with inotropes, pressors and ventilation. VBG showed severe metabolic acidosis (pH 7.042, bicarbonate 9.9) with hyperlactatemia (14mmol/l). Hyperglycaemic ketosis in non-diabetic gentleman was considered secondary to stress response or catecholamine storm and was treated with intravenous insulin. Serial echocardiograms showed consistently low LVEF (<30 %). Troponin-T and NT-pro-BNP were elevated: 591ng/l and 20,056ng/l, respectively. Once stabilised, heart failure management initiated. Cardiac MRI three weeks post-admission showed improving LVEF (49%), diffuse myocardial oedema and mid-wall patchy fibrosis, suggestive of fulminant myocarditis. Follow-up cardiac MRI (3 months) showed LVEF 64% with no RWMA or fibrosis. Post-discharge, the endocrine team organised plasma-free metanephrines, which were essentially normal. Noted no evidence of PPGL on CT-CAP.
Discussion
Acute presentation with hypertension, tachycardia, and hyperglycaemia suggested catecholamine storm. Subsequent cardiogenic shock with typical MRI appearance led to the diagnosis FAM secondary to cannabis use. FAM causes myocardial inflammation leading to severe LVSD and cardiogenic shock. Catecholamine excess, from PPGL or drugs (cannabis/stimulants), is a potential trigger. Prolonged adrenergic stimulation causes receptor desensitisation and myocardial stunning. Hence, LVSD can be reversible. Catecholamines stimulate glycogenolysis/gluconeogenesis, inhibit insulin secretion, and impair glucose uptake, causing hyperglycaemia.
Conclusion
A catecholamine storm does not always indicate an endocrine tumour. While PPGL is a classic cause, other non-endocrine causes should also be considered, as they can cause an identical clinical picture.

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EP19

Diagnosis of pheochromocytoma with lung metastases in a middle-aged hypertensive male following presentation of abdominal pain

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Introduction
Pheochromocytoma is a rare neuroendocrine tumor that arises from chromaffin cells in the adrenal medulla or extra-adrenal paraganglioma. Typical triad of symptoms includes episodic headache, palpitations, and sweating occurring in 24% of patients [1].
Case presentation
A 48-year-old male with uncontrolled hypertension and intermittent palpitations for two years presented with moderate right abdominal pain and discomfort for a 2-month duration. Initial ultrasonography revealed right suprarenal mass, and further CT imaging suggested 17cm×13cm×15 cm-sized right adrenal mass encasing the aorta, with non-enhanced density of 22 HU, enhanced density of 140 HU, absolute washout of 43%, relative washout of 32% and two small nodules in the right lung compatible with pulmonary metastases. Metanephrines were grossly elevated. Clinically or biochemically there was no evidence of excess cortisol, aldosterone or sex-steroids. He was referred to oncology following resection of tumour. Histology revealed malignant pheochromocytoma with Pheochromocytoma of the Adrenal gland Scaled Score (PASS) score of 8/20.
Outcome
Compression on the liver, hemorrhagic necrosis, or rupture of the tumor may lead to abdominal pain in pheochromocytoma [2]. High catecholamine levels are responsible for constipation, paralytic ileus, and megacolon [3]. Understanding atypical presentations of pheochromocytoma is crucial for reducing morbidity and mortality in suspected cases.
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EP20

Severe ACTH-Independent Cushing Syndrome Due to Adrenocortical Carcinoma Unmasked Following a Fall

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Introduction
Adrenocortical carcinoma (ACC) is a rare, hormone-producing cancer with an uncertain prognosis[#1]. It may present with excess adrenal hormones or symptoms of an abdominal mass. Although many cases are detected as adrenal incidentalomas, the likelihood of an incidentaloma being an ACC is low[#1]. We report a case in which a fall uncovered profound autonomous cortisol secretion from an underlying ACC.
Case History
A 74-year-old woman fell from her bed, sustaining a right ankle fracture. CT angiography, performed to exclude limb ischaemia, revealed a large left adrenal mass (10–11 cm) and splenic artery aneurysm. Biochemistry confirmed ACTH-independent hypercortisolism: ACTH <3 ng/l (<50), serum cortisol 1109 nmol/l (185–624), and 24-h urinary cortisol 3332 nmol/day (<200). Urine steroid profiling supported cortisol-secreting adrenal carcinoma. Serum testosterone and metanephrines were normal. Aldosterone (<60 pmol/l) and renin (0.4nmol/l/hr) were suppressed, consistent with cortisol-mediated mineralocorticoid axis suppression. CT adrenal imaging demonstrated a heterogeneous, calcified mass highly suspicious for ACC. She was commenced on spironolactone for refractory hypokalaemia and metyrapone to control cortisol excess. She was transferred to a tertiary centre for adrenalectomy assessment; however, her course was complicated by probable Pneumocystis pneumonia, marked deconditioning, and extensive pustular skin lesions. HSV-1 DNA was detected with secondary bacterial infection, attributed to cortisol-induced immunosuppression. Given her frailty and clinical deterioration, medical rather than surgical management was favoured. She was repatriated for rehabilitation and palliative care, with hypercortisolism controlled on ketoconazole and metyrapone.
Conclusion
This case illustrates how ACC may remain clinically silent until revealed by an unrelated event. Metabolic instability, frailty, and infection risk ultimately necessitated medical rather than surgical management. The case underscores the importance of prompt hormonal assessment and specialist referral when adrenal incidentalomas are identified.
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EP21

