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Abstract Unavailable
DOI: 10.1530/endoabs.109.PL1

Society for Endocrinology Starling Medal Lecture
PL2

Congenital hyperinsulinism: using genetics to improve diagnosis and knowledge of disease mechanisms
Sarah Flanagan
University of Exeter, Exeter, United Kingdom

Congenital Hyperinsulinism is the most common cause of persistent hypoglycaemia in childhood. The condition is clinically and genetically heterogeneous with over 35 different disease genes identified. Routine screening of these genes in individuals living with congenital hyperinsulinism identifies a pathogenic variant in ~50% of cases. Understanding the genetic cause of an individual's hyperinsulinism is critical as it will help to guide medical management. In recent years, genetic discovery efforts in congenital hyperinsulinism have focussed on screening for germline coding variants within genes known to have an important role in the pancreatic beta-cell. Much less attention has been afforded to the non-coding genome. This is largely because of the difficulties in interpreting the impact of non-coding variants on gene regulation. The Exeter Genomics Laboratory is an international referral centre for congenital hyperinsulinism, having received samples from over 4000 individuals living with this condition for genetic testing. Using state-of-the-art technology, we are improving our understanding of the genetics of this condition, which is leading to new knowledge of the pathways governing insulin secretion and importantly is providing more families with a genetic diagnosis. During this lecture I will show how we have developed methods to identify somatic variants in the known hyperinsulinism genes that are present in the pancreas but have until now remained undetected in leukocyte DNA. Results will also be presented from our genome sequencing studies which show how non-coding variants that disrupt the regulation of genes not normally expressed within the beta-cells, are a common cause of hyperinsulinism. These findings demonstrate, that for some, hyperinsulinism can present for the first time in adulthood- broadening the phenotypic spectrum associated with monogenic forms of hyperinsulinism.
DOI: 10.1530/endoabs.109.PL2

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PL3

Abstract Unavailable
DOI: 10.1530/endoabs.109.PL3

Society for Endocrinology Dale Medal Lecture
PL4

Growth hormone, DNA damage and cancer
Shlomo Melmed
Cedars-Sinai Medical Center, Los Angeles, USA

We explored the role of locally produced non-pituitary tissue GH (npGH) in regulating the normal epithelial microenvironment. In contrast to declining circulating pituitary GH occurring with age, both epithelial DNA damage and aging induce local npGH expression. DNA damage, a driver of age-related pathology, accumulates consequent to local npGH- mediated defective DNA damage repair (DDR). This build-up of unrepaired DNA damage results in chromosomal instability in aged mice and also in iPSC-derived human intestinal organoids. Disrupted mutant GHR signaling in fibroblasts derived from Laron syndrome patients, as well as observed in GHRKO murine colon, both reveal high expression of tumor-suppressor p53, with less DNA damage. Similarly, injection of a selective GHR synthesis inhibitor activates DNA repair with subsequent decreased epithelial DNA damage. By contrast, pegvisomant, induces colon p53 and p21 in colon epithelium of acromegaly patients, conferring protection from DNA damage. Consistent with these finidngs, in the aged human colon, local npGH is defined as a component of the senescence-associated secretory phenotype (SASP) and elicits paracrine epithelial GHR signalling to induce local DNA damage as evidenced by co-cultured WT and GH-expressing organoids developing chromosomal instability, somatic deletions, and EMT phenotypes. These adverse microenvironmental sequelae are induced by npGH-mediated suppressed DDR proteins, EMT and migratory protein dysruptions. WIP1 phosphatase mediates GH-induced dephosphorylated ATM, leading to inactivation of DDR proteins. Wip1 inhibition mitigates GH-induced DNA damage. npGH also triggers epithelial EMT and cell motility. Enriched gene ontology and KEGG analysis of colon organoids exposed to paracrine npGH revealed distorted ECM gene expression and focal adhesion pathways. Injecting of GH-expressing fibroblasts into murine prostate glands leads to EMT and DNA damage and phenotypic features consistent with benign prostate hypertrophy. Conclusions: Paracrine npGH enables a microenvironmental landscape favoring epithelial cell transformation. Blocking local GH action may benefit healthspan and ameliorate aging-associated disorders.
DOI: 10.1530/endoabs.109.PL4

British Thyroid Association Pitt-Rivers Lecture
PL5

Abstract Unavailable
DOI: 10.1530/endoabs.109.PL5

Society for Endocrinology Jubilee Medal Lecture
PL6

An accidental endocrinologist
Ashley Grossman
Green Templeton College, Oxford, United Kingdom. Barts and the London School of Medicine and Dentistry, QMUL, London, United Kingdom. Royal Free Hospital, London, United Kingdom

A career trajectory is rarely a straight line, or even a neatly curved line, but in my case it definitely meandered in different directions at different times. An early interest in psychology morphed into a devotion to language and psycholinguistics, but then this changed, after rather a trivial upset, into medicine, and possible psychiatry; in turn I have gradually moved via neurology through neuroendocrinology to endocrine oncology. I have always been lucky in moving to positions where I could follow my enthusiasms rather than any planned scheme, a path much less possible with our more structured approach to training in medicine. By way of *in vitro* pituitary studies, I worked with many colleagues to develop hypothalamic incubation systems, followed the close interplay between body and brain with studies into cytokine and gaseous neurotransmitters, and at the same time fortunately being gifted neuropeptides to explore neuroendocrine regulation. Over time, I moved into the molecular biological era and - with many collaborators - we were able to now investigate the molecular basis of many endocrine tumours, and the clinical development of diagnostic and therapeutic, especially theranostic, techniques. This path has also allowed me to work and, to some extent, help develop many nations progressing through their own problems in providing the best clinical care, both surgical and physician-led, to their populations. In my talk I hope to highlight the importance of motivation and enthusiasm in the fascinating world of clinical endocrinology, a branch of medicine more closely allied to rigorous basic science than probably any other branch of medicine, and to emphasise the role of serendipity, and allowing flexibility in one's research interests. But especially, we need to continue to

support the 'clinician scientist' as one able to mediate between the outstanding scientific discoveries, and their clinical application, as a two-way process.

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Society for Endocrinology International Medal Lecture

PL7

Abstract Unavailable

DOI: 10.1530/endoabs.109.PL7

Society for Endocrinology Medal Lecture

PL8

Endocrine dependence of maturation and developmental programming of mitochondrial oxidative phosphorylation (OXPHOS) function before birth

AL Fowden, KL Davies, EJ Camm, AJ Forhead & AJ Murray
Department of Physiology, Development and Neuroscience, University of Cambridge, Cambridge CB2 3EG, United Kingdom

At birth, requirements for energy in the form of ATP increase as the neonate takes on new postnatal functions such as pulmonary ventilation, thermoregulation and, in some species, locomotion. In many tissues, the morphological and physiological preparations for these neonatal adaptations begin before birth and depend on the natural rises in fetal cortisol and triiodothyronine (T_3) concentrations towards term. Recent studies in sheep have shown that these hormones also have an important role in the prepartum maturation of mitochondria, the major source of ATP. Mitochondrial content, oxidative capacity and abundance of electron transfer system (ETS) complexes of several fetal muscles increase towards term in parallel with the natural surge in fetal cortisol and T_3 concentrations. These prepartum mitochondrial changes can be stimulated prematurely by fetal cortisol infusion earlier in gestation and prevented by abolishing the rise in cortisol towards term by fetal adrenalectomy. Cortisol infusion also increased expression of the genes regulating mitochondrial biogenesis and OXPHOS efficiency while, conversely, adrenalectomy reduced these factors in late gestation. Similarly, prepartum development of muscle mitochondrial function was prevented by fetal thyroidectomy. In addition, prenatal overexposure to cortisol in late gestation altered mitochondrial OXPHOS function in specific muscles in adulthood. Muscle mitochondria are, therefore, responsive to the endocrine environment *in utero* and can be programmed developmentally with long term consequences for metabolism and ATP production postnatally.

DOI: 10.1530/endoabs.109.PL8

Clinical Endocrinology Journal Foundation Lecture

PL9

Improving the management of thyroid diseases: from the bench to the bedside

Kristien Boelaert
University of Birmingham, Birmingham, United Kingdom

Thyroid diseases are common, with thyroid dysfunction affecting up to 10% of the population and thyroid nodules occurring in 50% of people. Over the last 24 years my research has focussed on the pathogenesis, diagnosis and management of a wide range of thyroid conditions. In laboratory molecular studies I have explored novel oncogenes involved in the pathogenesis of thyroid cancers and how these affect the treatment of thyroid cancer with radioactive iodine. My clinical research has aimed to improve our knowledge of the prevalence, management and long-term outcomes of hyperthyroidism, managing thyroid disorders during pregnancy, as well as the causes of congenital hypothyroidism. In more recent years I have been actively involved and lead a number of large multi-centre clinical trials to evaluate the management of thyroid autoimmunity in fertility as well as the diagnosis and management of thyroid nodules. My research has changed clinical practice for these disorders and has been incorporated into national and international clinical guidance, patient information sources, and training pathways for clinicians. I have collaborated extensively nationally and internationally and worked with clinicians, scientists, health economists, policy-makers, and patient support groups aiming to improve the management of thyroid disorders in a clinically robust and cost-effective way. This lecture will provide an overview of my journey into thyroid diseases from the bench to the bedside.

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Debate

Motion: HRT should be used for the primary prevention of disease in menopausal women

D1.1

Abstract Unavailable

DOI: 10.1530/endoabs.109.D1.1

D1.2

HRT should be used by default for the primary prevention of disease in postmenopausal women

Richard Quinton
Imperial College London, London, United Kingdom. CNTW NHS Foundation Trust, Newcastle-on-Tyne, United Kingdom

The United Kingdom faces an unprecedented convergence of healthcare-related crises: an ageing population with extensive chronic healthcare needs; a crisis in social care, for which cross-party political agreement remains a distant mirage, and the inaccessibility of primary care services, as providers have prioritised meeting externally-set targets that unlock additional funding, ahead of providing accessible medical care according to clinical need. This has created a maelstrom of acute "medical" admissions that often lack dignity and sometimes even humanity, with risk factors for pain, disability, impaired QoL and hospitalisation in older age including sarcopenia, osteoporosis, cardio-metabolic syndrome, social isolation and poor mental health. The 4–5 year menopause transition heralds profound changes in physiology that accelerate biological ageing. The average woman loses 10% of bone mass and 10% of limb muscle mass; the lipid profile becomes pro-atherogenic; fasting glucose and HbA1c rise by 6%; sleep quality deteriorates and vulvovaginal atrophy precipitates sexual dysfunction or urinary urgency in 50%; 40% experience mood disorders, and divorce peaks, with most citing menopause as a contributing factor, irrespective of who initiated proceedings. HRT can mitigate most of these adverse effects and yet HRT scripts in are far below levels prior to the WHI study (2002), despite corrective messages in the media, and not helped by position statements emphasising the primary role of HRT as a treatment only for vasomotor and sexual symptoms. Even vaginal oestrogen is barely prescribed despite reducing actual or perceived UTIs. In the present UK healthcare environment (hours to get through to the surgery; weeks to secure routine appointment lasting 5 minutes that may not be with a doctor), it is unrealistic to expect women's needs to be met via patient-with-symptoms-consults-doctor-gets-counselled-receives-treatment. The only way forward is for a positive HRT discussion to be hard-wired into NHS primary care as per screening and vaccination.

DOI: 10.1530/endoabs.109.D1.2

Awards and Prizes

Teaching Achievement Award

TAA1

Empowering students in endocrine science: the establishment of the MSS summer school

Paul Foster
University of Birmingham, Birmingham, United Kingdom

As a key contributor to endocrine education at the University of Birmingham, Dr Foster leads the Cell Communications: Endocrinology and Pharmacology module for MBChB students (350/year) and oversees endocrine teaching for 1st-year dental students (85/year). Additionally, he provides significant teaching to 3rd-year BMedSci and Pharmacy students, including supervision of endocrine-focused final-year research projects. This Teaching Excellence Award highlights this work and the creation of the MSS Summer School. Established in 2016, the Department of Metabolism and Systems Science (MSS) Summer School offers an innovative 8–10 week program that immerses undergraduate students in endocrine-focused research. Participants undertake bespoke projects under the guidance of leading academics, gaining hands-on experience with techniques such as LCMS/MS metabolomics, confocal microscopy, and tissue analysis. Alongside technical skills, the program develops critical thinking and professional growth through journal clubs, seminars, and grant application training. The Summer School has expanded from six students to receiving over 70 applications annually, with cohorts averaging 15–20 participants. Projects encompass basic, translational, clinical, and bioinformatics sciences, providing a multidisciplinary research experience. Students actively contribute to group lab meetings and often publish their findings, significantly enhancing their endocrine academic and professional trajectories. This initiative demonstrates the transformative impact of immersive research experiences in inspiring students to pursue careers in endocrinology and related fields. Alumni have achieved notable milestones, including endocrine-based PhD placements and publications, underscoring the program's success. The MSS Summer School serves as a scalable model for integrating teaching excellence with research innovation. By embedding students in a dynamic research culture, the program equips them with essential skills and fosters future leaders in endocrine science. It highlights the value of research-intensive teaching as a cornerstone for advancing education and the field of endocrinology.

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Outstanding Clinical Practitioner Awards

OCP1

Crisis as a catalyst

Stefanie Baldeweg[1,2]
[1]University College London Hospitals, London, United Kingdom. [2]University College London, London, United Kingdom

The COVID-19 pandemic created unprecedented challenges in managing patients with endocrine conditions, particularly those requiring frequent monitoring and treatment dose adjustments. It is a real honour to be named Outstanding Clinical Practitioner by the Society for Endocrinology. I have been a Consultant endocrinologist for over 20 years. I am an allrounder and have strived to deliver excellence in clinical care at every encounter with patients, through service development, teaching and leadership. My most significant contribution to the endocrine community has been as Chair of the Clinical Committee of the Society. I have led the clinical community over 4 years, notably during the pandemic. I will present how the Society for Endocrinology developed and implemented innovative care protocols during nationwide lockdowns. The lessons learned continue to influence how we approach endocrine care, particularly for patients in resource-limited settings.

DOI: 10.1530/endoabs.109.OCP1

OCP2

Hungry for more: a tale of guts and hormones

Barbara McGowan[1,2]
[1]Guys & St Thomas' NHS Trust, London, United Kingdom. [2]Kings College London, London, United Kingdom

The lecture is about the journey which has led me to a career in obesity medicine. My interest in chemistry and molecules made biochemistry an easy choice to pursue as a first degree. What followed was a change in direction towards banking and finance, a world which opened up opportunities but could not suppress a strong desire to study Medicine. My PhD was all about gut hormones and appetite control, at a time when obesity was not recognized as a disease and there were no effective treatments. I was lucky to be in the right place at the right time to continue the journey into the science and clinical trials of gut hormone therapies, now approved as effective treatments in the NHS for people living with obesity.

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Nikki Kieffer Medal

NKM1

Abstract Unavailable

DOI: 10.1530/endoabs.109.NKM1

Emerging Researcher and Plenary Orals

Emerging Researcher Prize Lecture (Basic Science)

ER1.1

A developmental cell atlas of the human thyroid gland

Hassan Massalha[1,2], Mi K. Trinh[1], Erick Armingol[1], Liz Tuck[1], Alexander Predeus[1], Pavel Mazin[1], Carmen Sancho-Serra[1], Agnes Oszlanczi[1], Yvette Wood[1], Conor Parks[1], Toochi Ogbonnah[1], Holly J. Whitfield[1], Iva Kelava[1], Sam Behjati[1,3,4], Roser Vento-Tormo[1] & Nadia Schoenmakers[5,6]
[1]Wellcome Sanger Institute, Hinxton, United Kingdom. [2]University of Cambridge, Cambridge, United Kingdom. [3]Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom. [4]Department of Paediatrics, University of Cambridge, Cambridge, United Kingdom. [5]Department of Metabolism & Systems Science, School of Medical Sciences, College of Medicine and Health, University of Birmingham, Birmingham, United Kingdom. [6]Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom

The primary function of the thyroid gland is the synthesis and release of thyroid hormones, which are essential for health from embryogenesis to adulthood. Thyroid disorders occur frequently and include congenital hypothyroidism, which occurs due to aberrant thyroid development (thyroid dysgenesis) or impaired hormone synthesis and is particularly prevalent in trisomy 21 (T21). In contrast, thyroid carcinoma, an acquired disorder, is the most common endocrine malignancy in both paediatric and adult populations. Understanding the molecular basis of thyroid dysgenesis and paediatric thyroid carcinoma remains challenging, and requires an improved understanding of foetal thyroid development. To address this, we generated a comprehensive spatiotemporal atlas of the human thyroid during the first and second trimesters of pregnancy. Profiling over 200,000 cells with single-cell sequencing revealed key cell types involved in thyroid gland development, including the hormone-producing thyrocytes. We discovered that foetal thyroid follicular cells are heterogeneous epithelial populations consisting of two main functional subtypes (fTFC1, fTFC2), with fTFC2 expressing increased levels of PAX8, and spatial transcriptomics revealed subtype co-occurrence within individual follicles. While both fTFC1 and fTFC2 persist in adult thyroid, fTFC2 is a minor population amongst additional PAX8-positive follicular cell subsets. We observed thyroid dysgenesis in T21 age-matched specimens, and T21 thyrocytes showed transcriptional signatures of cytoskeletal disorganisation and altered interactions with the extracellular matrix, as well as compensatory activation of metabolic stress gene programs and upregulation of thyroid biosynthetic genes. In line with the altered proportions of fTFC2 in healthy foetal and adult thyroid, papillary thyroid cancer in children is transcriptionally enriched for the fTFC2 signature compared to that in adults. All together, these findings reveal thyrocyte heterogeneity across the lifespan and provide insights into thyroid development in health and disease, informing potential therapeutic interventions.

DOI: 10.1530/endoabs.109.ER1.1

Emerging Researcher Prize Lecture (Clinical)

ER1.2

Targeting human brown adipose tissue to improve cardiometabolic health

T'ng Choong Kwok
University of Edinburgh, Edinburgh, United Kingdom

Obesity is the leading preventable cause of morbidity and mortality worldwide. As a thermogenic organ, brown adipose tissue (BAT) holds promise as a pharmacological target for obesity and associated co-morbidities. Uncoupling protein 1 (UCP1) is the key thermogenic protein in BAT and is activated by cold-induced sympathetic stimulation. It remains unclear whether human BAT activity is reduced in obesity and cardiometabolic disease. In addition, our understanding of human BAT regulation remains limited, in part due to interspecies differences between human and murine BAT. RNA sequencing of human brown and white adipocytes identified the serotonergic and parasympathetic systems as two candidate pathways that were prioritized for further investigation. I hypothesised that: (1) *UCP1* expression in BAT was associated with favourable cardiometabolic risk factors; (2) the parasympathetic nervous system is a novel regulator of human BAT activity; (3) telotristat ethyl (a peripheral serotonin synthesis inhibitor) enhances human BAT and cardiometabolic health. To test these, I undertook several double-blinded placebo-controlled and case-control studies using techniques such as ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/MR, indirect calorimetry, thermal imaging and qPCR. (1) I demonstrated an inverse association between *UCP1* expression in BAT (n = 53 participants) but not WAT with ageing, adiposity, hypertension and insulin resistance. Additionally, *UCP1* expression and ^{18}F-FDG uptake by BAT were preserved in young obese adults. (2) Oxybutynin, a muscarinic acetylcholine receptor antagonist, inhibited ^{18}F-FDG uptake by BAT by ~20% during mild cold exposure and suppressed cold-induced thermogenesis. (3) Contrary to the hypothesis, telotristat ethyl inhibited ^{18}F-FDG uptake by BAT by ~25% and was deleterious to cardiometabolic health (suppressed cold-induced thermogenesis, reduced noradrenaline and increased cholesterol levels). Collectively, these studies demonstrated (1) an association between BAT dysfunction and adverse cardiometabolic profile, (2) the parasympathetic nervous system as a novel regulator of human BAT and (3) key interspecies differences in peripheral serotonin action on cardiometabolic health.

DOI: 10.1530/endoabs.109.ER1.2

Clinical Endocrinology Journal Foundation Best Abstract (Clinical)

ER1.3

Collagen-1 content as predictor for recurrence in clinically non-functioning pituitary neuroendocrine tumours (NF-PitNETs)

Ashutosh Rai[1], Ana Luís Carreira[2], Thomas Rice[3], Jack WilliamsWilliams[3], Kesson Magid[3], Aiste Mikalauskaite[3], Shruti Sabnis[3], Neil Dorward[4], Joan Grieve[4], Angelos Kolias[4], Danyal Khan[4], Hani J Marcus[4], Bishan Dass Radotra[5], Rajesh Chhabra[5], Pinaki Dutta[5], Márta Korbonits[3] & Federica Begalli[3]
[1]Panjab University, Chandigarh, India. [2]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal. [3]William Harvey Research Institute, Queen Mary University of London, London, United Kingdom. [4]UCL Queen Square Institute of Neurology, London, United Kingdom. [5]PGIMER, Chandigarh, India

Background
Incomplete resection (30-45%) or recurrence (7-12%) are common features in non-functioning pituitary neuroendocrine tumours (NF-PitNETs). However, we lack predictive biomarkers to help the management of these tumours. Collagen fibres are important structural components of the tumour microenvironment (TME) and have been associated with recurrence and aggressiveness in other cancers. However, their role in NF-PitNETs is unknown.
Method
We performed picrosirius red staining on 6 normal pituitaries (NP) and 73 NF-PitNETs; 49 full slides and 24 as part of tissue microarray, showing homogenous results. Collagens I and III were assessed via polarisation microscope. At least 4 fields of view were analysed from each sample. Additionally, we assessed collagen fibres characteristics: thickness and linearity (number of collagen fibre end points, number of fibre branch points, total length of fibres,), the structural complexity (fibre curvature, alignment, proportion of high-density matrix, ECM fractal dimension), fragmentation (hyphal growth unit), and compactness (matrix gaps, and lacunarity) using the TWOMBLI pipeline.
Results and Discussion
We observed significantly higher percentages of collagen-stained area in recurrent NF-PitNETs compared to non-recurrent and NP ($P < 0.0001$), with collagen I significantly increased, while collagen III significantly decreased in recurrent compared to non-recurrent tumours and NP ($P < 0.0001$). The study of the collagen fibres' characteristics revealed significant increase in number of fibres, thickness, length, structural complexity, and compactness in recurrent tumours compared to non-recurrent tumours and NP ($P < 0.0001$), while there was a significant decrease in fragmentation in recurrent tumours ($P < 0.0001$). These results show how recurrent NF-PitNETs are characterised by high-density matrix, which is associated with aggressiveness in other cancers. ROC analysis on the percentage of collagen-stained area showed its accuracy as prognostic marker for recurrence in NF-PitNETs (AUC = 0.88, $P = 0.006$).
Conclusions
This study highlight TME importance in PitNETs and crucially provides a powerful and easily applicable prognostic marker for recurrence in NF-PitNETs.

DOI: 10.1530/endoabs.109.ER1.3

Clinical Endocrinology Journal Foundation Best Abstract (Basic)

ER1.4

scRNAseq of orbital fat in thyroid eye disease reveals role of thyroid hormone signalling driving fibroblast function and identifies fibroblast-produced serum SPARC (osteonectin) as biomarker

Stephanie Hanna[1], Emma Robinson[1], Katie Boest Bjerg[1], Alexandros Delimichalis[1], Robert Andrews[1], Ilaria Muller[2,3],

Ebony Smith[4], Jadwiga Furmaniak[1], Marian Ludgate[1], Peter Taylor[1], Catherine Rennie[5], Dan Morris[4], Anjana Haridas[4], Vickie Lee[5] & Colin Dayan[1]
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Background
A subset of patients with Graves' disease (GD) develop thyroid eye disease (TED) , where orbital fat proliferates, resulting in protrusion of the eyes, disfigurement and even blindness. Antibodies that trigger GD can also cause TED. However, there remains a paucity of information about whether thyroid hormones can drive pathological processes in the orbital fat fibroblasts and the secretion of pro-inflammatory mediators by the fibroblasts. Furthermore, there is an unmet need to identify biomarkers that predict development of TED.
Methods
We profiled cells obtained from orbital decompressions in patients with TED, using scRNAseq, and examined mediators in the serum from healthy controls and participants in the CIRTED, INDIGO and Immunological Determinants of Graves' Disease studies.
Results
We found that fibroblasts were enriched for SLC16A2 (the T4/T3 transporter), DIO2 which catalyses conversion of T4 to T3, and THRA/B, the nuclear receptor for T3. In the serum we found that IGF1 was raised in subjects with thyroid disease but not further raised in those with TED. We wished to identify mediators from the fibroblasts released into the blood. We were particularly interested in SPARC (osteonectin) as highly produced by orbital fibroblasts in our scRNAseq analysis. Serum analysis identified that SPARC was significantly raised in people with thyroid disease compared to healthy controls. Furthermore, those with moderate to sight threatening TED had higher SPARC levels than those with thyroid disease alone or mild TED and their SPARC levels were positively correlated with FT3 and FT4.
Conclusion
Pathogenic processes in orbital fat are highly complex, involving TSHR, IGF1R (as targeted by teprotumumab) chemokine and cytokine signalling but also thyroid hormone signalling, resulting in elevated secretion of SPARC. This underscores the need to achieve euthyroidism to prevent development or progression of TED and suggests SPARC as a biomarker for the development of TED.

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Symposia

Disorders of bone mineral density mechanisms, consequences and management

S1.1

Secondary disorders: effects of diabetes on the bones

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Diabetes is characterised by hyperglycemia, but the two main types, type 1 diabetes (T1D) and type 2 diabetes (T2D), have distinct pathophysiology and epidemiological profiles. Individuals with T1D and T2D have an increased risk of fractures, particularly of the hip, upper arm, ankle, and nonvertebral sites. The risk of fractures is higher in T1D (+393%) than T2D (33%). The diagnosis of osteoporosis in individuals with T1D and T2D follows similar criteria as in the general population, but treatment thresholds may differ. There are changes in bone quality affecting bone matrix (the accumulation of AGES), changes in bone turnover (lower than usual), and changes in microarchitecture (such as cortical porosity) that better explain the fracture risk than BMD. Antiresorptive therapies, the first-line treatment for osteoporosis, are effective in individuals with T2D. Observational studies and post hoc analyses of previous trials have indicated that antiresorptive drugs, such as bisphosphonates and selective estrogen receptor modulators, are equally effective in reducing fracture risk and increasing bone mineral density (BMD) in individuals with and without T2D. Denosumab has shown similar effects on vertebral fracture risk but increases the risk of nonvertebral fractures. Considering the low bone turnover observed in T1D and T2D, anabolic therapies, which promote bone formation and resorption, have emerged as a potential treatment option for bone fragility in this population. Data from observational studies and post hoc analyses of previous trials also showed similar results in increasing BMD and reducing the risk of fractures in people with or without T2D.

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S1.2

Novel endocrine aspects of bone-kidney communication

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Fibroblast Growth Factor 23 (FGF23) is a hormone synthesized by bone osteocytes that controls serum phosphate concentrations by increasing renal phosphate excretion and decreasing renal production of 1,25-dihydroxyvitamin D3. Although this role has been known for several decades, the mechanisms that determine the regulation of FGF23 synthesis and secretion in response to variations in serum phosphate concentration are still poorly understood. In this talk, I will present data implicating PiT1/PiT2 transceptors expressed in bone in this sensing role and thus influencing the kidney (bone to kidney), and I will also present recent data illustrating the role of the kidney, a target of FGF23, in the endocrine regulation it exerts on bone to control FGF23 secretion (kidney to bone). Knowledge of these reciprocal regulatory loops will provide a better understanding of disorders of FGF23 homeostasis, which are often associated with significant morbidity and mortality.

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S1.3

Secondary disorders: effects of glucocorticoid treatment on bone

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Systemic glucocorticoid (GC) treatment has profound direct and indirect effects on the skeleton (1). At tissue level, GCs exhibit biphasic effects on osteoblast maturation, function, and lifespan. Osteoclast activity and survival is promoted through sclerostin and RANKL. Renal and gut calcium handling is adversely affected as is the sex hormone and GH axes. Secondary hyperparathyroidism contributes to the net loss of bone mass and degradation of architecture. Use is prevalent in the older age groups. In 2023, 9% of the Danish population aged 80 or older filled a prescription for sGCs compared with 3% for age 25-44 and 0.2% of those under 18. There is a general understanding that GCs shift the fracture threshold towards fractures occurring with minor BMD reduction. New data will be discussed. It is difficult to obtain unbiased data on BMD trajectories during sGC exposure because of entanglement of DXA referral and treatment intent, i.e. DXA monitoring also reflects a plan to intervene beyond a certain BMD threshold. BMD trajectories show considerable variation among GC users both in the short and the longer term with some patients experiencing little or no bone loss even with high doses (2). Fracture risk is particularly elevated with exposure to high GC doses, less so with intermittent dosing or lower daily doses. The impact of inhaled GCs is controversial; higher dosing flags a patient subgroup with more pronounced pulmonary disease, which in itself marks higher risk of fractures. There is a certain lack of data in younger adults and of evidence based guidelines in this age group. Clinical management guidelines across countries and societies show marked discrepancy in intervention thresholds and paths but good agreement in terms of choice of medications despite limited fracture data.

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Emerging Mechanisms and Treatments in Fatty Liver

S2.1

PNPLA3 and metabolic dysfunction-associated steatotic liver disease (MASLD)

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The I148M variant in PNPLA3 alone explains 10% of the risk of cirrhosis (UK Biobank). Of all subjects, 30-50% are heterogenous for the PNPLA3 I148M variant. Both MAFLD associated with insulin resistance (IR) ('MASLD-IR') and MAFLD caused by the PNPLA3 I148M variant ('MASLD-PNPLA3') predispose to all stages of MASLD. Patients with both IR and the PNPLA3 I148M variant are at particularly high risk of liver disease. IR increases while the PNPLA3 I148M variant decreases the risk of cardiovascular disease. This implies that the pathogenesis of 'MASLD-IR' and 'MASLD-PNPLA3' differ. *Substrate excess*. In 'MASLD-IR' compared to age-, gender,- and BMI-matched controls, there is, perhaps simply because of overeating and inactivity, marked substrate excess (glucose, fatty acids, amino acids) while substrates are unaltered in 'MASLD-PNPLA3'. *Substrate fluxes*. A dipose tissue lipolysis and de novo lipogenesis (DNL) are the two most important pathways contributing to steatosis in 'MASLD-IR'. DNL is low and lipolysis unaltered in 'MASLD-PNLA3'. Hepatic TG accumulation is thus purely a consequence of PNPLA3-I148M-induced changes in intrahepatic metabolism. *Human liver and adipose tissue lipidome.* The human liver lipidome in 'MASLD-IR' compared to matched controls is markedly enriched with saturated TGs and IR inducing ceramides. In PNPLA3 I148M carriers vs, non-carriers, the relative and absolute amounts of polyunsaturated fatty acids (PUFAs) in TGs are markedly enriched and there are no changes in bioactive lipids consistent with lack of insulin resistance in 'MASLD-PNPLA3'. The increase in PUFAs is due to retention of PUFAs in hepatic TGs. *Circulating lipids*. >'MASLD-IR' is characterized by increased circulating VLDL and low HDL. In IR individuals carrying the PNPLA3 variant, opposite, anti-atherogenic changes are observed. *Conclusions*. MASLD is more complex than its simple definition suggests. This knowledge has implications in the clinic for prediction of the individual risk of future liver and cardiovascular events and choice of therapies.

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S2.2

Abstract Unavailable

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S2.3

Liver disease in pregnancy

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Liver disorders can be precipitated by pregnancy, e.g. severe pre-eclampsia with HELLP (haemolysis, elevated liver enzymes and low platelets) syndrome, intrahepatic cholestasis of pregnancy (ICP) and acute fatty liver of pregnancy. Many women with liver disease need to be looked after by specialist physicians with an understanding of the impact of pregnancy on the disorder, the implication of some medications for the fetus, and also the potential risk of adverse pregnancy outcomes. Pre-pregnancy counselling and referral to specialist clinics will maximise the likelihood of good maternal and fetal health. Hepatic steatosis is increasingly reported in women of reproductive age. There is currently limited understanding of the prevalence and outcomes of steatotic liver disease in pregnancy. A US study reported that the proportion of pregnant women with metabolic dysfunction-associated steatotic liver disease (MASLD) tripled from 2007 to 2015. Pregnant women with MASLD had higher rates of maternal cardiometabolic disorders including gestational diabetes mellitus (GDM) and hypertension. They also had higher rates of pregnancy complications including preterm birth and postpartum haemorrhage. Furthermore, north American data report that MASLD is the commonest underlying cause of cirrhosis in pregnant women. This represents a considerable change from previous studies of cirrhosis in pregnancy where the principal underlying causes of cirrhosis were viral and autoimmune hepatitis. Cirrhosis remains associated with increased risk of serious maternal morbidity and mortality, principally from gastrointestinal haemorrhage. It is also complicated by maternal cholestasis, hypertensive disease, preterm birth and prolonged admission to the neonatal unit. Some gestational liver diseases are associated with subsequent maternal and offspring risk of hepatobiliary disease, including steatosis, MASLD and cirrhosis. Pregnancy represents a time when women and children at risk of fatty liver and associated metabolic disorders can be identified and interventions can be initiated to improve subsequent health outcomes.

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The adipose microenvironment: the missing link between obesity and cancer?

S3.1

Abstract Unavailable

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S3.2

Extracellular-vesicles from the peri-prostatic adipose tissue of obese, but not lean, men promote prostate cancer aggressivity

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Prostate cancer (PC) affects 1-in-8-men and obesity, termed a global epidemic by the WHO, affects 1-in-3. Obesity is the largest modifiable cancer risk-factor: every five-point increase in body-mass index increases risk of fatal PC by almost 10%. The peri-prostatic adipose tissue (PPAT), volume of which is associated with PC lethality/reduced therapy response, is an important component of the PC tumour-microenvironment. Adipose-tissue (AT) is the largest human endocrine gland, showing an altered secretome in obesity. PPAT can also secrete extracellular-vesicles (EVs) carrying cargo including microRNAs, which are involved in melanoma, lung, ovarian and breast cancer progression. Despite accumulating evidence showing the importance of AT secretome in tumour growth, its roles in PC progression are still poorly understood. This project investigates EV-mediated mechanisms of communication between PPAT and PC epithelial cells, and their clinical implications. To date, we established a biobank from >120 patients, with matching PPAT/tumour tissue and clinical information. We showed that PPAT EVs from obese but not lean patients, significantly increase proliferation and migration of PC cells *in vitro*. Obese PPAT EVs also reduce angiogenesis, consistent with chronic hypoxia observed in obese patient adipose. We performed small RNA-seq on PPAT EVs from obese/lean PC patients, and mRNA-seq on PC cells treated with these EVs. Top PPAT-EV dysregulated genes are associated with PC survival. Silencing of one such PPAT-upregulated gene, TBX1, repressed PC cell aggressiveness *in vitro*. We also optimized *in vitro* adipocyte differentiation from PPAT stem cells to demonstrate that PPAT effects are specifically attributable to mature-adipocytes. Finally, we showed that RNA-seq analysis of PPAT from genetically-engineered mouse models (GEMMs) modelling PC natural history, showed dramatic changes in tissue histology, immune response, lipid metabolism in PPAT of aggressive-*versus*-indolent tumours. Integrative analysis of these data will hopefully elucidate novel, actionable drivers of aggressive PC progression for personalized-medicine.

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S3.3

Abstract Unavailable

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Hot Topics in Diagnosis and Management of Pituitary Tumours

S4.1

Abstract Unavailable

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S4.2

Cabergoline for the treatment of non-functioning pituitary adenomas

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Non-functioning pituitary adenomas (NFPAs) are benign tumors that primarily manifest through pressure effects on surrounding structures. Transsphenoidal surgery serves as the primary intervention, particularly for large, symptomatic tumors, as it provides immediate decompression of adjacent tissues. However, post-operative tumor remnants present an ongoing clinical challenge, with a significant proportion of patients experiencing progressive tumor growth that necessitates additional surgery or radiation therapy. While no medical therapy has received regulatory approval for NFPA treatment, dopamine agonists, particularly cabergoline, have emerged as a promising therapeutic option. Clinical studies demonstrate that cabergoline can prevent remnant tumor growth in 50-60% of patients, with modest tumor shrinkage observed in 20-30% of cases. Preliminary evidence suggests this approach may reduce the frequency of additional therapeutic interventions, though more extensive studies are needed to confirm these findings. The therapeutic response appears independent of dopamine receptor expression levels, suggesting complex underlying mechanisms. Given the typically slow growth pattern of these tumors, developing tools to identify high-risk cases would enhance treatment stratification. The favorable safety profile of low-dose cabergoline, coupled with emerging evidence supporting its efficacy, positions it as a valuable option in the medical management of NFPAs, particularly for post-surgical remnants or when surgery is contraindicated.

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S4.3

Managing pituitary disease in adolescence

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Adolescence is a critical period of development, during which the immature child acquires physical and emotional maturity. The pituitary undergoes characteristic

changes in physical appearance and function that help orchestrate these developmental changes. Adolescents may have congenital pituitary insufficiency affecting single hormones, or insufficiency of all anterior and posterior anterior pituitary hormones, most commonly in the context of septo-optic dysplasia. Adolescence with septo-optic dysplasia may also experience visual impairment, special educational needs and autism, requiring particular attention and consideration at the time of transition to adult services. Acquired pituitary conditions include pituitary adenomas, most commonly prolactinoma in girls in the adolescent age group, and pituitary insufficiency due to brain injury or brain tumours and their treatment. Craniopharyngioma and germinoma show a peak in incidence during the adolescent years, while the cognitive and endocrine consequences of radiotherapy for brain tumours affecting younger children may become evident during this time. The experience of a life-threatening condition, and its treatment, pose unique challenges during adolescence when peer relationships become increasingly important together with a move towards independence from parents. Tumour treatment, lost time from school, time away from friends and greater dependence on parents may disrupt normal patterns of emotional, psychological and physical development. In this talk, we will use a case of a young patient diagnosed with a germinoma in early adolescence, to discuss the evolution of pituitary insufficiency and its treatment in the context of normal pituitary function during adolescence and consider how the disease and its treatment affects such patients as they move towards adult life.

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Thyroid Cancer from Bench to Bedside

S5.1

Cell motility in thyroid cancer

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Despite an excellent prognosis for the majority of people with thyroid cancer, a significant proportion of tumours progress to more advanced disease that is difficult to treat. Morbidity and mortality in thyroid cancer occurs as a result of locally invasive or metastatic disease. Therefore, a better understanding of the mechanisms that drive thyroid cancer cell motility and metastasis is required to develop new therapeutic strategies. This symposium will outline our current knowledge of the molecular and cellular mechanisms that regulate thyroid cancer cell motility and contribute to invasive and metastatic tumour progression.

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S5.2

Abstract Unavailable

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S5.3

Abstract Unavailable

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The benign, the bad and the ugly of adrenal lumps: an update

S6.1

Abstract Unavailable

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S6.2

The multiple facets of primary bilateral macronodular adrenal hyperplasia

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Primary Bilateral Macronodular Adrenal Hyperplasia (PBMAH) is an adrenal cause of Cushing's syndrome secondary to the development of bilateral benign adrenocortical macronodules responsible for variable levels of cortisol excess. The classic form causing overt-Cushing syndrome is rare, but mild form of the disease is nowadays more frequently diagnosed in patients with bilateral adrenal incidentalomas and Mild Autonomous Cortisol Secretion (MACS). Genomic studies identified molecular subgroups correlating with the clinical and morphological heterogeneity of PBMAH. *ARMC5* was identified 11 years ago as a new tumor suppressor gene responsible for PBMAH and germline alterations are found in about 20 % of the patients (Assié G, N Engl J Med, 2013; Bouys L, Eur J Endocrinol, 2023). More recently germline *KDM1A* alterations have been identified in more than 90 % of PBMAH causing Food-Dependent Cushing (Vaczlavik A, Genetics in Medicine, 2022; Bouys L, Eur J Endocrinol, 2025). These translational advances clearly demonstrate that PBMAH is the result of a molecular oncogenic process. In the 2022 revision of the WHO classification of adrenocortical tumors the term Bilateral Macronodular Adrenal Disease (BMAD) is proposed to reflect that. The clinical heterogeneity of PBMAH correlates with the molecular classification of PBMAH. *ARMC5* related PBMAH are more severe and with an equilibrated sex ratio. Treatment, especially surgery is more often done in these *ARMC5* patients. *KDM1A* related PBMAH are associated with Food-Dependent Cushing and mostly observed in female. Adrenal enlargement can be asymmetric. Diagnosed *KDM1A* patients are almost always treated, mostly by surgery. The remaining PBMAH with no know genetic defect today are observed in 2 groups from the morphological point of view and present specific genomic profiles (Violon F, Endocr Pathol. 2024). Cushing syndrome is usually less severe and patients are less often treated, especially with surgery. The perspective for patients management of these progress will be discussed.

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S6.3

Prognostication of adrenocortical carcinoma

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Adrenocortical carcinoma (ACC) is a rare aggressive endocrine cancer with a heterogeneous prognosis and limited treatment options. Initial tumor stage, resection status and Ki67 index are established clinical/histopathological prognostic factors, but do not always predict clinical outcome. Combined scores have been therefore proposed to improve prognostication of ACC. Hereby, the S-GRAS score has proved to have the best prognostic performance. Genome-wide multi-omics studies identified molecular patterns associated with poor prognosis, but required cost-intensive technologies and complex workup, precluding the adoption of the proposed prognostic biomarkers into clinical practice. More recently, targeted next-generation sequencing (NGS) has been validated for calling mutations, chromosome alterations and DNA methylation status in ACC samples. Still, all these studies were performed with snap-frozen samples that are not always available in clinical settings. In a retrospective project, we used DNA isolated from formalin-fixed paraffin-embedded (FFPE) specimens, readily available in clinical settings We applied targeted NGS for investigating alterations in 160 cancer-related genes and pyrosequencing for methylation in four genes and demonstrated that molecular profiling may improve prognostication of ACC. In following studies, we showed that the number of relevant genes relevant can be reduced to less than 10, making targeted sequencing even more applicable in clinical practice, paving the way towards precision medicine. It is now the task to prove that proposed techniques are feasible in real-life setting and biomarkers are clinically helpful to guide clinicians in patient care. Another important towards optimized management of patients with ACC would be the investigation of molecular alterations in circulating cell-free tumor DNA (ccfDNA). Previous studies showed that ccfDNA can be detected in a subset of patients and could be used for both prediction of clinical outcome and detection of early disease recurrences. Its application as prognostic biomarker or monitoring tool in clinical practice remain to be determined.

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Frontiers in Non Reproductive Actions of Sex Hormones Across the Lifecourse

S7.1

Age-related loss of GnRH expression and rhythmic release in cognitive disorders: a role for minipuberty?

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Pulsatile secretion of gonadotropin-releasing hormone (GnRH) is essential for activating and maintaining the function of the hypothalamic-pituitary-gonadal (HPG) axis, which controls the onset of puberty and fertility. Two provocative recent studies [1,2] suggest that, in addition to controlling reproduction, the neurons in the brain that produce GnRH are also involved in the control of postnatal brain maturation, odor discrimination, and adult cognition. I will discuss the development and establishment of the GnRH system, and especially the importance of its first postnatal activation, a phenomenon known as minipuberty, to its later functions, reproductive and non-reproductive. In addition, I will discuss the beneficial effects of restoring physiological, i.e. pulsatile, GnRH levels on olfactory and cognitive alterations in Down syndrome and preclinical models of Alzheimer's disease, as well as the risks associated with long-term continuous, i.e. non-physiological, GnRH administration in certain disorders [3]. Finally, I'll discuss the intriguing possibility that pulsatile GnRH therapy may hold therapeutic potential for the management of some neurodevelopmental cognitive disorders as well as pathological aging in the elderly. *This work was supported by National Grant no. ANR-17-CE16-0015 (GRAND), ANR-11-LABEX-0009 (DistAlz) and ANR-16-IDEX-0004 (I-SITE ULNE), and European Grant no. 101123221 (ERC-2023-PoC UPGRADE).*

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S7.2

Mapping the female brain: a spotlight on sex steroids across the lifespan

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Despite widespread sex differences in prevalence and presentation of numerous illnesses affecting the brain, there has been limited focus on the effects of endocrine aging on brain and mental health in females. The majority of preclinical studies have focused on males only, and clinical studies often analyzed data by covarying for sex, ignoring relevant differences between the sexes. This sex-neutral approach is biased and can contribute to failures of health care providers to deliver targeted treatments and services for all sexes. In my talk, I will spotlight female brain health by informing on the role of sex steroids, particularly estradiol, on the female brain across the lifespan. I will present our work on sex steroid fluctuations and their impact on the female brain across the menstrual cycle, pregnancy, and menopause using dense-sampling approaches, large population-based datasets, and machine learning tools. A better understanding of the dramatic changes in the female brain across the lifespan is a critical step towards mechanistic models explaining sex differences in disease susceptibility and a crucial prerequisite for the development of personalised mental health care.