A case of myxoedema presenting with type 2 respiratory failure

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A 61 year old female was admitted with cough, shortness of breath and bilateral leg oedema. She had type 2 respiratory failure on arterial blood gas and was treated as infective exacerbation of possible underlying chronic obstructive pulmonary disease with nebulisations, antibiotics and steroids. She required non-invasive ventilation in high dependency unit for type 2 respiratory failure. In view of her persistent bradycardia, hypotension and hyponatraemia (Na: 116 mmol/l (133-146)), thyroid function was done which showed severe hypothyroidism with free T4 <3.2 pmol/l (7.7-20.6) and TSH 38.15 mIU/l (0.30-4.80). Thyroid peroxisomal antibody was 704.3 IU/ml (<9.0). Random cortisol was 1484 nmol/l. ECG showed sinus bradycardia with low voltage QRS complexes. CTPA showed no pulmonary embolism but pericardial effusion up to 0.8 cm and small left-sided pleural effusion. Echocardiogram showed 10 mm pericardial effusion. She was started on Liothyronine and Levothyroxine which improved her bradycardia, hypotension and hyponatremia. She was discharged after her condition improved and has been followed up in Endocrinology clinic. Liothyronine has been tapered and stopped. Levothyroxine dose has been titrated. She is now symptom free and her current thyroid function is normal on Levothyroxine. This case highlights the diagnostic challenges in identifying severe hypothyroidism (myxoedema) in an acutely unwell patient and recognising its potential role as a contributing cause of respiratory failure. This patient had underlying severe hypothyroidism due to chronic autoimmune thyroiditis and possible underlying chronic obstructive pulmonary and presented with type 2 respiratory failure. The management consisted of treating her COPD and type 2 respiratory failure with medical therapy and non-invasive ventilation and replacement of thyroid hormones.

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EP22

Multifocal papillary thyroid carcinoma presenting on histological background of lymphocytosis

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A 24-year-old male presented with a gradually enlarging painless neck swelling. Noted to have a multiple nodules in thyroid consistent with multiple lymph nodes with enlarged cervical lymph nodes. Thyroid function noted to be normal. Tumor markers not done. Calcitonin normal. Ultrasonography and contrast-enhanced CT of the neck revealed a well-defined hypoechoic nodule in the left thyroid lobe with multiple cervical lymph nodes, classified as TIRADS-5. Fine-needle aspiration cytology suggested papillary thyroid carcinoma. The patient underwent total thyroidectomy with central neck dissection. Grossly, the left lobe measured 6 $\times$ 4.5 $\times$ 4 cm and showed a grey-brown friable nodule with papillary projections, while the right lobe appeared grossly unremarkable. Histopathological examination revealed papillary carcinoma, classic subtype, involving the left lobe with microscopic foci in the isthmus and right lobe. The tumor measured 5 $\times$ 3.5 $\times$ 4.2 cm, with lymphovascular invasion but no perineural invasion or tumor necrosis. Margins were close (<1 mm at multiple sites). Background lymphocytic thyroiditis and nodular goitre were present. A total of 15 lymph nodes were retrieved, 14 of which showed metastatic tumor deposits. The final pathological stage was pT3aN1Mx (AJCC 8th edition). This case highlights multifocal papillary thyroid carcinoma in a young adult with extensive lymph node metastases and lymphovascular invasion on a background of lymphocytic thyroiditis. Early recognition and surgical management with comprehensive histopathological evaluation are essential for prognosis and therapeutic planning.

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