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S7.3

Evaluating the complex interplay between androgen deprivation therapy, sleep disturbance and nocturia in prostate cancer. A systemic review of prospective studies, and consideration of the emerging role of transdermal oestrogen

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Insomnia in prostate cancer patients is common especially in those receiving androgen deprivation therapy (ADT). This review considers the evidence from prospective clinical trials exploring the impact ADT (mainly with LHRH analogue injections) has on sleep disturbance and will consider the relative contribution of hot flushes / night sweats as well as nocturia a common symptom associated with prostate cancer to insomnia. In addition, some initial investigations utilising transdermal oestrogen patches (tE2) will be presented as an alternative to LHRH analogue injections. A review was performed and identified 17 studies reporting on sleep disturbance and androgen deprivation therapy involving a total of 1417 patients. 7 were prospective non-randomised studies, 3 of which did not utilise an objective method of sleep assessment, and only 2 had a baseline assessment. The studies showed consistently that up to 68% patients on ADT subjectively reported poor sleep using self-reported questionnaires. Specifically, there was an increased prevalence of insomnia (as determined by the Insomnia Severity Index) in the order of 32-38%. The most frequently reported actigraphy parameters were the fragmentation index (FI), wake associated sleep onset (WASO), and daytime napping. The studies consistently showed a higher FI (>40%), and WASO (approximately 80-90 minutes), with a trend towards increase daytime napping, suggesting that those on ADT find it difficult to stay asleep at night with a more fragmented sleep pattern, for which they compensate by taking more daytime naps. There is conflicting data about the role of nocturia and the relative contribution this has on sleep disturbance compared to hot flash interference. In a subset analysis on 5 patients receiving tE2, preliminary investigations showed that they spent less time in bed at night with less nocturnal wakings and reduced daytime napping. Further studies are underway to better characterise the sleep profile in patients on tE2.

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Workshops

Basic Science Workshop: New ways to illuminate endocrine (patho)physiology

WS1.1

Visualising diabetes and obesity drug targets from the single molecule to the whole animal

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Glucagon-like peptide-1 receptor (GLP1R) and glucose-dependent insulinotropic polypeptide receptor (GIPR) have emerged as major drug targets for the treatment of type 2 diabetes and obesity. Drugs that target GLP1R and/or GIPR show profound effects on glucose levels, food intake and body weight. However, we still have limited knowledge of where GLP1R and GIPR are expressed in the body, which is holding back development of even more effective drugs. In the current presentation, I will introduce new technologies to visualize and interrogate GLP1R and GIPR expression from the single molecule to the whole animal. I will also discuss how these studies have led to new understanding of GLP1R and GIPR biology, with relevance for type 2 diabetes and obesity therapy, as well as ongoing clinical trials on neurodegenerative and inflammatory disease.

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WS1.2

Can total-body positron emission tomography (PET) imaging unravel multi-organ endocrine connectomes?

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The development of total-body Positron Emission Tomography (PET) scanners has galvanised the field of molecular imaging by broadening the horizons of systems biology research in the context of human physiology and pathobiology. This is because the whole human body can now be interrogated dynamically with total-body PET systems, consequently molecular responses occurring at different systems can be imaged simultaneously and integrated as functional connectomes. Traditionally, a connectome has been described as a comprehensive set of neuronal connections of a species' central nervous system. However, recent imaging developments have enabled the study of molecular connections across multiple organs. PET uses specific probes capable of reporting on different molecular processes *in vivo* and non-invasively. These probes are administered intravenously and through circulatory distribution reach all tissues in the body. Consequently, coupled with total-body PET, these probes can report on multi-organ molecular functionality with unprecedented temporal resolution. Recently, studies have reported distinct metabolic connectomes in cancer patients versus healthy controls using total-body PET imaging with [^{18}F]FDG, an analogue of glucose. In animals, complex bone metabolic connectomes have been reported. These metabolic connectomes have shown to be capable of identifying disease and serve as better prognostic markers than conventional single organs metrics used in the clinical setting, illustrating the value of multi-organ connectome analysis over conventional single organ studies. The endocrine system is distributed throughout the body and produces hormones with effects on multiple tissues and organs all over the human body. Consequently, total-body PET imaging can serve as an important enabler of endocrine system level research. This presentation will review the fundamental principles of PET imaging, describe latest developments with total-body PET technology and provide a few examples of how multi-organ connectomes can transform diagnosis, prognosis and treatment of human diseases.

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WS1.3

Abstract Unavailable

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Clinical Management Workshop: Calcium disorders in pregnancy

WS2.1

Calcium physiology in pregnancy and lactation

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Maternal calcium homeostasis undergoes major adaptations during pregnancy and lactation to meet the requirements of the developing fetus and infant. Early pregnancy is characterised by accrual of calcium in the maternal skeleton, which begins in the first trimester. This is mediated by a 2-5-fold increase in the synthesis of calcitriol by the renal proximal tubule, which leads to a doubling of intestinal calcium absorption during pregnancy. The increased calcitriol synthesis occurs independently of parathyroid hormone (PTH), and may instead be mediated by pregnancy hormones such as oestradiol, prolactin or human placental lactogen. Maternal circulating parathyroid hormone-related peptide (PTHrP) increases progressively throughout pregnancy and may also promote renal calcitriol synthesis. Increased intestinal calcium absorption suppresses PTH secretion and increases urine calcium excretion during pregnancy. Fetal accrual of calcium for skeletal development occurs mainly during the third trimester is supported by maternal increases in both calcium absorption and bone resorption. After childbirth, maternal calcium homeostasis involves a shift from renal calcitriol synthesis to increased mammary synthesis of PTHrP. High levels of PTHrP combined with lactational amenorrhoea and a hypo-oestrogenic state promote bone resorption in order to provide calcium for milk production. Thus, pregnancy and lactation are characterised by unique PTH-independent mechanisms for supplying calcium for fetal and infant development.

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WS2.2

Parathyroid disorders in pregnancy

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Managing parathyroid disorders in pregnant women requires careful consideration of the physiological changes in bone and mineral metabolism that occur during pregnancy. Diagnostic and therapeutic approaches for primary hyperparathyroidism (PHPT) and hypoparathyroidism differ significantly from those for non-pregnant patients. For PHPT, it is recommended to perform parathyroidectomy prior to pregnancy whenever possible, as maternal and fetal complications related to hypercalcemia tend to increase with the severity of hypercalcemia. If surgery is necessary during pregnancy, the second trimester is the preferred timing. Mild cases of PHPT are typically managed conservatively, primarily through hydration, though there is limited evidence to support drug treatments in this context. Women with hypoparathyroidism can be reassured that the condition does not typically impair fertility and carries a low risk of pregnancy complications if adequately managed. Regular monitoring is essential, as calcium and active vitamin D requirements may fluctuate during pregnancy, though they generally trend toward reduced dosages. Postpartum and lactation periods require close surveillance for women with parathyroid disorders, as they face an increased risk of hypercalcemia after delivery. Additionally, newborns of mothers with parathyroid conditions should have their calcium levels monitored closely in the days or weeks following birth. Intrauterine exposure to hyper- or hypocalcemia may affect their ability to regulate calcium metabolism postnatally.

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WS2.3

Pregnancy associated osteoporosis

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Pregnancy Associated Osteoporosis (PAO) is a rare condition which typically presents with back pain and height loss due to the occurrence of multiple vertebral fractures. Although symptoms often occur towards the end of the third trimester, the diagnosis is usually made post-partum. The estimated prevalence of the condition is about 4 in 100,000 women. The diagnosis should be suspected in a woman who experiences back pain so severe as to interfere with normal activities accompanied by height loss. The cause is unknown. It has been speculated that PAO may occur as the result of physiological bone loss in women who have pre-existing low bone mineral density (BMD) before pregnancy, exaggerated physiological bone loss, or a combination of both factors. There is evidence for a genetic component due to the frequent observation that women have a family history of osteoporosis. There have been few studies in which genetic analysis has been conducted but those that have been performed suggest that about one third

may have pathogenic variants in genes that regulate BMD or bone fragility. The diagnosis is usually can by a combination of spine x-ray, MRI and DEXA. Lumbar spine BMD is consistently lower than hip BMD in PAO, although it is not always possible to obtain spine BMD measurements due to the presence of vertebral fractures. The most used treatments for PAO are calcium and vitamin D supplements, bisphosphonates and teriparatide, although there is evidence that BMD improves even without treatment. The rate of recurrent fractures is about 12% and does not seem to be influenced by treatment. Further research is required to determine the cause of PAO, and to define the optimal mode of treatment to guide clinicians on how to manage this rare but serious disorder.

DOI: 10.1530/endoabs.109.WS2.3

Basic Physiology Workshop (Cutting Edge Session): New Insights into Hormonal Regulation of Behaviour

WS3.1

Integration of hunger and hormonal state gates infant-directed aggression

Johannes Kohl, Mingran Cao & Rachida Ammari
The Francis Crick Institute, London, United Kingdom

Social behaviour is profoundly shaped by bodily states. It is well-documented that individual states such as the estrous cycle or hunger affect behaviours such as mating or aggression. However, animals typically exhibit multiple such states simultaneously. How and where orthogonal states are integrated and how this shapes behaviour remains poorly understood. Here we report how hunger and hormonal state converge on neurons in the medial preoptic area (MPOA) to shape infant-directed behaviour. We first demonstrate that hunger can trigger pup-directed aggression in virgin female mice. This behavioural switch results from the inhibition of MPOA neurons by neuropeptide Y (NPY) release from Agouti-related peptide expressing neurons in the arcuate nucleus of the hypothalamus (ArcAgRP neurons). Next, we show that the rate of aggression is set by hormonal state, with MPOA neurons sensing the progesterone (P4) to estradiol (E2) ratio throughout the estrous cycle. Hunger and hormonal state converge on HCN (hyperpolarization-activated cyclic nucleotide-gated) ion channels, setting the baseline activity and excitability of MPOA neurons. Our findings provide a neural mechanism for the integration of orthogonal physiological states, enabling flexible switching of social behaviour.

DOI: 10.1530/endoabs.109.WS3.1

WS3.2

Abstract Unavailable

DOI: 10.1530/endoabs.109.WS3.2

WS3.3

Brainstem circuits regulating appetite suppression

Zachary Knight
UCSF, San Francisco, USA. HHMI, San Francisco, USA

The progress of meal is controlled by sensory feedback from the gut that is generated during eating. These sensory signals are transmitted by vagal afferents to the caudal brainstem, but how they are integrated in the brainstem to determine when a meal should end is unknown. A major challenge has been the inability to performing neural recordings in the caudal brainstem of awake, behaving animals. I will describe our work developing methods for brainstem recordings in behaving mice, and what these recordings have taught us about the signals that control food intake.

DOI: 10.1530/endoabs.109.WS3.3

How Do I...? Sessions

How do I. . .? 1

HDI1.1

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI1.1

HDI1.2

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI1.2

HDI1.3

How do i assess and manage HPA axis suppression from exogenous glucocorticoids?

Alessandro Prete
Department of Metabolism and Systems Science, University of Birmingham, Birmingham, United Kingdom

Glucocorticoids are widely prescribed as anti-inflammatory and immunosuppressive agents. This results in at least 1% of the population using chronic glucocorticoid therapy being at risk for glucocorticoid-induced adrenal insufficiency, a condition associated with considerable morbidity and mortality if not promptly recognised and managed. In cases where glucocorticoid-induced adrenal insufficiency develops or is suspected, a thorough clinical evaluation is essential, encompassing detailed history-taking, physical examination, and, where appropriate, biochemical testing. For patients discontinuing glucocorticoid therapy, individualised tapering protocols are crucial to minimise withdrawal symptoms and support adrenal function recovery. Patient education is a cornerstone of care, addressing key topics such as iatrogenic Cushing's syndrome, adrenal crisis prevention, and glucocorticoid withdrawal syndrome. This talk will focus on glucocorticoid-induced adrenal insufficiency management, with emphasis on national and international clinical guidelines.

DOI: 10.1530/endoabs.109.HDI1.3

HDI1.4

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI1.4

HDI1.5

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI1.5

HDI1.6

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI1.6

How do I. . .? 2

HDI2.1

How do i manage thyroid pathology after irradiation for other head and neck cancers?

Daniel Morganstein
Chelsea and Westminster Hospital, London, United Kingdom. The Royal Marsden Hospital, London, United Kingdom

External Beam Radiation is frequently used in the management of Head and Neck Cancer, including parathyroid cancer. The thyroid may also be exposed to radiation during mantle radiotherapy for Hodgkin's disease and breast cancer. Radiation can result in thyroid dysfunction in a high proportion of individuals with an intact thyroid prior to radiation. Primary hypothyroidism is the most common finding, in around 30% of patients, with a peak onset at around 2-3 years post treatment. Incidence may be increasing over time, possibly as a result of better recognition or longer survival. Hypothyroidism is most commonly diagnosed based on abnormal thyroid function tests rather than symptoms. Higher radiation doses to the thyroid are associated with higher risk. Less frequently, an acute thyroiditis can occur with transient thyrotoxicosis and more rapid progression to hypothyroidism. Older series report a risk of hyperthyroidism due to Grave' disease after mantle cell radiotherapy for Hodgkin's disease. In contrast the rate of hypothyroidism after treatment of breast cancer was low. Those with hyperthyroidism require close observation, with beta blockade as required, and prompt initiation of levothyroxine on progression to hypothyroidism. Amongst those with de novo hypothyroidism, sub-clinical hypothyroidism may occur first, but the risk of progression to clinically overt hypothyroidism is high. Finally, radiotherapy for nasopharyngeal tumours may include the pituitary and carry a risk of secondary hypothyroidism.

DOI: 10.1530/endoabs.109.HDI2.1

HDI2.2

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI2.2

HDI2.3

How do i approach hyperprolactinaemia whilst on antipsychotics and antidepressants?

Steven Hunter
Royal Victoria Hospital, Belfast, United Kingdom. Queen's University, Belfast, United Kingdom

Drug-induced hyperprolactinaemia is common. Approximately half of those taking antipsychotics develop hyperprolactinaemia due to blockade of the dopamine type 2 receptor. The propensity to cause hyperprolactinaemia varies markedly between antipsychotics. Regular monitoring before and during treatment will identify those with anti-psychotic induced hyperprolactinaemia. If prolactin exceeds 3000 mU/l a pituitary adenoma should be ruled out by MRI. Otherwise treatment is only necessary in cases with symptoms of hyperprolactinaemia or hypogonadism. Treatment options include dose reduction or change in antipsychotic treatment, sex steroid replacement or dopamine agonist therapy which should be done in consultation with psychiatry. By contrast antidepressants may cause modest hyperprolactinaemia in some patients by modulation of serotonin or noradrenaline levels. Routine monitoring is not recommended unless symptoms related to hyperprolactinaemia develop. Management is by dose reduction or switching to an alternative antidepressant with reassessment of prolactin levels and consideration of other causes if prolactin exceeds 1000 mU/l.

DOI: 10.1530/endoabs.109.HDI2.3

HDI2.4

How do i investigate and manage hypophosphataemia without hyperparathyroidism?

Holly Mabillard[1,2] & John Sayer[1,2]

[1]Newcastle University, Newcastle Upon Tyne, United Kingdom. [2]Newcastle Hospitals NHS Foundation Trust, Newcastle Upon Tyne, United Kingdom

Phosphate is essential for numerous physiological processes, including skeletal mineralisation, energy production, enzymatic reactions, cell membrane structure, and neurological function. Disruptions in phosphate balance, particularly hypophosphataemia, can cause significant morbidity but are often overlooked due to its exclusion from routine blood tests and the non-specific nature of its symptoms. This talk will explore the regulation of phosphate homeostasis, which is controlled by 1α,25-dihydroxyvitamin D3, parathyroid hormone (PTH), and fibroblast growth factor 23 (FGF23). These hormones govern phosphate absorption in the gut, its exchange between bone and extracellular spaces, and its excretion via the kidneys. Serum phosphate levels vary with age, making it vital to interpret results using appropriate reference ranges to avoid missed diagnoses, particularly in children. The causes of hypophosphataemia are broadly categorised into: (1) inadequate intake or absorption, often linked to malnutrition or gastrointestinal conditions; (2) redistribution, seen in conditions like diabetic ketoacidosis (DKA) treatment and refeeding syndrome; and (3) renal phosphate loss, as occurs in hyperparathyroidism or genetic conditions like X-linked hypophosphataemic rickets. Severe hypophosphataemia can lead to muscle weakness, respiratory failure, cardiac dysfunction, and bone pain due to reduced ATP production and oxygen transport. Management depends on identifying the underlying cause. Dietary supplementation is effective for nutritional deficiencies, while intravenous phosphate replacement may be necessary in acute, severe cases. Long-term treatment requires addressing the root cause, such as treating malabsorption or reducing renal phosphate losses. This presentation will outline practical approaches to diagnosing and managing hypophosphataemia, including simple diagnostic pathways and evidence-based treatments. Timely recognition and appropriate intervention are key to preventing complications, highlighting the crucial role endocrinologists play in improving outcomes for these patients.

DOI: 10.1530/endoabs.109.HDI2.4

HDI2.5

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI2.5

HDI2.6

Abstract Unavailable

DOI: 10.1530/endoabs.109.HDI2.6

Meet the Expert Sessions

Nurse

MTE1

Best practice in management of turner syndrome

Helen Turner
Department of Endocrinology, Oxford, United Kingdom

Turner Syndrome (TS) is characterized by a karyotype containing one X chromosome and complete or partial absence of the second sex chromosome, associated with one or more typical clinical manifestations of TS in a phenotypic girl/woman. It is common, affecting 50/100 000 females and unlike many conditions managed by endocrinologists it requires life-long care, can affect many different organs, with different conditions arising at different stages of life and often requiring multidisciplinary input. The recent 2024 International Guidelines for Management of Turner Syndrome provide a useful resource to help inform best practice, and covers the areas of (1) diagnosis and genetics, (2) growth, (3) puberty and estrogen treatment, (4) cardiovascular health, (5) transition, (6) fertility assessment, monitoring, and counselling, (7) health surveillance for comorbidities throughout the lifespan, and (8) neurocognition and its implications for mental health and well-being. The session will enable discussion of the updated guidelines including a selection of key issues/updates as well as ongoing questions to enable optimisation of care for all girls and women with TS.

DOI: 10.1530/endoabs.109.MTE1

Best Practice in Managing Turner s Syndrome

MTE2

Abstract Unavailable

DOI: 10.1530/endoabs.109.MTE2

Treatment resistant prolactinomas

MTE3

Managing early life adrenal tumours

Ruth Casey
Cambridge University Hospital, Cambridge, United Kingdom

This presentation will focus on malignant tumours of the adrenal gland arising in childhood including phaeochromocytomas and their extra adrenal counterpart paragangliomas, neuroblastoma and adrenocortical carcinomas. Differences in the tumour biology, rates of genetic predisposition, clinical presentations and approaches to management, together with rare disease incidence and therapeutic challenges in paediatric compared with adult patients, mandate close expert cross-disciplinary teamwork. This presentation will focus on specific aspects of diagnosis and management unique to children with malignant adrenal tumours and will draw from recent international guidelines in this field.

DOI: 10.1530/endoabs.109.MTE3

Adrenal tumours in children, adolescents and during transition: update on management

MTE4

Abstract Unavailable

DOI: 10.1530/endoabs.109.MTE4

Advances in medical therapy for Graves ophthalmopathy

MTE5

Advances in medical therapy for graves' ophthalmopathy

Catherine Napier
Newcastle upon Tyne Hospitals, Newcastle upon Tyne, United Kingdom

The management of thyroid eye disease has evolved significantly over the last 5-10 years. While methylprednisolone remains the mainstay of treatment for patients with active, moderate to severe disease, newer immunotherapies are changing how we manage this heterogeneous condition. Emerging therapeutic options add complexity to management decisions, but have the potential to hugely benefit our patients.

DOI: 10.1530/endoabs.109.MTE5

Mechanisms of Cancer Cachexia

MTE6

Neuroendocrine mechanisms in cancer cachexia

Anthony Coll
University of Cambridge, Cambridge, United Kingdom

Understanding the processes that govern body weight is highly relevant to clinical practice as disorders of energy homeostasis cause significant morbidity and mortality. Cachexia is a syndrome of negative energy balance where muscle and fat mass are progressively lost. It affects a high proportion of patients living with cancer and is strongly associated with both reduced tolerance to anti-cancer therapy and reduced survival. Despite this, the pathophysiology of cancer cachexia remains poorly understood and, until very recently, there has been no effective, evidenced-based treatments for cancer cachexia. A robust evidence base supports the primacy of the brain and central neuronal pathways in the control of appetitive behaviour, body weight and body composition. However, it is unclear how these key homeostatic mechanisms which regulate energy balance are perturbed in cancer cachexia. A better understanding of how the pathways controlling appetitive behaviour are subverted or affected in cachexia will bring much needed mechanistic insight into a condition with unmet clinical need. In this session I will review evidence to support the hypothesis that in cancer cachexia, tumour-derived factors, acting both independently and in concert with factors derived from non-cancer tissues, can be prime drivers of the phenotype. Acting through neural mechanisms involving appetite, subsequent changes in behaviour directly contribute to the adverse changes in body composition. I will review in particular how work from model organism systems has greatly contributed to the development of emerging therapies that target GDF-15 (Growth Differentiation Factor 15), a member of the TGF-β superfamily. I will highlight how targeting GDF15 signalling shows real potential in both ameliorating the side effects of chemotherapy and increasing body weight in cancer cachexia.

DOI: 10.1530/endoabs.109.MTE6

Current Management of Hyperparathyroidism

MTE7

Abstract Unavailable

DOI: 10.1530/endoabs.109.MTE7

Tales of the unexpected in the adrenal MDT

MTE8

Tales of the unexpected in the adrenal MDT

Irina Bancos
Mayo Clinic, Rochester, USA

Adrenal tumors are common, diagnosed in around 5% of adults undergoing abdominal cross-sectional imaging. When evaluated by endocrinologists, adrenal adenomas are diagnosed in 85% of patients with adrenal tumors, other benign

tumors, such as myelolipomas or cysts, in 3-6%, pheochromocytomas in 2-4%, adrenal carcinomas in 4-6%, and other malignant tumors in 1-3%. Imaging and hormonal assessments are key in determining the etiology of adrenal mass, though a thorough review of clinical presentation, medical history, and genetics can aid the diagnosis. Recent 2023 guidelines on adrenal incidentalomas recommend a multidisciplinary tumor board (MDT) review of any patients with indeterminate adrenal tumors. In addition, rare and unusual presentations benefit from the MDT review. In this presentation, we will review presentation, management, and outcomes of several rare, unusual, or thought-provoking clinical cases reviewed and discussed at MDT.

DOI: 10.1530/endoabs.109.MTE8

Nurse Sessions

Nurse Session 1

NS1.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS1.1

NS1.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS1.2

NS1.3

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS1.3

Nurse Session 2

NS2.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS2.1

NS2.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS2.2

NS2.3

The role of the endocrine specialist nurse in supporting patients treatment needs in acromegaly

Anna Hawkins
BHRUT, Essex, United Kingdom

From a patient's first experience of a symptom, through their journey to diagnosis, there is often very little support available for rare conditions such as Acromegaly. Patients know they are unwell; they are looking for answers, but these can be slow to come and for some diagnosis can take many years. From the day a patient meets their endocrine specialist nurse (ESN) they have an advocate who will help to explain their journey so far and the future one take lies ahead of them. Patients living with Acromegaly have many challenges. The ESN is vital in supporting patients through the different treatment phases of this life changing condition.

DOI: 10.1530/endoabs.109.NS2.3

Nurse Session 3

NS3.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS3.1

NS3.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.NS3.2

Other Sessions

What is New?

WIN1

Abstract Unavailable

DOI: 10.1530/endoabs.109.WIN1

WIN2

Abstract Unavailable

DOI: 10.1530/endoabs.109.WIN2

Endocrine Emergencies – The Sequel

EE1.1

Myxoedema

Peter Taylor
Cardiff University, Cardiff, United Kingdom

Myxoedema coma is a rare life-threatening condition characterised by profound hypothyroidism and altered mental status. Despite its name most patients are not comatose and the presentation is that of decompensated profound hypothyroidism. Due to widespread easy access to thyroid function testing it is very unusual for myxoedema coma to be the first presentation of undiagnosed hypothyroidism. The typical patient is usually an elderly female patient with well-established hypothyroidism (either auto-immune or following definitive treatment for hyperthyroidism), who has poor compliance with levothyroxine with a precipitating event triggering the emergency presentation. Prompt thyroid hormone and glucocorticoid replacement combined with supportive care on a HDU/ITU unit if appropriate is key although mortality may still be as high as 50%.

DOI: 10.1530/endoabs.109.EE1.1

EE1.2

Abstract Unavailable

DOI: 10.1530/endoabs.109.EE1.2

EE1.3

Abstract Unavailable

DOI: 10.1530/endoabs.109.EE1.3

Endocrinology in the Era of 'Fake News'

FN1.1

A selfish guide to research integrity

Ralitsa Madsen
University of Dundee, Dundee, United Kingdom

In the pursuit of scientific knowledge, maintaining research integrity is not merely a moral imperative but also a selfish endeavour. The first part of this talk will highlight that research integrity is about much more than isolated cases of research misconduct. Many researchers unintentionally engage in so-called questionable research practices without realising the potential harm they can cause to the scientific community, the broader society, and their own careers. The prevalence of such practices, including p-hacking, HARKing (Hypothesising After the Results are Known), data cherry-picking, and selective reporting, will be discussed in the context of wider research culture. The second part of the talk will focus on practical solutions that support high levels of research integrity while also benefitting researchers on the ground by increasing the efficiency and visibility of their research. The third and final part of the talk will highlight the many challenges and opportunities emerging from the rise of generative artificial intelligence (AI), with tools like ChatGPT now commonly used by students and researchers alike. Best-practices for the use of such tools in academic research will be discussed, with reference to key policies and nationwide discussions that everyone ought to be aware of.

DOI: 10.1530/endoabs.109.FN1.1

FN1.2

In the era of "fake news" – media misconception

Joyce Harper
Institute for Women's Health, UCL, London, United Kingdom

The World Health Organization (WHO) emphasizes the critical need for comprehensive health education to support the survival, well-being, and development of young people. Yet, education in schools often falls short, leaving media as a dominant source of information. Platforms like TikTok, Instagram, and Dr. Google have become go-to resources, with over 61% of adolescents turning to social media for sexual and reproductive health information. While media can educate and advocate, it also perpetuates misinformation through sensationalism, oversimplified claims, and conflicts of interest, especially when influencers and even professionals market products or services. Our research examined how reproductive health education is portrayed on TikTok and Instagram, revealing inaccuracies and highlighting the challenges of using social media as a tool for health education. For instance, Anti-Mullerian Hormone (AMH) testing is falsely marketed as a measure of fertility despite evidence showing the contrary. This test is heavily promoted to young women as empowerment and even funded by some governments, such as France and Greece. Similarly, the menopause market has exploded, with supplements claiming to relieve symptoms, balance hormones, and promote well-being. However, these claims often rely on testimonials and distorted interpretations of scientific data rather than robust evidence. In the fertility field, IVF clinics continue to market unproven add-ons and inflated success rates, despite warnings from regulatory bodies like the Human Fertilisation and Embryology Authority and the European Society of Human Reproduction and Embryology. The unchecked marketing of tests, supplements, and treatments undermines trust in healthcare, leading to delayed medical advice, stigmatization, and potential harm. We urgently need a coordinated response from healthcare professionals, educators, and media outlets to combat misinformation. By promoting evidence-based resources and engaging with the public on trusted platforms, we can reclaim the narrative and safeguard health.

DOI: 10.1530/endoabs.109.FN1.2

FN1.3

Abstract Unavailable

DOI: 10.1530/endoabs.109.FN1.3

Legends of Endocrinology

LE1.1

Extraskeletal vitamin D: from pathological oddity to supplementation trials

Martin Hewison
University of Birmingham, Birmingham, United Kingdom

Vitamin D has always been an endocrinology 'outsider'. Although it is clearly fundamental for mineral homeostasis and bone health, it had its beginnings in nutrition and most people aren't bothered that active 1,25-dihydroxyvitamin D (1,25D) is a steroid hormone so long as they can buy vitamin D capsules from their local supermarket. When I joined the vitamin D research team at the Middlesex Hospital in 1985 vitamin D was undergoing a further departure from mainstream endocrinology. This was start of the era of 'non-classical vitamin D' - effects of 1,25D beyond the skeleton. My presentation will describe how this facet of vitamin D evolved from disease phenomenology to the fundamental mechanisms that form the basis of the many high profile vitamin D supplementation trials over the last few years. The evolution of 'Extra-skeletal vitamin D' has occurred in parallel with my own career, and I will describe some of the key discoveries that were made during my time in London, Birmingham and Los Angeles, and the wonderful colleagues who contributed to our current understanding of vitamin D.

DOI: 10.1530/endoabs.109.LE1.1

LE1.2

Abstract Unavailable

DOI: 10.1530/endoabs.109.LE1.2

LE1.3

50 years of fascination by insulin and antibodies (standing on the shoulders of giants!)

Kenneth Siddle
Cambridge University, Cambridge, United Kingdom

My career has been shaped by two real legends of endocrinology, Nick Hales and Steve O'Rahilly. Nick first introduced me to both the fascination of insulin action and the power of antibodies as analytical reagents, when for my PhD I set up immunoassays for cyclic nucleotides and applied these in studies of metabolic regulation. After Cesar Milstein described techniques to produce monoclonal antibodies, I used that technology in the development of immunoassays for polypeptides and then in the study of cell surface receptors. In the 1980s, with commercial support my lab established ultrasensitive, two-site immunoassays for glycoprotein hormones and, in collaboration with Nick, specific assays for proinsulin. However my focus turned back to the mechanism of insulin action as my group developed large panels of monoclonal antibodies for insulin receptors and IGF-1 receptors. In the early 1990s Nick recruited Steve O'Rahilly to the department, who immediately became an inspiring colleague. My group discovered that the structurally related receptors for insulin and IGF-1 can assemble as heteromeric hybrids and, in collaboration with Steve, we studied mechanisms underlying specificity in the actions of insulin and IGFs. An intriguing property of many anti-receptor antibodies was their ability to activate receptors and act as insulin-mimetics, an action that extends to some mutant receptors that are not responsive to insulin itself. As my own career draws to a close, my former colleagues Rob Semple and Gemma Brierley are now exploring the potential to use anti-receptor antibodies as therapeutics in insulin-resistance syndromes. For more than 50 years I have been excited to see advances in understanding insulin receptor structure and function and the mechanism of insulin action, while collaborations have always been central to my own productivity and the satisfaction. It has always been a lot of fun!

DOI: 10.1530/endoabs.109.LE1.3

Endocrine Network Sessions

Adrenal and Cardiovascular

EN1.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN1.1

EN1.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN1.2

EN1.3

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN1.3

Bone and Calcium

EN2

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN2

Endocrine Consequences of Living With and Beyond Cancer

EN3

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN3

Reproductive Endocrinology

EN4.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN4.1

EN4.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN4.2

Metabolism, Obesity and Diabetes

EN5

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN5

Neuroendocrinology

EN6

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN6

Thyroid

EN7.1

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.1

EN7.2

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.2

EN7.3

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.3

EN7.4

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.4

EN7.5

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.5

EN7.6

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN7.6

Cancer

EN9

Abstract Unavailable
DOI: 10.1530/endoabs.109.EN9

Oral Communications

Bone and Calcium

OC1.1

Burosumab in adults with X-linked hypophosphataemia – audit data from the Queen Elizabeth University Hospital, Glasgow

Nathan Smith, Paul Connelly & Maria Talla
Queen Elizabeth University Hospital, Glasgow, United Kingdom

Background
X-linked hypophosphataemia (XLH) is a rare genetic disorder due to inactivating PHEX mutations, leading to elevated FGF23, renal phosphate wasting, and decreased 1,25 dihydroxy-vitamin D levels. Conventional therapy for XLH consists of activated vitamin D and oral phosphate replacement, but this is often poorly tolerated. Burosumab is a recombinant human monoclonal antibody against FGF23 and unlike conventional therapy, targets the underlying pathophysiology of XLH.
Methods
A retrospective audit was carried out on five adult patients (>18 years) attending the Queen Elizabeth University Hospital in Glasgow with a diagnosis of XLH and confirmed PHEX mutations who are receiving subcutaneous Burosumab every 4 weeks. Activated vitamin D and oral phosphate were discontinued 7 days prior to initiation of Burosumab therapy.
Results
All patients had a history of lower limb deformities and previous orthopaedic interventions. Four patients experienced recurrent dental abscesses, four had previous fractures/pseudofractures and one had a Chiari malformation. The median age at Burosumab initiation was 37 years (IQR 20–39), with a median dose of 80 mg (IQR 70–90). The median height was 148.5 cm (IQR 140.5–157.0), and the median BMI was 32 (IQR 27.2–39.4). The median treatment duration was 272 days (IQR 263–348). Prior to Burosumab initiation, all patients had low serum phosphate levels (median 0.65 mmol/l, IQR 0.55–0.68). Serum phosphate normalised in all patients within 4 weeks of treatment, with sustained levels observed at 12 weeks (median 0.96 mmol/l, IQR 0.9–1.0).
Conclusions
Burosumab appears well tolerated and effectively normalises serum phosphate levels in adults with XLH. However, further data is required to understand the impact of this treatment on the long-term complications of XLH.

DOI: 10.1530/endoabs.109.OC1.1

OC1.2

The impact of implementation of NICE guidance on preoperative imaging sequence in primary hyperparathyroidism

Manjeet Kaur Sehemby, Ammar Rafique, Kanwarpreet Dhamija, Shahad Yahya, Sanjay Vydianath & Harit Buch
New Cross Hospital, Wolverhampton, United Kingdom

Background
Parathyroid imaging facilitates parathyroidectomy in patients with primary hyperparathyroidism. Preoperatively, concordance between ultrasonography (US) and Scintigraphy (RN) was sought in all patients, until the publication of NICE guidance in 2019, which recommended a sequential approach, with RN to be considered only if it "further guides surgical approach". Since 2020 we initially request US and reserve RN scan for patients in whom US is negative/equivocal or in patients with chances of multiglandular disease.
Patients and Methods
We retrospectively reviewed records of 94 patients who underwent parathyroidectomy (unilateral neck exploration (UNE)) from 2021-2023. Clinical, biochemical, imaging and surgical findings were recorded. We compared the number of RN scan requests and cure rate during this period whilst following sequential imaging approach, to those obtained between 2014-2019 when US and RN were requested simultaneously in all patients.
Results
$N=$ 94, mean age 68 years, 79% females, mean serum calcium 2.93mmol/l. The overall cure rate was 92%. US was unequivocally positive in 65(69%) patients. Following UNE, 62/65(95%) patients were cured and in all patients who were cured, surgical findings were concordant with US. 29(31%) patients had equivocal US findings and went on to have further imaging studies. In this cohort 24/29 (83%) patients were cured. As each RN scan cost is £400, between 2021-2023 we made a cost saving of £26000 (65 patients). The table shows that the cure rates, overall and in each sub-group, were almost identical between both time periods ($P=$ns for all).

2011-2018	**Overall**	**Concordant imaging**	**Discordant imaging**
	145/160 (91%)	88/93 (97%)	51/61(83%)
2021-2023	**Overall**	**Single scan**	**Sequential dual scan**
	86/94 (92%)	62/65 (95%)	24/29 (83%)

Conclusion
Implementation of NICE guidance on imaging sequence in patients with primary hyperparathyroidism prior to UNE led to significant cost saving without adversely affecting the cure rate.

DOI: 10.1530/endoabs.109.OC1.2

OC1.3

Management of long term post-surgical hypoparathyroidism; need for improvement and potential for remission

Muhammad Fahad Arshad[1,2], Nisha Thambuchetty[2] & Saba P Balasubramanian[1,2]
[1]University of Sheffield, Sheffield, United Kingdom. [2]Sheffield Teaching Hospitals, Sheffield, United Kingdom

Introduction
Several international guidelines have recommended regular monitoring in patients with long-term hypoparathyroidism; however, care remains suboptimal. Also, patients with post-surgical hypoparathyroidism (PoSH) can be weaned off calcium/ vitamin D supplements with pro-active attempts. Aim of this study was to evaluate compliance of European Society of Endocrinology (ESE) guidelines in real-world in patients with PoSH cohort and determine the proportion of patients weaned.
Methods
All patients with PoSH (requiring supplements >6 months post-operatively) over 10 years (2009-2018) were identified using healthcare records at a tertiary centre. Demographic, clinical, and biochemical data was collected and using ESE guidelines as set standards, clinical practice was audited. Intention to adhere to ESE guidelines was evaluated and if supplements were successfully weaned.
Results
51 patients with PoSH were identified and median (IQR) age was 49.7 (32.4-61.4) years with female/male ratio of 3:1. Most patients had thyroid surgery ($n=46$), followed by parathyroid surgery ($n=4$), or both ($n=1$). The median (IQR) follow-up duration was 51 (23-72) months. Key findings showed that 63% ($n=32$) patients did not have vitamin D levels of >75 nmol/l during follow-up. 24% ($n=12$) patients had urine biochemistry performed, of which 42% (5/12) had hypercalciuria. At least one episode of hypercalcaemia, hyperphosphatemia, and hypomagnesemia was recorded in 15% ($n=8$), 65% ($n=33$) and 24% ($n=12$) patients, respectively. Intention to adhere to ESE guidelines was 61% and 35% ($n=18$) patients were weaned off supplements at a median (IQR) interval of 21.5 (8.1-61.3) months. The median (IQR) annual rate of rise in eGFR was 1.9 (0.7-5.0) ml/min/1.73m^2/year, however, recovery in renal functions was observed in those weaned.
Conclusion
This study illustrates the need for improving monitoring in patients with PoSH. Significant number of patients can be weaned off supplements with pro-active efforts. Patients with PoSH are at greater risk for decline in renal functions.

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OC1.4

Retrospective analysis of DEXA scans in patients with primary hyperparathyroidism: importance of forearm scanning in osteoporosis diagnosis

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Background
Primary Hyperparathyroidism (PHPT) is characterized by excess production of parathyroid hormone (PTH) causing hypercalcaemia and reduced bone density. Dual-energy X-ray absorptiometry (DEXA) is the gold standard investigation for assessing bone mineral density (BMD) and diagnosing osteoporosis. Standard DEXA scans typically include hip and lumbar spine while forearm osteoporosis is the hallmark of PHPT-induced bone loss. This study was aimed at evaluating how often DEXA scans included the forearm and whether the forearm scans revealed a high prevalence of osteoporosis as compared to the hip and spine.
Methods
A retrospective review was conducted on patients diagnosed with PHPT over a period of 5 years. DEXA scan results were analyzed based on whether the forearm was included and T scores were compared between the 3 sites.

Results
A total of 347 patients with primary hyperparathyroidism (PHPT) who had undergone DEXA scans were identified. Among them, only 178 (51%) had scans that included the forearm. When defining osteoporosis as a T-score of -2.5 or lower, osteoporosis was detected in 70 patients (39%) in the forearm, while only 26 (14%) had it in the hip, and 18 (10%) in the lumbar spine. The average T-scores were -1.94 in the forearm, -1.34 in the femoral neck, and -0.76 in the lumbar spine. Notably, 22 patients (12.3%) had normal T-scores in the hip and spine but showed osteopenia or osteoporosis in the forearm. Relying solely on two-site DEXA may underestimate the extent of bone disease in patients with PHPT.
Conclusion
This study highlights the importance of including the forearm in DEXA scans in patients with PHPT as recommended by NICE NG132. Routine inclusion of the forearm may result in increased detection of a recognised complication of PHPT, and improved risk stratification with more accurate decision making for definitive management.

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OC1.5

Sustained improvement in renal function with palopegteriparatide in adults with chronic hypoparathyroidism: 2-year results from the phase 3 pathway trial

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Individuals with chronic hypoparathyroidism managed with conventional therapy (active vitamin D and calcium) are at increased risk for renal complications and declines in renal function. In clinical trials, palopegteriparatide treatment enabled independence from conventional therapy (no active vitamin D and ≤600 mg/day elemental calcium) and maintained serum biochemistries within normal ranges. This post hoc analysis examines the impact of palopegteriparatide treatment on renal function in adults with chronic hypoparathyroidism through week 104 of PaTHway, a phase 3 trial with a randomized, double-blind, placebo-controlled 26-week period and ongoing 156-week open-label extension. Changes in renal function were assessed using estimated glomerular filtration rate (eGFR). At week 104, 93% (76/82) of participants remained in the trial. Of those, 82% had normal albumin-adjusted serum calcium levels (2.07-2.64 mmol/l), 97% were independent from conventional therapy, none required active vitamin D. Mean (SD) serum phosphate (1.1 (0.2) mmol/l) and albumin-adjusted calcium x phosphate product (2.5(0.4) $mmol^2/l^2$) were normal. At week 104, mean (SD) eGFR was 77.8 (14.8) mL/min/1.73m^2. With palopegteriparatide treatment mean eGFR increased 8.9 (11.0) mL/min/1.73m^2 ($P<.0001$) from baseline to week 52, which was sustained through week 104 with a mean (SD) change from baseline of 9.0 (10.3) mL/min/1.73m^2 ($P<.0001$). By week 104, 61% and 44% of participants had an increase in eGFR of ≥5 mL/min/1.73m^2 and ≥10 mL/min/1.73m^2, respectively. Palopegteriparatide treatment normalized mean 24-hour urine calcium within 26 weeks, maintaining levels below 6.2 mmol/day through week 104 (4.0 (2.3) mmol/day). No cases of nephrolithiasis were reported with palopegteriparatide. Most TEAEs were mild or moderate; no new safety signals reported. These findings demonstrate the sustained renal safety of palopegteriparatide and suggest that PTH replacement therapy with palopegteriparatide and independence from conventional therapy may not only preserve but improve renal function in adults with chronic hypoparathyroidism.

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OC1.6

CKD-MBD in the diabetic-renal clinic: an under-managed pathology?

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Introduction
Diabetic kidney disease (DKD) is a common cause of chronic kidney disease (CKD). In CKD bone mineralisation disorder (CKD-MBD), imbalanced feedback between phosphate, calcium, vitamin D, and parathyroid hormone (PTH) causes bone mineralisation loss, architecture damage and increased fracture risk. Treatment involves pharmacological interventions and dietary modification. Kidney Disease Improving Global Outcomes (KDIGO) have published guidance to aid management.
Aims
This project aimed to audit the quality of CKD-MBD management in a tertiary centre DKD clinic compared to the KDIGO CKD-MBD guideline.
Methods
119 patients attending DKD clinic between September and November 2023 were retrospectively reviewed. Patients with an eGFR >60 ml/min/1.73m^2 were excluded. Data collected included demographics, biochemistry, renal replacement therapy status, pharmacological treatment, dietetic advice, bone mineral density (BMD) measurements and fractures.
Results and Discussion
Most patients received appropriate biochemical monitoring, but calcium was more intensively monitored compared to phosphate and PTH. Only 29% of patients had received a prior radiological BMD measurement. Treatment findings relevant to clinical practice included 63% of patients with hyperphosphatemia receiving dietician delivered low-phosphate dietary advice. Also, 36% of CKD G5d patients treated with vitamin D analogues for secondary hyperparathyroidism (SPTH) had a most recent PTH measurement outside the recommended target range of 2-9 multiples the upper limit of normal. 10% of patients had a recorded fracture, these occurred more frequently in lower eGFR patients not on dialysis. 6% of CKD stage G3a-G3b patients, who may be suitable for bisphosphonates, were prescribed the treatment. No patients were treated with Denosumab.
Conclusion
Clinicians working with DKD patients should be aware of the KDIGO guidance for CKD-MBD, particularly around dietary recommendations and treatment targets in SPTH patients. Improving BMD measurement frequency in suitable patients may help identify patients that would benefit from pharmacological intervention; few patients in this audit were benefiting from these treatments.

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Endocrine Cancer and Late Effects

OC2.1

Glutamine antagonism as a new treatment approach in adrenocortical carcinoma

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Deregulation of cell metabolism is a hallmark feature of cancer that remains underexplored in adrenocortical carcinoma (ACC), despite the urgent need for better medical treatment options. We employed a recently developed transgenic mouse model of ACC, driven by gain-of-function β-catenin and loss-of-function p53 mutations (BPCre), to characterize *in vivo* ACC metabolism and identify putative targetable vulnerabilities. We used a combination of targeted metabolomics by liquid chromatography-mass spectrometry and RNA-seq to compare tissue metabolism in BPCre ACC tumours to normal adrenals. We identified widespread metabolic dysregulation in ACC (64/176 polar metabolites significantly dysregulated, false discovery rate [FDR]<0.05); most prominent changes pertained to arginine, proline and glutamate metabolism, nucleotide and nucleotide sugar metabolism, and glutathione metabolism. Lipidomic analysis revealed extensive dysregulation of triglyceride metabolism. Orthogonal analysis by RNA-seq revealed congruent metabolic pathway alterations. Given the prominent dysregulation of several glutamine-dependent metabolic pathways in BPCre tumours, we hypothesized that glutamine catabolism may represent a

targetable metabolic vulnerability in ACC. Pharmacological targeting of glutamine metabolism by the glutamine antagonist 6-Diazo-5-Oxo-L-Norleucine (DON) effected marked cytotoxicity against four mouse and human ACC cell lines (IC50 0.03-4.07 uM). The effect was rescued only by nucleoside substitution, suggesting that glutamine contribution to *de novo* nucleoside biosynthesis is the critical metabolic dependency in ACC. *In vivo*, treatment with the DON pro-drug JHU-083 achieved marked tumour growth inhibition (TGI) against subcutaneous mouse ACC implants in both immunocompetent (mean TGI 86%) and immunodeficient mice (mean TGI 67%), as well as against human NCI-H295R xenografts. Tumour immunophenotyping by flow cytometry revealed significantly increased infiltration with Natural Killer cells, likely potentiating the anti-tumour effect of JHU-083 in immunocompetent mice. Tissue metabolomics of JHU-083-treated implants revealed extensive depletion of purine metabolites. This works imparts new insights into ACC metabolism and provides pre-clinical evidence supporting glutamine antagonism as a new treatment approach in ACC.

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OC2.2

The androgen mediated interplay between cytoplasmic AR and G3BP1 as a driver of endocrine therapy resistance in breast cancer

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In postmenopausal women, aromatase inhibitor (AI) therapy is the gold-standard first line treatment for ER-positive breast cancer. Unfortunately, many patients will suffer recurrence due to acquired AI resistance, creating an urgent need to elucidate the underlying mechanisms. Accumulating evidence shows that androgen/androgen receptor (AR) signaling is involved in AI resistance due to the androgenic environment dominating post-treatment. Exploration of the AR protein interactome via LC-MS/MS in AI resistant cells identified AR protein partners previously linked with castrate resistant prostate cancer, such as stress granule core component, G3BP1. Plant polyphenol (EGCG), an inhibitor of G3BP1 interaction, was used to explore the impact of stress granule (SG) complex inhibition across isogenic AI-sensitive and AI-resistant breast cancer cell lines utilising 3D bioprinted models of disease. Co-immunoprecipitation and confocal fluorescence imaging approaches were used to investigate the effect of EGCG and androgens (classical and 11-oxygenated) on G3BP1-AR protein complex formation. To date, our study has shown that androgen responsive AI resistant cells are exquisitely sensitive to disruption of SG formation. The interaction between extra-nuclear AR and G3BP1 is confirmed to be closely linked to cytoprotective mechanisms through its influence on SG formation, which is further modulated by the androgen/AR signaling pathway. Activation of the androgen/AR signaling pathway by both classical and 11-oxygenated adrenal androgens resulted in enhanced SG formation in AI-resistant LetR cells albeit through different mechanisms. In summary, exploration of the dynamic interplay between AR and G3BP1 will help us better understand the mechanisms of AI resistance in ER-positive breast cancer. Investigating the impact of AR protein and AR mRNA in SG regulation will help elucidate the complex and context dependent AI resistance mechanism regulated by androgen/AR in ER positive tumors. Further studies will focus on exploring the transcripts sequestered within SGs under exposure to various androgenic ligands.

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OC2.3

Serum untargeted metabolomics reveals widespread metabolic dysregulation in adrenocortical carcinoma

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Dysregulation of cell metabolism is a hallmark feature of cancer, which remains under-explored in adrenocortical carcinoma (ACC). Dissecting ACC tumour metabolism is of high translational importance, with the potential to identify new treatment targets as well as diagnostic or prognostic biomarkers. In this prospective, multi-centre study, we collected pre-operative serum samples from 54 patients with ACC (65% women; 11% with isolated glucocorticoid excess; 7% with isolated androgen excess; 52% with mixed hormone excess; 22% metastatic at the time of tumour diagnosis) and 291 age-, sex- and body mass index-matched controls with benign, non-aldosterone-producing adrenocortical adenomas (ACA; 36% non-functioning, 48% mild autonomous cortisol secretion, and 16% adrenal Cushing's syndrome). We completed untargeted profiling of polar and non-polar metabolites by ultra-high performance liquid chromatography-tandem mass spectrometry. ACC patients had a distinct serum metabolome, with 437 significantly dysregulated metabolites compared to ACA (false discovery rate [FDR] <0.05), of which 24 showed a >2-fold change between the two groups. Pathway analysis revealed widespread dysregulation of amino-acid and nucleotide metabolism, including arginine and proline metabolism; branched-chain amino-acid biosynthesis; glycine and serine metabolism; alanine, aspartate and glutamate metabolism; and pyrimidine metabolism (FDR <0.05). There was also wide dysregulation of steroid metabolites and lipids, most prominently affecting glycerophospholipids, ceramides and sphingolipids, and triglycerides. The extensive changes in the serum metabolome of ACC patients in comparison to patients with ACA persisted when patients were stratified for the presence of Cushing's syndrome. There were also notable differences among ACC patients depending on whether the tumour had a low ($<10\%$), intermediate (10-19%) or high ($\geq 20\%$) Ki67 proliferation index ($n=5$ dysregulated metabolites, FDR <0.05). This study reveals for the first time distinct and extensive changes in the serum metabolome of ACC patients, providing new insights into tumour biology.

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OC2.4

The development of humanised 3D bioprinted models of endocrine resistant breast cancer

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Introduction

Recent reports from our group, and others, have shown that an androgenic steroid environment is associated with poor response to therapy and facilitates anchorage-

independent growth of breast cancer cells. Additionally, hormone receptor-positive breast cancer is challenging to study *in vitro* as they do not readily form organoids/patient-derived xenografts (PDX) or fully recapitulate the tumour endocrine microenvironments. Using modern 3D bioprinting techniques and newly gained proficiencies in steroid detection, this study aims to define the utility of 3D bioprinting as a novel method in modelling androgens-mediated treatment resistance in breast cancer.

Methods

Using well-established breast cancer cell line models of endocrine resistance, we determine the influence of the steroid precursor androstenedione (A4) and other steroid ligands (E2, R1881, 11KT) in *in vitro* 2D and 3D-printed models.

Results

Various breast cancer cell lines retain cell viability post 3D bioprinting. Increased cell growth in response to androgens in 3D bioprinted cells compared to conventional 2D culturing highlights the efficiency of integrating the tumour steroid microenvironment into this model. Interestingly, androgens impacted the sensitivity of 3D bioprinted breast cancer cell lines to anti-AR therapies. Preliminary data suggest that primary breast tumours can be successfully disaggregated and bioprinted to generate 3D structures that resemble their respective *in vivo* histological phenotypes *ex vivo*. Patients' tumour-associated conditioned medium derived from primary tumour-associated adipocytes were steroid profiled by LC-MS/MS, with results suggesting that individual tumour steroidogenesis impacts tumour growth and potentially facilitates endocrine resistance.

Conclusion

Integrating the tumour steroid microenvironment with 3D bioprinting might serve as a novel prognostic tool based on individual tumour steroid microenvironment. Successfully developing humanised models of breast cancers via 3D bioprinting would provide an alternative to existing *ex vivo* and *in vivo* models, potentially facilitating further research in uncovering the role of androgens in driving treatment resistance in breast cancer.

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OC2.5

Adrenal masses differentiation through the measurement of circulating cell-free DNA concentrations

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Background

Ruling out malignancy in adrenal masses (AM) is a clinical challenge. We demonstrated that circulating cell-free DNA concentrations (ccfDNA-C) are higher in patients with adrenocortical carcinoma (ACC) compared to healthy subjects (HS). However, ccfDNA-C have not been compared among different types of AM.

Objectives

To assess the potential role of ccfDNA-C for AM differentiation.

Methods

We enrolled 81 patients (45 females) with adrenocortical adenoma (ACA, $n=55$), other benign AM (OB, $n=5$), ACC ($n=11$), pheochromocytoma ($n=3$) and adrenal metastases from other primary tumours (MET, $n=7$). Blood samples, clinical, hormonal and radiological data were collected at first referral. AM with heterogeneous radiological appearance and/or size >4 cm or plain Hounsfield Units >10 and not associated with overt adrenal hormone excess were labelled as "undefined AM" ($n=36/81$, 18 ACA, 5 OB, 6 ACC, 7 MET). ccfDNA was isolated with a commercial kit and ccfDNA-C were measured with fluorometer. Age, sex and tumour size adjusted univariate analysis was conducted to assess ccfDNA-C distribution. We tested the diagnostic performance of our previously published HS-derived cut-off (>0.146 ng/μL) with positive (PPV) and negative predictive value (NPV) for ACC recognition.

Results

ccfDNA-C were higher in ACC than in OB ($P=0.001$), MET ($P<0.001$), and ACA ($P=0.069$) but comparable to PHEO ($P=0.402$). Our ccfDNA cut-off predicted ACC with PPV = 33.33% and NPV = 96.3% in the entire cohort. Considering undefined AM, ccfDNA-C were higher in ACC than in each AM group ($P<0.001$) and our cut-off showed PPV = 50.0%, NPV = 100.0% in predicting ACC. The same cut-off was confirmed by logistic regression and showed Odds Ratio: 6.515 (95% Confidence of Interval: 1.936-21.911), $P<0.001$, sensitivity 81.8% and specificity 74.3% with same PPV and NPV.

Conclusions

In undefined AM, high ccfDNA-C seem to be ACC-specific and ccfDNA-C $>$ 0.146 ng/μL is useful for ACC discrimination. Further samples are being tested to increase statistical power.

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OC2.6

Combinatorial drug strategy targeting sodium iodide symporter (NIS) activity enhances radionuclide uptake in breast and thyroid settings *in vivo*

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Background

Radioiodide (RAI) ablation therapy is hampered by diminished NIS expression, as well as intracellular retention of NIS away from the plasma membrane, especially in aggressive NIS-expressing cancers such as thyroid and breast. Recently, we reported that $Cu(DDC)_2$ – a copper metabolite of the FDA-approved drug disulfiram – elicited a dual effect on NIS function, markedly inducing NIS expression and RAI uptake across thyroid cancer cell lines and in human primary thyrocytes[1]. Here, our objective was to address the hypothesis that combining drugs with distinct modes of action on NIS function, such as $Cu(DDC)_2$ with a histone deacetylase inhibitor (HDACi), would have a maximal effect on NIS activity *in vivo*.

Methods

SAHA (vorinostat) was used as a candidate HDACi. NIS function was monitored by RAI (^{125}I) uptake assays in vitro and SPECT/CT imaging via technetium-99m pertechnetate (^{99m}Tc) uptake in a MDA-MB-231 breast cancer xenograft model.

Results

$Cu(DDC)_2$, as well as SAHA, induced significant RAI uptake in multiple breast cancer cell types (1.8-6.0-fold; $P<0.001$) and in stable NIS-expressing MDA-MB-231 cells (3.6-fold; $P<0.001$), accompanied by increased NIS protein. Given the additive effect of $Cu(DDC)_2$ and SAHA on NIS protein levels in thyroidal TPC1-NIS cells (~1.9-fold higher than either treatment alone), we next progressed to *in vivo* orthotopic models (MDA-MB-231;$89\pm16mm^3$;day 26 post-inoculation). SPECT/CT imaging revealed that SAHA (100 mg/kg/day) and nano-encapsulated $Cu(DDC)_2$ (5 mg/kg/day) robustly increased ^{99m}Tc uptake in MDA-MB-231 tumours (2.3-fold; $P<0.05$;OTSU threshold;$n=3$) and thyroid glands (1.6-fold; $P<0.001$) compared to controls. Biodistribution studies revealed no differences in other tissues, or any change in body weight.

Conclusions

Our study identifies a new combinatorial strategy to stimulate NIS activity *in vivo*, with potential clinical application for improving radionuclide-based therapies and imaging across multiple cancer settings;

[1]Brookes K *et al*. Dual agonism of sodium iodide symporter function *in vivo*.bioRxiv 2024,02.27.582332.

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Reproductive Endocrinology

OC3.1

Kisspeptin: a novel tool to interrogate hypothalamic function in women presenting with menstrual disturbance

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Background
Polycystic Ovary Syndrome (PCOS) and Functional Hypothalamic Amenorrhoea (FHA) are the two commonest causes of menstrual disturbance. A fundamental abnormality that underpins these conditions is altered hypothalamic function, being increased in PCOS but reduced in FHA. Kisspeptin is a potent stimulator of hypothalamic GnRH secretion, and thus could be a novel tool to interrogate hypothalamic function in women presenting with menstrual disturbance.
Methods
Healthy women ($n=43$), women with PCOS ($n=65$), FHA ($n=44$), or congenital hypogonadotropic hypogonadism (CHH) ($n=10$) aged 18-35yrs not currently taking hormonal treatments, underwent two study visits, where they received an intravenous bolus of kisspeptin to interrogate hypothalamic function, and of GnRH to interrogate the pituitary response. Serum reproductive hormones were monitored 15-minutely for 8hrs.
Results
The mean (SD) of the maximal rise in LH (IU/l) after kisspeptin was 9.1 (10.3) in healthy women, 6.7 (5.7) in women with PCOS, 18.8 (12.5) in women with FHA, and 0.9 (1.0) in women with CHH. The mean (SD) of the maximal rise in FSH (IU/l) after kisspeptin was 3.7 (3.2) in healthy women, 2.1 (1.6) in women with PCOS, 9.3 (3.2) in women with FHA, and 0.6 (0.5) in women with CHH. The maximal rise in FSH after kisspeptin could differentiate women with lean PCOS (BMI <25 kg/m^2) from those with FHA (area under ROC 0.95, $P<0.0001$). The maximal rise in FSH after kisspeptin could differentiate women with FHA from women with CHH (auROC 0.99, $P<0.0001$), whereas the equivalent auROC for FSH rise after GnRH was 0.74 ($P=0.027$).
Conclusion
Kisspeptin offers a novel approach to assessing hypothalamic function in patients presenting with different reproductive disorders causing oligo / amenorrhoea. Our data reveals for the first time that the hormonal response to kisspeptin has promising diagnostic potential to aid in the evaluation of women presenting with menstrual disturbance.

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OC3.2

Changes in 11-oxygenated androgen metabolism after bariatric surgery in patients with obesity are mediated by downregulation of aldoketoreductase type 1C3 (AKR1C3) activity

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The circulating androgen pool is comprised of classic androgens and those derived from the 11-oxygenated pathway. Aldoketoreductase type 1C3 (AKR1C3), which activates androstenedione (A4) to testosterone (T) in the classic pathway and 11-ketoandrostenedione (11KA4) to 11-ketotestosterone (11KT) in the 11-oxygenated pathway, is highly expressed in adipose tissue. Expression is increased in obesity and serum 11KT levels correlate with body mass index. Here we hypothesised that weight loss induced by bariatric surgery impacts on 11-oxygenated androgen metabolism by reducing expression of AKR1C3 in adipose tissue. Multisteroid profiling of serum and 24-hour urine samples by liquid chromatography tandem mass spectrometry was performed pre and postoperatively in patients undergoing bariatric surgery. Baseline anthropometric and metabolic data were collected before and after surgery. A total of 60 patients were included [$n=40$ female; median BMI 49.3 (IQR 45.1-54.6) kg/m^2; median age 50.5 (IQR 43.3-56.6) years]. Median % weight loss was 17.6 (IQR 13.7-21.2)% at a median of 18.0 (IQR 16.8-20.3) weeks postoperatively. Weight loss resulted in a significant reduction in serum levels of A4 ($P<0.05$) in women, while dehydroepiandrosterone and T increased significantly in men ($P<0.05$ for each). Urinary (5αTHF+THF)/THE, a marker of systemic 11b-hydroxysteroid dehydrogenase type 1 activity, was not significantly altered by weight loss. Serum levels of 11β-hydroxyandrostenedione, 11KA4 and 11β-hydroxytestoterone did not change significantly after bariatric surgery. In contrast, serum levels of 11KT decreased significantly [1.5 (IQR 1.0-2.7) vs 1.3 (IQR 0.87-1.8), $P<0.05$)]. The ratio of serum 11KT/11KA4, a surrogate marker of AKR1C3 activity, also reduced significantly postoperatively ($P<0.05$). This is the first *in vivo* study to demonstrate the impact of bariatric surgery on 11-oxygenated androgen metabolism. Reduced serum levels of the active 11-oxygenated androgen 11KT reflect lower AKR1C3 activity in adipose tissue. Our data reinforce the critical links between obesity and perturbations in androgen metabolism in men and women.

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OC3.3

Quantification and identification of pharmacological and psychological components of the androgen withdrawal syndrome in men: a community-dwelling cross-sectional study

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Background
A recent meta-analysis estimated that men <30 years old have a 6% lifetime prevalence rate of androgen abuse. Androgen abuse increases mortality 3-fold by exposing men to cardiovascular and psychiatric diseases, suicide and violent crime. Up to 30% of men abusing androgens develop a dependency syndrome causing high relapse rates within the first year of cessation. However, clinical and biochemical characteristics of androgen withdrawal have not been quantified previously.
Methods
Ethics-approved cross-sectional study of 286 community-dwelling men: no androgen use (Control; $n=50$); current androgen abuse (Current; $n=125$); cessation of androgen abuse within previous year (Withdrawal; $n=111$). Total International Index of Erectile Function-15 (IIEF-15), Beck Depression Inventory-II (BDI-II), Generalised Anxiety Disorder-7 (GAD-7) and 36-item Short Form Survey (SF-36) questionnaires, fasting morning blood sampling and urine toxicology testing were performed.
Results
Men stopping androgen abuse within the previous year had worse sexual function (IIEF-15: 69.0 [IQR 62.0, 73.0], Controls; 62.0 [IQR 47.0, 71.0], Withdrawal; $P=0.0135$), depression (BDI-II: 3.0 [0.0, 8.0], Controls; 8.0 [2.0, 18.0], Withdrawal; $P=0.0005$), and anxiety (GAD-7 1.0 [0.0, 3.0], Controls; 2.0 [0.01, 6.0], Withdrawal; $P=0.0271$) scores compared with healthy men. Lower total testosterone levels were linearly correlated with worsened sexual function ($P<0.05$). Multivariable analysis suggested that androgen cessation (coefficient -10.8 [95% CI -5.6, -17.2]; $P<0.001$) and psychiatric comorbidity (coefficient -6.5 [95% CI -13.0, -1.3] $P=0.03$) were independently associated with poor sexual function, and that pre-diagnosed psychiatric illnesses (OR 2.39 [95% CI 1.60, 3.57]; $P<0.001$) and lower serum total testosterone (OR 0.85 [95% CI 0.88, 0.94]; $P=0.002$) were independently associated with depression.
Conclusions
This study provides the first quantitation of acute androgen abuse withdrawal symptoms in men. Our data reveal potential pharmacological and psychological components of androgen withdrawal, which could be targeted to develop novel therapies supporting androgen withdrawal, none of which currently exist.

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OC3.4

Luteinizing hormone receptor (LHR) signaling in granulosa lutein (GL) cells from women with polycystic ovary syndrome (PCOS): therapeutic potential of an allosteric inhibitor of LHR action

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Polycystic ovary syndrome (PCOS) is characterised by aberrant luteinizing hormone (LH) secretion and action. A primary signalling pathway of LH receptor (LHR) to drive its steroidogenic actions is via its ability to activate Gas/cAMP. Both LHR internalization to the very early endosome (VEE) and negative regulation by the adaptor protein APPL1 play a key role in shaping LHR cAMP signal profiles. Therefore, a targeted modulation of LHR signalling at a spatial level could play an important role in designing a novel treatment for PCOS. Granulosa-lutein cells (GLCs) were obtained from women with or without PCOS as a by-product of egg collection for IVF. Cultured cells were subjected to LH stimulation (with or without treatment with an siRNA for APPL1) and the effects assessed on cyclic AMP (cAMP) production, steroidogenic gene expression, and steroid secretion. We then examined the impact of Org-42599, an LHR-selective, allosteric modulator, on LH signalling in GLCs from both groups. PCOS-derived GLCs exhibited enhanced responses following LH stimulation, without change in LHR gene or protein expression. Dose-response studies indicated higher sensitivity to LH in PCOS GLCs. Both control and PCOS-derived GLCs showed equivalent dependence on LHR internalisation for acute ligand-induced cAMP signalling. APPL1 knockdown in control GLCs resulted in enhancement of LH-induced cAMP but, in contrast, inhibition of APPL1 markedly reduced LH-mediated cAMP in PCOS GLCs, implying that the increased LH-LHR activity in PCOS involves reprogramming of APPL1 from a negative to a positive regulator of LHR-mediated cAMP signalling. The allosteric LHR inhibitor Org-42599 both decreased LH-induced cAMP signalling in PCOS-derived GLCs, and restored APPL1-dependent negative regulation. In summary, we show alteration in LHR-cAMP signalling in GLCs from PCOS involves rewiring of APPL1-dependent mechanisms. Selective targeting of LHR signalling with modulators such as Org-42599 offers a promising therapeutic approach for 'correcting' LH-dependent dysfunction in steroidogenic cells.

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OC3.5

Androgen receptor sensitivity assessed by genetic polymorphism in the testosterone treatment of male hypogonadism

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The Androgen receptor (AR) CAG repeat polymorphism in exon 1 within human populations encodes for a polyglutamine stretch which varies between 9 to 35 repeats. The greater the number of CAG repeats the less sensitive the receptor in relation to biological functions. It is known that lesser the AR sensitivity the higher the circulating testosterone levels are required to provide normal AR stimulation. Notably CAG repeat numbers are positively associated with LH, FSH, waist circumference, % body fat, leptin and insulin. In clinical practise some men with symptoms of hypogonadism may not be diagnosed or if diagnosed may not respond to testosterone therapy. The aim of this study was to examine the relationship between AR sensitivity, testosterone (total, free, bioavailable) and symptom response between men who were treatment responders vs non-responders. Hypogonadal men ($n=32$), diagnosed by clinical guideline criteria for testosterone deficiency were treated with transdermal gel and were assessed at 3, 6 and 12 months. Symptoms were assessed using the validated AMS (Aging Male Symptom) score which was correlated with TT, calculated freeT and BioT / CAG ratios. At 6 months the study cohort was divided into responders (AMS $<$ 33% improvement) and non-responders by AMS score ($>33\%$ improvement). Non-responders had ARCAG repeats mean $21.8+3.9$ v responders $18.7+2.7$ ($P=0.03$). ARCAG repeats showed significant potential ($P=0.028$) in differentiating non-responders from responders to treatment with sensitivity of 95.2%, specificity of 50%. No correlation was found in relation to TT, freeT or BioT or T/CAG repeat ratios. This study showed that non-responders to treatment had significantly higher numbers of ARCAG repeats i.e. more insensitive AR. This study findings may indicate the need for higher post-treatment T levels in non-responders and / or men with a higher number of the ARCAG repeats >22. There is a clinical benefit of assessing the ARCAG.

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OC3.6

Rapid onset of action of intranasal vs intravenous kisspeptin supports a direct kisspeptin-activated olfactory-reproductive pathway in humans

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Background
The most well-described pathway for kisspeptin's activation of the reproductive axis relies on activation of kisspeptin receptors on GnRH-neurons in the hypothalamus. However, recent evidence has identified an extra-hypothalamic population of GnRH-neurons within the olfactory bulb that also express kisspeptin receptors. Intranasal delivery of kisspeptin could directly activate these olfactory bulb GnRH-neurons to stimulate reproductive hormone release and identify a novel olfactory pathway. Here, we compared reproductive hormone responses following intranasal and intravenous kisspeptin administration for the first time in humans, providing mechanistic insight and evidencing a novel, non-invasive clinical route of administration.
Methods
Healthy men received 12.8 nmol/kg of kisspeptin-54 either intranasally (4 sprays, $n=12$) or as an intravenous bolus ($n=5$). Reproductive hormone levels were measured every 15mins for 6hrs post-administration. The median time to maximal reproductive hormone response was compared using the Mann-Whitney test.
Results
Both intranasal and intravenous kisspeptin-54 elicited significant gonadotrophin and testosterone responses. Although the peak LH response was lower after intranasal compared to intravenous administration (mean $\pm$ SEM (IU/l): 4.5 ± 0.6 above baseline for intranasal vs 11.3 ± 1.4 for intravenous, $P<0.0001$), the LH peak occurred much earlier following intranasal kisspeptin-54, with a median time of 38mins (IQR:30-79) compared to 300mins (IQR:285-308) for intravenous administration ($P=0.0002$). Similar temporal patterns were observed for FSH, peaking at 38mins (IQR:30-79) after intranasal administration vs 345mins (IQR:345-360) with intravenous kisspeptin-54 ($P=0.0002$). Testosterone also peaked earlier after intranasal kisspeptin-54, reaching a median maximum at 165mins (IQR:109-240), compared to 345mins (IQR:240-360) with intravenous kisspeptin-54 ($P=0.0116$).
Discussion
The strikingly faster onset of hormonal responses following intranasal compared to intravenous kisspeptin-54 suggests that this route capitalises on a direct olfactory-reproductive pathway via kisspeptin receptors on olfactory GnRH-neurons. These findings have important clinical implications for kisspeptin administration in common reproductive and psychosexual disorders and support the existence of a novel olfactory-reproductive pathway.

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Thyroid

OC4.1

Pre-gestational and gestational care of hypothyroid women at cambridge university hospital nhs foundation trust (CUH)

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Introduction
Inadequate hypothyroidism management during pregnancy can jeopardize obstetric outcomes, therefore optimal pre-conceptual and antenatal care are mandatory. This audit compares care at CUH with standards specified in local guidelines based on the American Thyroid Association recommendations (2017).
Aims and Objectives
- Evaluate pre-conceptual and antenatal management of hypothyroidism at CUH
- Assess the reasons for deviation from local standards.
- Develop a plan to improve future care in this area.

Method
A retrospective review of notes was conducted for 272 women with hypothyroidism or a need for levothyroxine during pregnancy at CUH. The

study assessed adherence to local guidelines and categorized non-compliance based on whether the patient was in primary care or receiving care at CUH.

Results

The following results were observed against the established standards.

Standard	Result(met)	CUH(non-compliant)	Primary-care (non-compliant)
TSH < 2.5 mU/l at conception	49%	19%	81%
TFT checked following positive pregnancy test	75%	39%	61%
Levothyroxine increased appropriately	70%	26%	74%
TFT and TSI checked at first contact	83%	7%	93%
TFT checked at advised frequency	83%	21%	79%
Mean TSH < 3 mu/l	78%	Not applicable	
TSI checked at 28 weeks	70% checked at/after 28 weeks, 36% checked before 28 weeks.		
Appropriate foetal and neonatal monitoring if TSI positive at 28 weeks	5% were positive (66% referred to neonatology, 22% moved centre, 11% not referred to neonatology)		
TFT checked 6 weeks postpartum	<50% (limited data, recommended post-discharge in primary care)		

Aim:100% for all but >80% for 6 weeks post-partum TFT checks.

TFT-Thyroid function test

TSI-Thyroid stimulating immunoglobulin

TSH-Thyroid stimulating hormone

Conclusion

Although adherence to local standards was excellent in some domains, this audit highlighted inadequacies, especially in achieving a pre-conceptual TSH of <2.5mU/l. To address this, a card has been designed for patients with hypothyroidism to summarize the key management requirements in preconceptual and antenatal care.

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OC4.2

Towards enhancing sodium iodide symporter function in thyroid cancer: HiBiT tagging and CRISPR-driven drug discovery

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Background

Sodium iodide symporter (NIS) is pivotal to iodide transport, and essential for therapeutic and imaging applications in differentiated thyroid cancer (DTC). However, its efficacy is often compromised by diminished activity at the plasma membrane (PM) . We aimed to design a new high-throughput platform for screening drugs capable of enhancing endogenous NIS activity. Thus, we inserted an 11 amino acid HiBiT luminescence tag into 6 different locations within three extracellular loops of NIS and appraised their impact on radioiodine uptake.

Methods

HiBiT tag was inserted within the 1st, 3rd and 6th extracellular loops of NIS, at positions adjacent to Leucine-85, Glycine-214, Threonine-221, Cysteine-483, Aspartic acid-513, and Arginine-516. All 6 constructs were transiently transfected and appraised via radioiodine uptake assays, Western blotting, and Nano-Glo extracellular detection, to validate their impact on NIS expression and function, in the presence and absence of drugs known to modulate NIS function.

Results

Three plasmids retained functional iodide uptake in both TPC1 and Hela cells. Specifically, positions Cysteine-483, Aspartic acid-513, and Arginine-516 transported iodide, with increases of 2.8-fold, 3.9-fold, and 2.6-fold in TPC1 cells, and 6.1-fold, 6.9-fold, and 6.6-fold in Hela cells, respectively, compared to the pcDNA 3.1 vector ($P<0.05$ in TPC1; $P<0.01$ in Hela). Luminescence assays reinforced these findings, confirming that HiBiT-tagged NIS correctly localised to PM. Drug treatments – including the HDACi SAHA – induced parallel increases in iodide uptake and luminescence, confirming functionality of HiBiT-tagged NIS.

Implications

These proof-of-principle data suggest that HiBiT-tagging of NIS, particularly within the 6th extracellular loop, represents a viable strategy for progressing to CRISPR-mediated gene editing to facilitate the development of cell lines with endogenously tagged NIS, and hence novel high-throughput drug screening. This would pave the way for the first HTS of endogenous NIS activity, with the ultimate potential to improve therapeutic strategies for patients with refractory thyroid cancer.

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OC4.3

Outcome of treatment for mild graves' disease: could less be more?

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The standard first-line therapy for uncomplicated Graves' hyperthyroidism is 12-18 months of anti-thyroid drugs (ATD) in most centres, with about 50% chance of long-term remission. However, as sensitive FT3 assays were introduced since this became established practice in the 1980s, there are no good data that inform the outcome or natural history of mild Graves' disease, which is now routinely detected and treated. The outcome of 87 patients with mild Graves' disease, defined as TSH $\leq$0.05 mU/l, FT4 <30 pmol/l, FT3 <9.0 pmol/l, and TRAb 1.8-5.0 IU/l was followed in the 2 largest centres in Tyne & Wear. Patients with eye disease and those who did not tolerate ATD were excluded. Fifteen patients (17%) had spontaneous remission of hyperthyroidism that was sustained for 12 months without treatment. Thyroid status at one year after stopping treatment was available for 52 patients who completed at least 12 months of ATD (median treatment length was 18 months). Forty five patients (87%) remained in euthyroid (in remission) and 7 (13% relapsed). Outcome of ATD was not available for 20 patients for several reasons (9 patients who did not complete 12 month's ATD, 6 patients did not stop ATD, 4 patients stopped the ATDs but have not completed the 12 months follow up yet and 1 patient made a personal choice for RAI). Treatment of mild Graves' hyperthyroidism is not always necessary, as spontaneous remission is not infrequent (17%). In addition, 12 months or more of ATD treatment gives an excellent outcome (87% remission). Shorter treatment courses would have fewer side-effect and use less NHS resource, so should be considered.

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OC4.4

De-prescribing levothyroxine in primary care – results of a feasibility study

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Introduction

Levothyroxine is the third most commonly prescribed medication in the UK, with an annual cost to the NHS of £52 million. Due to the fluctuating nature of thyroid function, guidelines for hypothyroidism management recommend that an elevated Thyroid Stimulating Hormone (TSH) should be confirmed with repeat testing, prior to commencing treatment. International research has demonstrated that levothyroxine is routinely prescribed contrary to such guidance and frequently for those with normal thyroid function. The goal of this research is to determine the acceptability of de-prescribing levothyroxine.

Methods

Patients registered with five general practices in North-East England were invited to participate. All were taking levothyroxine for at least six months and never had a documented TSH >10mU/L. Those with a history of thyroid cancer, thyroidectomy or pituitary disease were excluded. Participants discontinued levothyroxine for a six-week period. All completed a ThyPRO-39 quality of life questionnaire prior to intervention and again at the end of the study period, along with assessment of free T4, TSH & TPO antibodies at six weeks. The primary outcome was the proportion of patients who remain euthyroid, off levothyroxine, at 6 weeks.

Results

102 participants were enrolled. 94 (92.2%) completed 6 weeks of levothyroxine withdrawal, with 8 patients restarting early, primarily due to symptoms. 60.8% of those completing the discontinuation period were either euthyroid or had TSH in

the subclinical hypothyroidism range (4.4-10mU/L). 50% of those with subclinical hypothyroidism chose not to restart treatment at trial conclusion, with higher TPO-Ab levels positively predicting those who recommenced. 65.7% of the whole cohort reported feeling either "the same" or "better" at the end of the study period.
Conclusion
Most patients prescribed levothyroxine for presumed primary hypothyroidism do not develop overt hypothyroidism 6 weeks after discontinuation of medication, highlighting the potential for de-prescribing levothyroxine in select patients, without impacting patient well-being.

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OC4.5

Subclinical hypothyroidism and its impact on cardiac function post-acute myocardial infarction: a prospective cohort study

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Background
Subclinical hypothyroidism (SCH) is defined as elevated thyroid stimulating hormone (TSH) levels coupled with normal free thyroxine levels. SCH is associated with increased systemic vascular resistance, left ventricular systolic and diastolic dysfunction. Acute myocardial infarction (AMI) represents a leading cause of mortality and morbidity worldwide. AMI can progress to left ventricular systolic dysfunction and heart failure which predicts lower overall survival.
Aims
(i) Evaluate how SCH affects systolic and diastolic function in patients, post-AMI (ii) Assess the prevalence of SCH, post-AMI. (iii) Explore predictors of systolic or diastolic dysfunction post-AMI.
Methods
Patients with AMI (both ST-elevation and non-ST-elevation), were recruited across 6 hospitals in the North-East of England for a 2-year longitudinal prospective cohort study. Thyroid function tests were performed. patient medical characteristics were recorded. Systolic function was evaluated by the left ventricular ejection fraction on echocardiography. Diastolic function parameters included The E wave to A wave ratio (E/A ratio), mitral valve deceleration times (MVDecT) and E/e' ratio.
Results
Out of 1835 patients there were 321 cases with SCH representing 17.4% of the cohort. SCH was a significant predictor of prolonged MVDecT ($P=0.043$) & ($B=0.072$). Increased TSH levels were significant with having an increased E/A ratio ($P=0.003$) & ($B=0.009$). Significant predictors of systolic dysfunction were male sex, ST-elevation MI, current smokers, and alcohol consumption. Significant predictors of diastolic dysfunction were increasing age, increased BMI, male sex, and SCH.
Conclusion
SCH is prevalent among patients post-AMI and it is a significant predictor of diastolic dysfunction.

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OC4.6

Evaluating the difference between thyroid function test (TFT) results (thyroid stimulating hormone (TSH) and free thyroxine (FT4)) in managed hypothyroidism vs screened untreated/euthyroid individuals: analysis of a whole city population database

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Introduction
Over 10 million TFTS are carried out in England annually, most requests coming from primary care. This study aimed to investigate differences in laboratory thyroid-hormone-status in managed hypothyroidism vs untreated/euthyroid individuals taking into accounting diagnostic code/levothyroxine amount prescribed.
Methods
Using a city-wide population record, we analysed TSH/FT4 simultaneous results from 47,869 consecutive diagnosed hypothyroid individuals by medication dose and 393,101 untreated/euthyroid individuals over 14 years. For those on medication we only included those diagnosed >2 years and who had more than 2 years of tests. For those not on medication we included results from those patients who had a single test or 2 tests with more than 5 years between tests.
Results
The FT4 distribution for levothyroxine treated individuals was similar in shape vs untreated individuals but shifted towards higher FT4 even at the lowest dose of levothyroxine, with an increasing separation of the distributions as levothyroxine dose increased (F value = 1.5 increasing to F value = 4.2). In contrast the TSH distribution was substantially different for untreated individuals vs those on levothyroxine where the distribution was massively skewed to low/ undetectable TSH with a 'hockey stick' configuration, even for those on low daily doses of levothyroxine. For those not on thyroid-hormone replacement, 90% of individuals were within the TSH reference range. For those on medication only 43% were within TSH reference range. For men vs women median levothyroxine dose was higher in all decades, with the highest median daily dose at age 50-59years (men: 107 mg. women 96 mg). Median T4 rose (women > men) and TSH fell progressively (women > men) by age in treated individuals.
Conclusion
We have here described that distribution of FT4/TSH is different in people on and off levothyroxine treatment and that degree off difference increases in treated individuals by levothyroxine daily dose. The distribution of TSH is 'unphysiological' even at low levothyroxine dose.

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Adrenal and Cardiovascular

OC5.1

Can voxel analysis of [11C]Metomidate PETCT be used to detect micronodular disease and predict outcome from adrenalectomy?

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Background
[^{11}C]Metomidate PET-CT (MTO) is a non-invasive method of lateralisation for the diagnosis of unilateral Primary Aldosteronism An SUVmax lateralisation index of 1.25 of tumour:contralateral normal gland has previously been established. Despite lateralisation, most patients do not have complete PASO clinical success after adrenalectomy, which may be due to the presence of bilateral disease. Using entire gland voxel analysis, we seek to test the hypothesis that multifocal, bilateral disease has a more uniform isotope uptake compared to unilateral disease, in which a single discrete nodule has higher uptake than the remainder of the ipsilateral and contralateral gland.
Methods
40 adrenal glands on pre-operative MTO scans were analysed. Those with complete PASO biochemical and clinical success were compared to those with medically managed bilateral disease. Glands were manually outlined on CT by combining the region of interest (ROI) on each CT slice into a volume of interest (VOI) encompassing the entire gland. The following parameters were calculated from all voxel SUV values within the gland: mean, maximum, total gland uptake (TGU, volume x SUVmean), standard deviation (SD), skewness (asymmetry of distribution) and kurtosis (distribution around the mean).
Result
The contralateral 'normal' gland of the patients who were cured post-operatively had a smaller mean volume ($4.38\ cm^3 \pm 1.46$) and markers of tracer uptake (SUVmean 11.46 ± 3.6, max 17.69 ± 4.71, TGU 50.42 ± 23.3) than the 'unilateral' diseased gland ($7.59\ cm^3 \pm 2.52$, mean 15.68 ± 3.95 max 31.79 ± 12.77, TGU 310.4 ± 103.23) . The bilateral glands had values between 'normal' and 'unilateral' ($6.24\ cm^3 \pm 3.67$, mean 13.9 ± 2.75, max 22.08 ± 5.26, TGU 90.37 ± 66.67). The 'unilateral' gland was more positively skewed with a less negative kurtosis.
Conclusion
This exploratory, retrospective analysis identifies potential novel radiological measures of CYP11B2 activity, using all available voxel data, that may provide additional information to the standard analysis of SUVmax values alone.

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OC5.2

Hypothalamic-pituitary-adrenal axis activation precedes metabolic dysfunction in obesity in a porcine model

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The temporal relationship between obesity, hypothalamic-pituitary-adrenal (HPA) activation and metabolic disease is complex and poorly understood. It is difficult to model the HPA response to calorie overconsumption in humans/rodents. In this study, we hypothesise that HPA activation precedes metabolic dysfunction in a porcine model of obesity. Adult female pigs (LandraceXHampshire, $n=7$) underwent phenotyping before and during 12 weeks of high calorie feeding (HCF) (9,000 kcal/day vs 3500 kcal/day/100 kg pig). Unstressed blood sampling was achieved by use of vascular access ports. Average weight gain was 5 ± 0.5 kg/week. Subcutaneous adipose (MRI/ultrasound) increased by 34+/-9.2% with minimal increase in visceral adipose. Pigs developed relatively "metabolically-healthy" obesity with no change in fasted insulin/glucose or response to oral glucose tests. There was, however, a reduction in glucose infusion rate during an euglycaemic-hyperinsulinaemic clamp at 12 weeks compared to baseline (9.5 ± 2.38 vs 5.1 ± 0.91 mg/kg/min, $n=4$, $P=0.03$). Plasma/salivary cortisol and cortisone were quantified by LC-MS/MS weekly; plasma concentrations were unaltered with HCF. Salivary cortisone, however, increased by 12 weeks (0.95 ± 0.38 vs 1.52 ± 0.32nM, $P=0.04$). Diurnal rhythm was assessed by 8-hourly sampling (0800hrs, 1400hrs, 2200hrs). All measured plasma/salivary glucocorticoids were increased at 1400hrs at 6 and 12 weeks, concentrations at 2200hrs were not different. The response of cortisol to ACTH (Synacthen) stimulation was increased at 6 and 12 weeks (AUC 207 ± 23 vs 318 ± 39, $P=0.03$). There was a small but non-significant reduction in suppression response to oral dexamethasone (1 mg) at 12 weeks. Liver biopsies showed hepatic expression of corticosteroid binding globulin (CBG) was significantly reduced by HCF. Hyperinsulinaemia has been posited as the driving force for HPA activation in obesity. Our data suggest the opposite - that high-calorie feeding alone is sufficient to activate the HPA axis and reduce CBG expression, and this precedes changes in insulin sensitivity/hyperinsulinemia.

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OC5.3

Incident changes of the 1 mg-overnight dexamethasone suppression test correlate with long-term clinical outcomes in patients with adrenal incidentalomas: results from the multi-centre DEX-AI and CORTEX-AI ENSAT studies

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Introduction
Patients with adrenal incidentalomas (AI) should undergo a 1 mg-overnight dexamethasone suppression test (1 mg-DST) to exclude cortisol excess (non-functioning adrenal tumours, NFAT; serum cortisol $\leq$50 nmol/l) or diagnose mild autonomous cortisol secretion (MACS; serum cortisol $>$50 nmol/l). Guidelines recommend repeating 1 mg-DST only if treatment is intended; however, data underpinning this recommendation are scarce.
Methods
Retrospective multi-centre study including patients with benign AI with at least two 1 mg-DST and follow-up $\geq$3 years. Incident 1 mg-DST changes were correlated with clinical and radiological characteristics. Cox proportional hazard regression was used to calculate effect estimates of clinical outcomes.
Results
2525 patients from 25 centres were included, with a median follow-up of 6.7 years (range 3-22.9). 1 mg-DST incident changes were observed in 22.5% of patients: 9.0% NFAT developed MACS (NFAT→MACS); 7.7% MACS developed normal 1 mg-DST (MACS→NFAT); 7.7% had 1 mg-DST results fluctuating around the 50 nmol/l cutoff. Most 1 mg-DST changes (~60-70%) occurred within 3 years of the baseline 1 mg-DST. NFAT→MACS patients had larger tumours, more frequently bilateral, were more likely to be smokers and had a higher prevalence of hypertension, type 2 diabetes, osteoporosis, and cardiovascular events than those with persistently normal 1 mg-DST (NFAT→NFAT). MACS→NFAT patients were younger with smaller and more frequently unilateral tumours than those with persistently abnormal 1 mg-DST (MACS→MACS). At the last available clinical follow-up, there was a progressive increased risk of hypertension, type 2 diabetes, dyslipidaemia, and cardiovascular events across the spectrum of NFAT→NFAT, NFAT→MACS, MACS→NFAT, and MACS→MACS. Only MACS→MACS patients had significantly increased age- and sex-adjusted risk of composite cardiovascular events (hazard ratio 1.50 [95%CI 1.04-2.15] vs. NFAT→NFAT, $P=0.03$).

Conclusions
Incident 1 mg-DST changes are frequent in patients with benign AI and correlate with tumour characteristics and clinical outcomes. Repeating 1 mg-DST within 3 years may be advocated to risk-stratify patients during long-term follow-up.

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OC5.4

Ciclesonide as an improved therapeutic treatment for the respiratory consequences of preterm birth

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Cortisol is an essential regulatory hormone for normal mammalian respiratory development prior to birth. The potent synthetic glucocorticoids betamethasone and dexamethasone (DEX) are used in the NICU to treat the respiratory complications of human preterm birth. There are however emerging concerns of their deleterious effects in other fetal organs such as the brain that has led to the search for more efficacious compounds with reduced systemic side-effect profiles. Here we have assessed the asthma steroid ciclesonide (CIC), a novel prodrug and agonist of the glucocorticoid receptor (GR) as an alternative treatment for the consequences of preterm birth. We have previously demonstrated that postnatal administration of CIC and DEX both stimulate key biomarkers of lung development, but unlike DEX, CIC does not induce growth retardation, reduce brain weight or reduce neural myelination levels. Here we show in primary cultures of mouse fetal lung fibroblasts that CIC and its active metabolite desisobutyryl-ciclesonide (Des-CIC) induce very similar but not identical transcriptome changes to Dex that were absent in GR-null fetal lung fibroblasts indicating that Des-CIC induced changes were mediated via the GR. Key target genes included known GR-regulated proteins, such as Fkbp5, Crispld2, Tgm2 and Zbtb16, that drive reduced cell proliferation and lung extracellular matrix remodelling. In contrast to Dex, neonatal rats treated with Des-CIC did not cause reduced body weight, reduced IGF-1 serum levels or chronic hyperglycaemia. However, Des-CIC was as effective as DEX in reducing expression of proinflammatory cytokine mRNAs in a bleomycin-induced rat model of lung injury. Structural studies indicate that Des-CIC acts as a GR super-agonist. Overall, these results suggest CIC may be an effective synthetic GC prodrug to promote lung maturation and reduce lung injury in the neonatal period driven by the selective GR modulator activity of its *in vivo* active metabolite, Des-CIC.

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OC5.5

Cardiovascular risk profile of low-dose prednisolone and its effect on the quality of life in patients with adrenal insufficiency: the HYPER-AID observational study

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Aim
To assess the cardiovascular risk of low dose prednisolone in patients with adrenal insufficiency (AI), and how switching from hydrocortisone to prednisolone affects their quality of life (QOL).
Methods
In this prospective observational study, patients with AI were switched from hydrocortisone to 2-4 mg of prednisolone and followed up for 4 months. We assessed cardiovascular risk using blood pressure, waist and hip circumferences, lipid profile and C-reactive protein. QOL was assessed using a customized modified SF-36 questionnaire. We compared baseline and follow-up means using paired t-test.
Results
Sixty-two participants were enrolled, of which 48 completed the study. The mean (SD) age at enrolment was 54.5 ± 13 years. Twenty-seven (56.3%) were female while 8 (16.8%) had primary AI. The mean duration on glucocorticoids was 11.4 ± 8.6 years. At follow-up, we observed a significant reduction in weight from 90.6 kg to 89.6 kg ($P = 0.007$). There was a significant reduction in systolic blood pressure (BP) of up to 6mmHg ($P = 0.027$) but not the diastolic BP. There was no difference in the ratios of waist to hip circumference ($P = 0.183$). The use of prednisolone was associated with no changes in LDL-cholesterol, total cholesterol, HDL, non-HDL, triglycerides or CRP ($P > 0.05$ for all). We observed an increase in subjective energy scores as well as total quality of life scores ($P = 0.003$ and $P = 0.019$ respectively). There were however no changes in the subjective general health, wellbeing and nausea scores. Patients reported prednisolone to be more convenient compared to hydrocortisone ($P = 0.002$).
Conclusion
Prednisolone has similar cardiovascular risk profile to hydrocortisone. The reduction in weight and systolic blood pressure, convenience, the improvement in energy levels and subjective general health offer additional advantages over hydrocortisone.

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OC5.6

Salivary cortisone vs serum cortisol in the overnight dexamethasone suppression test: results of a utility evaluation at one centre

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Introduction
Saliva hormone measurements are increasingly being applied in every day clinical practice. In relation to salivary cortisol / cortisone measurement there is a particular advantage, with minimal chance of cross reaction with prescribed glucocorticoids and greater convenience. We here evaluated the utility of these measurements in patients undergoing an overnight dexamethasone suppression test (ONDST).
Methods
Individuals undergoing an ONDST had parallel measurement of serum cortisol and salivary cortisone at 0900 following midnight dexamethasone(1 mg). Salivary cortisone was measured by electrospray positive ion mode liquid chromatography tandem mass spectrometry (1). The threshold for adequate suppression of salivary cortisone was < 2.7 nmol/l; serum cortisol was $<$ 50nmol/l.
Results
Results for 25 individuals (24% men (median age 53.0) and 76% women (median age 55.6) were analysed. In 40% of individuals an adrenal adenoma was present; in 53% Cushing's Syndrome was suspected on the basis of clinical features. Serum cortisol failed to suppress <50 nmol/l in 14/25 cases. We found a strong correlation between 0900 salivary cortisone and serum cortisol after 1 mg ONDST (beta coefficient $= 0.31$, [95% CI 1.4-4.9], $P = 0.001$). When performance of post-dexamethasone salivary cortisone (<2.7 nmol/l) alone in relation to suppression of serum cortisol (<50 nmol/l) was analysed, agreement was 72.3% between tests (Cohens Kappa 0.30 $P = 0.02$), with a positive predictive value of 70% of salivary cortisone (using serum cortisol as the standard) and negative predictive value of 100% in relation to ruling out cortisol excess.
Conclusion
We have demonstrated test validity and clinical utility in substitution of salivary cortisone for serum cortisol in the ONDST as a first-line test. Salivary cortisone could therefore be used as an alternative sampling method which does not require venepuncture or attendance at hospital. Application of the test has the potential for significant savings of money and time.
Reference: Jones RL *et al. J Chromatogr B Analyt Technol Biomed Life Sci*. 2012;881-882:42-48. doi:10.1016/j.jchromb.2011.11.036

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Metabolism, Obesity and Diabetes

OC6.1

Diet-responsive NtsR1-expressing enteropancreatic neurons mediate a glucoregulatory effect of monounsaturated fatty acids

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The ingestion of foods rich in monounsaturated fatty acids (MUFAs), such as olive oil, stimulates the secretion of neurotensin, a neuropeptide and gut hormone, from intestinal enteroendocrine cells. Neurotensin has established effects in the central nervous system, and has been more recently implicated in peripherally promoting lipid abortion, but its role in glucose homeostasis remains unclear. Neurotensin acts via three receptors including the NtsR1. We hypothesise that neurotensin mediates the glucoregulatory effects of specific MUFAs. Administration of exogenous neurotensin acutely improved glucose tolerance in both lean and diet-induced obese mice and stimulates insulin release via the NtsR1. The glucoregulatory effect of oral olive oil was blocked by an NtsR1 antagonist or a lipase inhibitor. Oleic acid, known to stimulate neurotensin release, is the major MUFA constituent of olive oil and also improved glucose tolerance in mice. Using NtsR1 reporter mice, we visualised NtsR1-expressing neurons which originate in the proximal duodenum and extend towards islets in the pancreas. The function of enteropancreatic neurons is currently unknown, and they have been found in both mice and humans. Surgical separation of the proximal duodenum and adjacent pancreas blocked the glucoregulatory effects of oral olive oil and exogenous neurotensin. Specific ablation of NtsR1-expressing enteropancreatic neurons through injection of cre-dependant diptheria toxin receptor-encoding AAV into the pancreas of NtsR1-NeoCre mice also blocked the glucoregulatory effects of olive oil and neurotensin and enhanced the glucose excursion in mice in a fast-refeed study. These data suggest that NtsR1-expressing enteropancreatic neurons mediate the glucoregulatory effects of exogenous neurotensin and endogenous neurotensin release following olive oil ingestion and are therefore potential targets for future interventions to improve glucose homeostasis.

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OC6.2

Evaluating setmelanotide treatment for 12 months in patients aged 6 to 12 with rare melanocortin-4 receptor pathway–related diseases: reduction of weight parameters

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Background
Impaired melanocortin-4 receptor (MC4R) signaling due to rare genetic defects such as biallelic variants in *POMC* or *PCSK1* (leading to proopiomelanocortin [POMC] deficiency) or *LEPR* (leading to leptin receptor [LEPR] deficiency), or Bardet-Biedl syndrome (BBS) may result in hyperphagia and severe obesity. Previously, setmelanotide in patients aged 2-17 years was well tolerated and improved hunger severity and weight-related measures. Here, we report changes in weight measures after 12 months of setmelanotide in paediatric patients aged 6 to 12.
Methodology
Patients from index clinical trials with on-treatment measurements at Baseline and Month 12 were included. Changes in weight, body mass index (BMI) and BMI z-score per World Health Organization methodology from Baseline to 12 months of setmelanotide were assessed.
Results
A total of 11 paediatric patients were analyzed: 4 with POMC deficiency, and 7 with BBS. In both patient groups, mean (standard deviation [SD]) BMI z-score, BMI and weight were reduced at 52 weeks (Table). All 11 patients (100%) achieved a clinically significant reduction in BMI z-score from Baseline to Week 52 of at least 0.2 points. No new adverse events were reported.
Conclusions
Setmelanotide leads to clinically significant improvements in weight-related measures in paediatric patients aged 6 to 12 with obesity related to POMC deficiency or BBS. The therapeutic goal of weight stabilization in this age group is exceeded. These data support setmelanotide use in these ages in approved indications of hypothalamic MC4R pathway disruptions.

Table 1. Change from Baseline to Week 52 in weight-related parameters by indication (absolute and percentage)

	BMI z-score	BMI (kg/m^2)	Weight (kg)
POMC (n = 4)	−1.46 (0.60)	−6.68 (3.31)	−12.05 (7.17)
	−42.53% (17.78)	−20.52% (9.02)	−14.54% (8.30)
BBS (n = 7)	−0.99 (0.50)	−3.56 (2.08)	−3.87 (5.60)
	−28.24% (24.85)	−10.40% (7.64)	−4.59% (7.67)

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OC6.3

Canine genome-wide association study identifies DENND1B as a canine and human obesity gene which regulates melanocortin signalling

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Obesity is an important heritable disease, but its genetic basis is not clearly understood. In dogs, selective breeding renders some breeds, including Labrador retrievers, particularly susceptible to obesity and makes trait mapping tractable. We performed a canine genome-wide association study (GWAS) for obesity in 241 Labrador retrievers. We showed polygenic risk affects individual susceptibility to weight gain in an obesogenic environment and that owners of at risk dogs must exercise greater restraint to keep at-risk dogs slim. To test if genes identified on the canine GWAS were relevant to human obesity, we examined regions orthologous to those mapped in dogs in human data sets. Specifically, we tested for association with BMI in a GWAS on 806,834 participants from the GIANT study; an exome-wide association study (ExWAS) of rare, deleterious exome variants from 454,787 individuals from the UK Biobank study; rare variant enrichment tests in the Severe Childhood Onset Obesity Project; and the Severe Obesity in Pakistani Population (SOPP) cohort. This approach identified some form of genetic association with human obesity for each of the top five canine loci. The lead association in dogs was with rs24430444 within the gene DENN domain containing 1B (DENND1B) with the risk SNP being associated with ~7% greater body fat. In humans, DENND1B was significantly associated with BMI in the GWAS and ExWAS studies and a homozygous variant found in DENND1B was a candidate for causing severe obesity in a patient from SOPP. We demonstrated that DENND1B regulates signalling and trafficking of MC4R, a hypothalamic receptor which has a central role in energy homeostasis. In summary, our work used canine genetics to identify novel obesity genes and mechanisms relevant to both dogs and humans.

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OC6.4

Associations between PCSK9 gene missense variants, blood glucose and type 2 diabetes

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Background
Lipid-lowering medication has dramatically reduced cardiovascular events and associated mortality. Statins (HMG-CoA reductase (HMGCR) inhibitors), the most widely used class of lipid-lowering medication, are associated with an

increased risk of new onset type 2 diabetes. Similarly, inactivating mutations in *HMGCR* are associated with an increased risk of new onset type 2 diabetes. Medications that inhibit the activity or production of proprotein convertase subtilisin/kexin type 9 (PCSK9) are novel agents that potently lower cholesterol. Conflicting data about reduced PCSK9 activity and the risk of developing type 2 diabetes have been reported in the literature. Exploring genetic factors may provide additional insights and inform clinical practice.

Aim

To evaluate the relationship between genetic variants in *PCSK9* and type 2 diabetes.

Methods

Using the UK Biobank dataset, we performed single-variant analyses and utilised regression (PLINK), Burden, SKAT, SKAT-O tests and hierarchical clustering to test for associations between *PCSK9* missense SNPs and metabolic traits (LDL cholesterol, random glucose and type 2 diabetes) in 469,835 individuals with whole-exome sequencing data.

Results

Single-variant association analysis revealed associations between rs374014696 (Ala242Val, OR [95% CI] 0.51 [0.40-0.65], $P = 1.022\times10^{-7}$) and rs773660398 (Ala44Thr, OR: 1.50 [1.26-1.78], $P = 6.735\times10^{-6}$) alternative alleles and higher random glucose values. Clustering and burden tests highlighted three distinct clusters of *PCSK9* missense variants. Cluster 1 variants were associated with lower LDL and higher glucose levels. Cluster 2 variants were associated with lower risk of type 2 diabetes. Cluster 3 variants were associated with lower LDL levels, higher glucose levels and higher risk of type 2 diabetes.

Conclusions

Our data suggest that a proportion of coding missense *PCSK9* gene variants are associated with lower cholesterol levels, higher random glucose levels and increased risk of type 2 diabetes. Further research is required to determine if similar risks are present in more diverse populations.

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OC6.5

iPSC-derived hepatocytes offer a novel platform for modelling metabolic dysfunction-associated steatotic liver disease (MASLD) *in vitro*

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is a disease spectrum ranging from intrahepatic lipid accumulation to fibrosis, cirrhosis, and hepatocellular carcinoma. Despite the severity, there are no efficacious therapies, mainly due to the complexity of disease and the lack of predictive pre-clinical models. We hypothesised that iPSC-derived hepatocytes (Opti-HEP) offer a suitable platform for the development of *in vitro* MASLD models recapitulating all aspects of the disease phenotype. Wild-type iPSCs and iPSCs harbouring the MASLD risk-associated PNPLA3-I148M variant were differentiated to Opti-HEP. Differentiation status was determined by qPCR, immunocytochemistry, western blotting, colorimetric assays, and ELISA. Wild-type and disease Opti-HEP were treated with a mixture of fatty acids, glucose, or a combination of both for 7 days. Differences in lipid accumulation, insulin sensitivity, hepatic inflammation, and CYP450 expression were determined by qPCR, western blotting, and BODIPY staining. Wild-type and PNPLA3-I148M Opti-HEP demonstrated mature hepatocyte phenotype, as evidenced by liver maturity marker expression (albumin, alpha-1-antitrypsin, HNF4A), urea secretion, gluconeogenesis, and CYP450 activity. Fatty acid and glucose treatment of wild-type Opti-HEP significantly increased lipid accumulation compared to vehicle-treated cells, and this effect was further exacerbated in PNPLA3-I148M cells. High glucose treatment impaired AKT phosphorylation (Ser473) in wild-type and PNPLA3-I148M Opti-HEP suggestive of insulin resistance, whilst fatty acid treatment resulted in ~20% reduction in Opti-HEP viability alongside increases in pro-inflammatory cytokine *IL-1β*, *IL-6*, *IL-8*, and *TNFα* expression. Endorsing these findings, fatty acid and glucose treatment significantly decreased drug metabolising genes expression (*CYP3A4*, *CYP2B6*, *CYP2C9)*, suggesting impaired drug metabolism activity. We have successfully produced iPSC-derived hepatocytes with comparable functionality to that observed in primary human hepatocytes. By applying dietary and genetic interventions associated with MASLD development, we have generated a novel model that recapitulates the MASLD phenotype *in vitro*, offering an efficient pre-clinical platform for the large-scale efficacy screening of novel therapeutics against the disease.

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OC6.6

Development of the hormone cell atlas

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Hormones are secreted by diverse cell types across endocrine and non-endocrine tissues, acting via cognate receptors to coordinate cellular responses. A systematic understanding of hormone production and action across human tissues, at cell type resolution, is lacking. We have developed the Hormone Cell Atlas, a unique single cell transcriptomic resource integrating 46 tissues from over 1000 donors, from which we map the expression of over 500 genes encoding hormones and their receptors. We profile cross-tissue, sex-specific expression of genes involved in peptide, steroid and amine-derived hormone production, defining classical endocrine and non-professional hormone-producing cell types. We survey the expression and specificity of G protein coupled receptors, nuclear hormone receptors and enzyme-linked receptors in central and peripheral tissues, including those representing major drug targets, and uncover previously uncharacterised sites of hormone action. We next leverage the Hormone Cell Atlas to assemble cell type specific intracellular hormone regulatory networks. Focusing on adipose tissue, we identify regulatory networks in adipocytes centred on the glucocorticoid receptor (*NR3C1*) and thyroid hormone receptor beta (*THRB*), and validate downstream targets in primary human adipocytes cultured *in vitro*. Investigating depot and BMI-dependent patterns of hormone production and receptivity, we highlight the androgen receptor (*AR*) as a prominent and BMI-associated transcript in subcutaneous adipocytes, explore associated transcriptional signatures, and offer new insights into hormonal regulation of adipose tissue function. Finally, using our directory of hormone-receptor interactions, we assemble a system-wide, hormone-mediated cellular interaction network, including feedback and crosstalk within and across classical endocrine axes. The Hormone Cell Atlas, accessible via a searchable web-based portal, will provide a valuable resource for understanding hormone regulation and action in health and disease.

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Neuroendocrinology and Pituitary

OC7.1

Lowering the day 5 postoperative cortisol cutoff value to avoid over-diagnosis of secondary adrenal insufficiency following pituitary surgery

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Background

Identifying patients who develop secondary adrenal insufficiency (SAI), requiring longterm glucocorticoid replacement (GR) following trans-sphenoidal pituitary surgery (TSS) is crucial to prevent life-threatening Addisonian crisis. An early morning day 5 cortisol value may reliably assess hypothalamo-pituitary-adrenal (HPA) axis functioning. However, the cut-off which can reliably predict SAI is yet to be elucidated.

Method

This is a retrospective cohort study of 88 consecutive patients who underwent TSS at Charing Cross Hospital between 2019 and 2023. Receiver Operating Characteristic (ROC) curves were generated to evaluate the different predictive values of cortisol levels on postoperative day 5, using the Abbott Alinity cortisol immunoassay. We excluded 34 patients leaving 54 patients for analysis. Area Under the curve (AUC) was calculated from the ROC curve.

Results

SAI prevalence within this study was 31%. The currently used cortisol cutoff concentration of >358 nmol/l to exclude SAI demonstrated 100% sensitivity and a specificity of 53.85%. Lowering this threshold to >308 nmol/l maintained 100% sensitivity while improving specificity to 75.86%. A Day 5 cortisol <206 nmol/l predicts poor HPA function with a sensitivity of 70.59% and 100% specificity. Day 5 cortisol (AUC$=0.9645$) and Day 4-7 (AUC$=0.8679$) cortisol provided better predictive values for SAI compared to Day 2/3 samples (AUC$=0.8095$).

Conclusion

Day 5 serum cortisol >308 nmol/l reliably indicates an intact HPA axis. Values <206 nmol/l reliably detects SAI. Patients with Day 5 serum cortisol

measurements between 206-308 nmol/l should be discharged on glucocorticoid therapy and undergo a dynamic test post-operatively to ascertain their true HPA function.

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OC7.2

The MRAP2 accessory protein directly interacts with melanocortin-3 receptor to enhance signalling

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The central melanocortin system links nutrition to energy expenditure, with melanocortin-4 receptor (MC4R) controlling appetite and food intake, and MC3R regulating timing of sexual maturation, rate of linear growth and lean mass accumulation. Melanocortin-2 receptor accessory protein-2 (MRAP2) is a single transmembrane protein that interacts with MC4R to potentiate it's signalling, and human mutations in MRAP2 cause obesity, with hyperglycaemia and hypertension. Previous studies have been unable to consistently show whether MRAP2 affects MC3R activity. Here we used single-molecule pull-down (SiMPull) to confirm that MC3R and MRAP2 interact. Analysis of fluorescent photobleaching steps showed that MRAP2 forms monomers or occasionally homodimers at cell surfaces, while MC3R is predominantly monomeric. When co-transfected, MC3R and MRAP2 readily form heterodimers most commonly with a 1:1 (~74%) or 1:2 (~17%) stoichiometry. snRNA-seq of human hypothalamic neurons showed MRAP2 was expressed in 57% of MC3R-positive neurons, while spatial transcriptomics revealed *MRAP2* transcripts are present under the same spatially barcoded spots as *MC3R* transcripts in regions of the human hypothalamus with roles in energy homeostasis and appetite control, including the arcuate nucleus, ventromedial hypothalamus and periventricular region. We then showed that MRAP2 enhances MC3R cAMP signalling, impairs β-arrestin recruitment, and reduces receptor internalisation in HEK293 cells. Structural homology models revealed putative interactions between the two proteins and alanine mutagenesis of five MRAP2 and three MC3R transmembrane helix-6 residues significantly reduced MRAP2 effects on MC3R signalling. Finally, we showed genetic variants in MRAP2 that have been identified in individuals that are overweight or obese prevent MRAP2's enhancement of MC3R-driven signalling. Thus, these studies reveal MRAP2 as an important regulator of MC3R function and provide further evidence for the crucial role of MRAP2 in energy homeostasis.

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OC7.3

Venous thromboembolism risk in cushing's disease, acromegaly and non-functioning pituitary adenomas: insights from three UK tertiary centres

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Objective
To assess risk of venous thromboembolism (VTE) in patients with Cushing's disease (CD) compared to GH-secreting and non-functioning pituitary adenomas (NFAs). Timing and risk factors for VTE were recorded, with a detailed focus on VTEs in CD patients.
Design
A Retrospective, observational cohort study.
Methods
Patients diagnosed with acromegaly, NFA, or CD across three UK centres (OUH, QEHB, UHBW) between 2010 and 2021 were included. Chi-square, Kaplan-Meier survival, and Cox regression were performed to compare VTE cumulative probability and identify predictors. For the Cox regression, the period of study began four years prior to the diagnosis of pituitary tumour to capture VTEs prior to adenoma diagnosis.
Results
Among 827 patients (107 CD, 502 NFA, 218 acromegaly) followed for median 7 ± 3 years, VTE rates were 11.2% in CD, 0.4% in NFA, 2.7% in acromegaly. Patients with CD had higher VTE risk compared to NFA (OR 21.05, 95% CI 5.83 to 76.02, $P < 0.001$) or acromegaly (OR 4.48, 95% CI 1.63 to 12.30, $P = 0.002$). Kaplan-Meier analysis showed shorter time-to-event in CD ($p < 0.001$). Cox regression identified CD diagnosis (HR = 35.40; 95% CI 7.75 to 161.71; $P < 0.001$) and diabetes mellitus (HR 3.84; 95% CI 1.51 to 9.76; $P = 0.005$) as predictors of VTE. Eight/12 VTEs were diagnosed within one year pre- or post-diagnosis of CD. Four VTEs occurred shortly after transsphenoidal adenectomy (1-, 24-, 33-, and 35-days post-surgery). In contrast, VTEs in NFA and acromegaly patients occurred over a broader time interval (from four years before to twenty years post-diagnosis).
Conclusion
This study re-emphasises the increased risk of VTE CD patients specifically when comparing to patients with acromegaly or NFA. VTEs in patients with CD presented even one year following the diagnosis of hypercortisolaemia suggesting consideration should be given to what is the optimal duration of prophylaxis.

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OC7.4

Impact of prolactin to cellular respiration in hypothalamic neurons

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The pituitary lactogenic hormone prolactin (PRL) has well recognized role on metabolism and energy homeostasis, besides the classic physiological actions in lactation and reproduction in humans and rodents. Both persistent hyperprolactinemia (>25 µg/l) and low PRL levels (<7 µg/l) have negative impact on metabolism, indicating the complexity of PRL to the control of metabolism. Although it is known that prolactin may indirectly influence the control of energy homeostasis by causing hypothalamic leptin insensitivity, it has not been reported whether PRL has a direct effect on cellular respiration of hypothalamic neurons, which we hypothesise that may alter the energy sensing mechanism of hypothalamic cells, causing alteration to central control of the metabolism. Preliminary tests of dosage and duration for PRL treatment of immortalised hypothalamic cells mHypoE-37 were performed to establish the optimal protocol to mimic hyperprolactinemia. The chronic treatment for 3 consecutive days with PRL at 300ng/ml and 400ng/ml had robust effects, observed by the increased gene expression of PRLR and STAT5. These chronic treatments decreased the basal respiration of the cells subjected to a Glucose/Pyruvate Oxidation Stress in the SeahorseÛ apparatus. The oxygen consumption rate (OCR) was maintained lower after a surplus acute injection of PRL. Chronic treatment with PRL has also decreased the ATP production, as observed during the challenge with the ATP synthase inhibitor oligomycin, and the maximal oxygen consumption triggered by FCCP. These preliminary results suggest that PRL may alter the cellular respiration of hypothalamic neurons, although further investigation is required.

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OC7.5

A within patient comparison of 11C-methionine (Met) and 18F-fluoroethyltyrosine (FET) PET for the imaging of pituitary tumours – a pilot study

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Background
Pituitary MRI does not always reliably identify sites of *de novo*, residual or recurrent pituitary adenoma (PA). Some patients are therefore denied potentially curative intervention (e.g. transsphenoidal surgery or stereotactic radiosurgery) or undergo suboptimal treatment because of the absence of a clear target. Molecular imaging can complement anatomical imaging to aid tumour localisation. To date, [11C]methionine PET (Met-PET), is the preferred radiotracer for pituitary imaging. However, with a short half-life (20 min) access is limited to centres with an on-site cyclotron. Recently, [18F]fluoroethyltyrosine (FET-PET) (half-life 110 min) has been proposed as an alternative amino acid radionuclide, which could increase access to functional pituitary imaging.
Methods
We have conducted the first within patient comparison of [11C]Met-PET and [18F]FET-PET across a spectrum of pituitary tumour subtypes. In the initial pilot phase, 4 corticotropinomas, 3 thyrotropinomas, 2 somatotropinomas and 1 prolactinoma (with either de novo or residual disease) were assessed. Five patients had suspected cavernous sinus extension (CSE). Both qualitative and quantitative [standardised uptake values (SUV) normalised to cerebellum] tumoral uptake were assessed.
Results
Although all pituitary tumour subtypes showed focal [18F]FET uptake, in all cases PA were more readily localised [both qualitatively (visual inspection) and quantitatively (SUVmax)] using [11C]Met-PET. Importantly, unlike [11C]Met, significant physiological uptake of [18F]FET was observed in the normal CS in all patients, which resulted in tumoral CSE being less readily appreciated when compared with [11C]Met-PET.
Conclusions
[18F]FET-PET can aid localisation of all functioning PA subtypes. However, our findings suggest that tumour-to-background uptake ratios are superior for [11C]Met-PET, especially when there is CSE. Therefore, whilst [18F]FET-PET may facilitate increased access to molecular pituitary imaging, [11C]Met-PET is likely to remain the radiotracer of choice for the most challenging cases with low volume disease and/or CSE.

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OC7.6

Management of cystic macroprolactinoma – a UK & ireland multi-centre study

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Background
Prolactinomas are managed primarily using dopaminergic agonists (DA). Cystic macroprolactinomas have been considered an exception to this rule, particularly when the chiasm is involved as the cystic component is considered less likely to respond to DA.
Methods
Data were collected regarding management of cystic macroprolactinomas from 18 UK and Irish endocrine centres. Cystic macroprolactinomas were defined as $>$ 10mm, cystic component $>$ 50% adenoma diameter and prolactin $>$ 2000mIU/l.
Results
117 patients were identified meeting the inclusion criteria (median age at presentation 32.0, IQR 21.0-50.0yrs, 57F). Of these, 14 presented with apoplexy. Of the remaining 103 patients, three underwent primary surgery for visual field (VF) deficits. Decompression of the chiasm and restoration of VFs was achieved in all, however, all remain on DA. One hundred patients received DA as primary therapy (median age 36.5, IQR 20.0-50.3yrs; 51F; median duration 50, IQR 10.0-93.3mths). Cabergoline was the DA of choice ($n = 99$; median dose 1.0, IQR 0.5-1.5 mg/wk). At last follow-up, prolactin levels had declined from 9863 (IQR 4099-25369)mIU/L to 390 (IQR 125-954)mIU/l. Tumour shrinkage occurred in 79, with reduction in median adenoma and cyst diameter from 18.0 (IQR 14.0-26.0)mm and 13.5 (IQR 7.0-18.0)mm to 14 (IQR 11.0-19.0)mm and 8.3 (IQR 4.3-13.0)mm respectively. Baseline chiasmal compression and VF defects were present in 37 and 30 respectively. Of these, 27 showed relief of chiasmatic compression and 20 improved VFs. Four showed no improvement in either chiasmal compression or VFs; data were not available for six. Seventeen patients underwent surgery as secondary treatment for persistent VF defects, failure of tumour shrinkage/enlargement, or DA intolerance. Of these, 11 remain on DA. Five patients experienced apoplexy during treatment.
Conclusions
These data support a high degree of efficacy for primary DA therapy in cystic macroprolactinoma and provide data helpful to inform outcomes.

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Oral Poster Presentations

Neuroendocrinology and Pituitary

OP1.1

Characterisation of the acromegalic arthropathy in patients <50 years of age

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Background
The acromegalic arthropathy is a disease-specific, progressive, degenerative arthropathy. Degenerative arthropathies such as osteoarthritis are infrequent below the age of 50 years. We characterised the prevalence of acromegalic arthropathy in patients ≤50 years of age.
Methods
We undertook a multicentre, cross-sectional study, utilising validated questionnaires in patients with acromegaly, aiming to examine distribution of arthropathy, severity of pain, and treatment modalities employed.
Results
Of the total cohort, 107/411 patients were ≤50 years of age (median 41, 18-50 years; 47F; 44.9% with active disease) and 304 were >50 years (median 65, 51-88 years; 163F; 35.5% with active disease). The most painful joint was similar to the overall cohort (lower back [20.8%], knees [16.0%] and hips [12.3%]). The median number of painful joints was 5 (range 0-25). 36.4% and 10.3% of those < 50 years complained of moderate or severe joint pain respectively, compared with 45.7% and 14.1% of those >50 years. 56% and 29.9% of patients aged ≤50 years were taking at least one or two regular analgesics respectively, whereas the corresponding percentages for those >50 years were 61.4% and 37.2%. The most frequently used analgesics in patients aged ≤50 years were paracetamol (39.3%), oral non-steroidal anti-inflammatory drugs (NSAIDs; 29.9%), topical NSAIDs (9.3%), and codeine (15.0%). Four individuals were taking more potent opioids and 6 atypical analgesics. 16.8% of these patients had received at least one joint injection, however only three patients (2.8%) had undergone joint replacement therapy for a total of five joints (2 shoulders, 2 hips and 1 knee). In those aged > 50 years 29.9% had received at least one joint injection and 22.0% (n = 67/304) had at least one joint replaced.
Conclusions
Patients with acromegaly aged ≤50 years have significant arthropathy burden characterised by pain, requirement for analgesics and joint injections, however joint replacement was uncommon.

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OP1.2

Kisspeptin administration does not induce anxiety in humans

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Background
Kisspeptin is a critical endogenous activator of the reproductive system, with escalating clinical interest as a novel therapeutic agent for reproductive and psychosexual disorders. However, conflicting animal data suggest that kisspeptin can have anxiolytic, neutral, or anxiogenic effects. Given the rapid development of kisspeptin-based therapeutics, it is important to clarify kisspeptin's effects on behavioural, biochemical, and physiological measures of anxiety in humans.
Methods
Ninety-five eugonadal participants (n = 63 men, n = 32 women) completed a double-blind, randomised, placebo-controlled, crossover protocol (mean age ± SEM 30.9 ± 0.9yrs, BMI 24.0 ± 0.4 kg/m^2). Participants attended for a 75-minute intravenous kisspeptin-54 infusion (1nmol/kg/h) and again for a rate-matched placebo. Blood sampling (for reproductive hormones and cortisol) and heart rate measurements took place at 15-minute intervals throughout the infusions. Participants completed a state anxiety psychometric questionnaire ('STAI Y1-State') before and at the end of the infusions to assess for any dynamic effects of the infusions on anxiety.
Results
Intravenous kisspeptin robustly increased serum LH to similar levels previously described using this administration protocol, confirming that the dose was biologically active ($P < 0.001$). As expected, kisspeptin had no significant effects on downstream sex-steroid levels during the 75-minute study period, thereby excluding these as possible confounders. State anxiety was not significantly altered by kisspeptin (mean difference in 'STAI Y1-State' scores during the infusions: kisspeptin -0.4 ± 0.8, placebo 1.3 ± 0.8, P = 0.09). Moreover, kisspeptin had no significant effects on circulating cortisol (P = 0.73) and heart rate (P = 0.52) during the infusions.
Summary
This is the largest study demonstrating that administration of a biologically active dose of kisspeptin to humans does not affect behavioural, biochemical, and physiological measures of anxiety. Given that animal studies have yielded contradictory results, this provides key clinical data and reassurance that kisspeptin does not induce anxiety in humans and so supports the advancing development of kisspeptin-based therapeutics for reproductive and psychosexual disorders.

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OP1.3

Recovery of hypopituitarism in macroprolactinomas: a comparison of medical vs. surgical treatment. Results from a European multicenter retrospective study

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Context
Macroprolactinomas not only cause hypogonadism, but also other pituitary dysfunctions, like deficiency of adrenocorticotrophic hormone (ACTH) and thyroid-stimulating hormone (TSH). While dopamine agonist treatment shows varying recovery rates of these insufficiencies, surgical outcomes are less studied, and a direct comparison between treatments is lacking.
Objective
To evaluate recovery of pituitary dysfunction in medically vs surgically treated patients with macroprolactinoma.
Design
Retrospective multicenter study including 104 patients with macroprolactinoma (44 surgically vs 60 medically treated) with at least two hormonal deficiencies before treatment.
Results
Before surgery, all patients presented with hypogonadotropic hypogonadism, 25 (57%) with ACTH-deficiency, and with 32 (73%) TSH-deficiency. 10 months post-surgery, prolactin normalized in 25 (57%) patients, while 19(43%), 15 (60%) and 10(31%) recovered from hypogonadism, ACTH-deficiency, and TSH-deficiency, respectively. Before medical therapy, hypogonadism was observed in all patients, ACTH-deficiency in 31 (52%), and TSH-deficiency in 50 (83%). After 12 months under dopamine agonists, prolactin levels normalized in 36 (60%) patients, 25(42%) recovered from hypogonadism, 17 (55%) from ACTH-deficiency, and 14(28%) from TSH-deficiency. No significant difference in recovery rates between surgical and medical treatment for hypogonadism (OR 1.633, p=0.338), ACTH-deficiency (OR 0.462, p=0.319), or TSH-deficiency (OR 0.584, p=0.339) was observed. Initial tumor size was a significant negative predictor of recovery for all hormone deficiencies (always p<0.05), while prolactin normalization was a predictor of recovery of hypogonadism (p<0.001).

Conclusion
Both surgical and medical treatment allow for hormonal recovery in patients with macroprolactinoma, with no significant advantage for either approach. Initial tumor size and prolactin-normalization are predictors of recovery outcomes.

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OP1.4

Risk factors for disorders of sodium and water balance in the early post-operative period following pituitary surgery

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Background
Arginine vasopressin deficiency (AVP-D) and hyponatremia are recognised complications of pituitary surgery and if left untreated can both increase morbidity and mortality. This study therefore aimed to investigate risk factors for the development of AVP-D and hyponatremia in patients following pituitary surgery.
Methods
A single-centre retrospective study was conducted in patients who underwent pituitary surgery between January 2016 and March 2024. Patient demographics, tumour characteristics, pre-operative and peri-operative data were collected.
Results
264 surgery cases were analysed (132 females, 132 males). The cohort consisted of 106 functioning pituitary adenomas, 147 non-functioning pituitary adenomas, seven Rathke's cleft cysts and four craniopharyngiomas. 36 (14%) patients developed isolated AVP-D, of which three patients developed permanent AVP-D, and 26 (10%) patients developed isolated hyponatremia. Five (2%) patients developed a biphasic response (AVP-D followed by hyponatremia), and no patients developed a triphasic response (biphasic response followed by another phase of AVP-D). Craniopharyngiomas were the only subtype associated with an increased risk of developing AVP-D ($P = 0.03$). Multiple logistic regression analysis showed that the independent predictors of developing hyponatremia were: pre-operative use of diuretics (OR = 5.23; 95% CI = 1.37-18.67; $P = 0.01$), lower pre-operative serum sodium (OR = 0.83; 95% CI = 0.71-0.96; $P = 0.01$) and gross total resection (OR = 2.96; 95% CI = 1.23-7.52; $P = 0.02$). The only independent predictor identified for AVP-D was cerebrospinal fluid (CSF) leak (OR = 2.56; 95% CI = 1.13-5.70; $P = 0.02$).
Conclusion
Since lower pre-operative serum sodium levels were identified as a risk factor for developing post-operative hyponatremia, individuals with pre-operative serum sodium values in the lower half of the reference range should be particularly closely monitored. Withholding diuretics peri-operatively may reduce the risk of hyponatraemia and further research is warranted to determine the optimal duration to hold diuretics peri-operatively and whether this may have any negative consequences. The association between CSF leak and AVP-D likely reflects the resection of a larger and more invasive tumour.

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Metabolism, Obesity and Diabetes

OP2.1

The impact of GLP-1 receptor agonist-induced weight loss on 22 cancers in the next ten years using a markov state-transition model

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Background
Obesity is a major risk factor for many cancers. Glucagon-like peptide-1 (GLP-1) receptor agonists are highly effective and in-demand agents for weight loss. There is a lack of published modelling studies describing the broader implications of GLP-1 agonist-induced weight loss on cancer incidence.
Methods
A Markov cohort state-transition model was devised to evaluate the impact of GLP-1 receptor agonist (GLP-1RA) -induced weight loss on future cancer incidence. Contemporary data on weight distribution, cancer incidence, and body mass index (BMI)-associated cancer risk were integrated into the model. As an exercise to demonstrate the impact of extensive GLP-1RA uptake in the adult population on future cancer cases, a closed cohort with no mortality was modelled over 10 years. Two scenarios were assessed, GLP-1RAs were made available to all people with obesity (BMI > 30) or only those with severe obesity (BMI > 35).
Findings
When simulating individuals with obesity (BMI > 30) or severe obesity (BMI > 35) moving into lower BMI categories from GLP-1RA use, reductions in overall cancer cases were seen. This effect was greatest for uterine, kidney, liver and colon cancer, changing the landscape of new cancer cases over the next decade.
Interpretation
Targeted weight control measures using GLP-1RA could reduce new cancer cases. Based on our models, the potential risk of thyroid cancer is balanced by a reduction in new cases of other cancer types. Although the model has limitations and should not be viewed as a forecast, this study highlights that implementing effective weight loss programmes could enhance the health of the population over the next decade through a reduction in cancer cases.

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OP2.2

GLP-1R in β-cells mediates the effects of ingested protein and alanine on glucose tolerance

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High-protein diets (HPDs) improve glucose tolerance. One possible mechanism is through the stimulation of the gut hormone glucagon-like peptide-1 (GLP-1) secretion from enteroendocrine L-cells in the gut in response to the amino acid products of protein digestion. The secreted GLP-1 can then act on the GLP-1 receptor (GLP-1R) on the pancreatic β-cell to increase insulin release and improve glucose tolerance. The Pdx1CreERT/GLP-1R fl/fl mouse line, characterised by knockout of GLP-1R in duodenal homeobox 1 (Pdx1)-expressing pancreatic β-cells after tamoxifen induction, was created by crossing over the tamoxifen-inducible Pdx1-Cre/Esr1 mice (Jax 024968) with GLP-1R fl/fl mice (kindly provided by Professor Randy Seeley, University of Michigan). The impact of amino acids on intraperitoneal glucose tolerance and insulin secretion was assessed in mice both before and after GLP-1R knockout from the β-cell. Additionally, ileal mouse organoids were utilised to examine how alanine influences GLP-1 secretion and the involvement of SLC38A2 in this process. We investigated the role of GLP-1 in mediating the effects of ingested protein and of alanine, an amino acid produced by protein digestion thought to play a key role in metabolism. Whey-induced improvements in glucose tolerance and insulin secretion were attenuated in mice with GLP-1R knocked out in β-cells compared to mice with intact GLP-1R. Similarly, the effects of alanine on glucose tolerance and insulin secretion were also blunted in mice with GLP-1R knocked out in β-cells. These results suggest that GLP-1 signalling in the pancreatic β-cell is at least partially responsible for mediating the beneficial effects of whey and alanine on glucose tolerance via an insulin-dependent pathway. Exploiting this system may facilitate dietary approaches to the prevention and treatment of type 2 diabetes.

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OP2.3

Which fuel for the fire? clock protein REV-ERBα regulates energy substrate utilisation in mice

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Nuclear receptor REV-ERBα (NR1D1) is a core component of the molecular circadian clock, a transcription-translation feedback loop which oscillates over

24 hours. REV-ERBα is a constitutive repressor, and we have previously shown that it has extensive, genome-wide binding activity in mouse liver. This repressive function is greatest during the day (inactive period), and is diminished at night. Mice with global deletion of the *Rev-erbα* gene have a markedly abnormal metabolic phenotype, including heightened adiposity and disordered eating behaviour, and it has been challenging to elucidate the function of REV-ERBα in this model. We have employed a mouse model of inducible, hepatocyte-targeted Rev-erbα deletion, to investigate the role REV-ERBα plays in regulating liver metabolism. We find that the day-night rhythm in respiratory exchange ratio (RER) is altered with liver *Rev-erbα* deletion, implying an alteration in the day-night rhythm of lipid and carbohydrate utilisation, at a whole animal level. We find that liver REV-ERBα is required to maintain circulating glucose levels during a daytime fast, but not at night. Integration of transcriptome and cistrome datasets suggests that enzymes important for modulating glycogen synthesis and breakdown (*Ppp1r3b, Ppp1r3c*) are targets of REV-ERBα repression, as is a regulator of pyruvate dehydrogenase activity (Pdk4), which determines whether products of glycolysis or beta-oxidation enter the tricarboxylic acid (TCA) cycle. Taking our findings together, we propose that REV-ERBα exerts rhythmic regulation over critical enzymes involved in energy substrate utilisation. In this manner, REV-ERBα contributes to circadian control of the use of carbohydrate or lipid as fuel, thus playing a key role in the maintenance of energy homeostasis over the day-night cycle.

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OP2.4

Regulation of metabolic homeostasis via pancreas-projecting enteric neuronal signaling

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Enteric neurons located in the myenteric plexus of the proximal duodenum have been found to relay neural signals directly to the pancreas, yet their role in regulating pancreatic hormones release and maintaining metabolic homeostasis remains unclear. The gastrointestinal tract detects nutrients, initiating signaling pathways that regulate metabolic hemostasis. Our findings observed that the consumption of high-dose whey protein and extra virgin olive oil reduced blood glucose levels and improved glucose tolerance. To clarify the contribution of enteric-pancreatic neuronal communication to these effects, we performed a surgical procedure that severed the neuronal connections between the proximal duodenum and pancreas, effectively disrupting the enteric neurons that project to the pancreas. This separation diminished the beneficial effects of olive oil on glucose tolerance, suggesting a role for enteropancreatic neurons in nutrient-triggered metabolic regulation. Interestingly, the effects of high-dose whey protein on glucose tolerance remained unaffected by this intervention, suggesting alternative signalling pathways mediate this effect. To further explore the pancreas-projecting enteric neurons, we isolated and co-cultured longitudinal muscle myenteric plexus (LMMP) neurons and pancreatic islets, providing a novel approach to study the effects of specific hormones and nutrients on enteropancreatic neurons and their resulting effects on pancreatic hormone secretion. Immunocytochemistry confirmed the expression of secretin receptors on LMMP neurons. Administration of secretin resulted in a significantly greater insulin release when pancreatic islets were cultured with neurons than when they were cultured alone, suggesting a possible role for enteropancreatic neurons in mediating the effects of secretin on insulin release. This research provides insight into the complex interactions between the enteric nervous system and pancreatic hormone secretion. It highlights the significant influence of enteric neural pathways on the regulation of metabolic responses to nutrient intake and suggests future directions for exploring their therapeutic potential for metabolic disorders.

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Adrenal and Cardiovascular

OP3.1

Waking salivary cortisone vs the short synacthen test in screening for adrenocortical insufficiency: results of a service evaluation: evaluation of the relation of waking salivary cortisone to a 30/60minute SST

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Introduction
Saliva cortisol/cortisone measurements can be applied in every day clinical practice (minimal chance of cross reaction with prescribed glucocorticoids) and are an alternative to the Short Synacthen test (SST) (92,000 done each year in England) to evaluate adrenocortical function.
Methods
A service evaluation of waking salivary cortisone vs serum cortisol in 30/60minute SST was undertaken. We retrospectively studied patients who attended the investigation unit at a tertiary centre. They provided a waking saliva sample for measurement of salivary cortisone, by tandem mass spectrometry. Waking salivary cortisone level (pass >17nmol/l;borderline 7-17nmol/l; fail<7nmol/l) was compared with 30minute+60minute serum cortisol post 250micrograms SST (pass defined as 30 or 60 minute cortisol 450nmol/l or more).
Results

Number of Tests	Salivary Cortisone Pass	Salivary Cortisone Borderline	Salivary Cortisone Fail
SST Pass	18	4	2
SST Fail	0	2	2

Results for 24 individuals (21% men: mean age 43 years); 79%women: mean age 45.3 years) were analysed. The reason for the test was as follows: weaning off glucocorticoids-14, low serum cortisol-10, fatigue-2, hypopituitarism-2. For the SST 86% of individuals were a pass and 14% did not reach threshold (ie a 'fail'). Everyone deemed a pass on salivary cortisone also passed the SST. Of the 14% that failed SST, none were a pass on the salivary cortisone. Of those that were borderline/fail on salivary cortisone, 60% were a pass on SST. Positive predictive value for salivary cortisone=100%, sensitivity=75% and specificity=100%. Negative predictive value=40%.
Conclusion
Waking salivary cortisone did not falsely categorise anyone as having normal adrenocortical function. Of those that passed the SST 75% also passed on the basis of salivary cortisone. Waking salivary cortisone could therefore be used as an alternative 1st line screening test (cost £16) which does not require venepuncture or attendance at hospital vs SST (cost £300+).

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OP3.2

Simulation via instant messaging - bedside application (SIMBA) event co-designed by experts and patients enhanced clinicians' confidence in managing adrenal conditions

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Background
Simulation via Instant Messaging - Bedside Application (SIMBA) is a virtual simulation-based medical training model that improves clinicians' confidence. Simulation-based learning (SBL) fosters interactive learning, bridging theoretical and practical clinical skills, while patient and public involvement (PPI) enriches healthcare professionals' understanding of patient needs. Despite SBL and PPI's recognised benefits in improving patient-centred care, PPI remains inconsistently integrated into medical education. This study evaluates the effects of combining PPI with SBL on healthcare providers' confidence and clinical performance in managing adrenal disorders.
Methods
A hybrid two-day SIMBA event in Birmingham, UK, utilised nine case-based adrenal disorder scenarios designed with PPI input. Patients contributed their insights through workshops, providing feedback on the case scenarios to align them with real patient experiences. Participants' confidence was measured with pre- and post-SIMBA surveys, and performance was assessed using the Global Rating Scale (GRS). Statistical analysis was conducted using Stata software.

Results
Among 64 participants, confidence in managing adrenal disorders significantly improved post-simulation ($P < 0.00001$), with 92% favouring SBL over traditional learning methods. PPI integration allowed healthcare providers to adopt a more patient-centered approach, positively impacting patient feedback. Participants noted increased awareness of rare diagnoses and a commitment to evidence-based medicine, further improving patient care. Qualitative feedback highlighted the model's accessibility and value, though participants suggested logistical improvements.
Conclusion
Integrating PPI in SBL for our SIMBA session enhanced healthcare providers' confidence and patient-centered clinical practices. The SIMBA model's accessible and effective format has potential for broader applications across medical disciplines. Future studies should assess long-term clinical impact and include objective measures of practice changes, particularly in diverse and resource-limited settings.

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OP3.3

Enhancing adrenal vein sampling: the role of plasma metanephrines in diagnosing primary aldosteronism

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Introduction
Adrenal vein sampling (AVS) is the gold standard for diagnosing primary aldosteronism (PA) subtypes, but cortisol's long half-life and potential co-secretion complicate its use. Plasma metanephrines (MN), with a shorter half-life and a higher adrenal vein (AV) to peripheral vein (PV) gradient, may provide a more reliable alternative.
Method
We retrospectively analysed 131 AVS procedures (January 2018-May 2023) in patients with confirmed PA. Receiver operating characteristic (ROC) curve analyses were used to assess the utility of plasma MN using established aldosterone-to-cortisol (AC) ratios as reference criteria. Cannulation success was defined by an AV/PV cortisol ratio >2, while unilateral disease was indicated by an AV/AV AC ratio >2 with contralateral suppression <0.5 of the PV.
Results
ROC analysis revealed an optimal MN selectivity index (SI) of >3, achieving 99% sensitivity, 100% specificity, and an area under the curve (AUC) of 1.0. Successful cannulation was confirmed in 126 patients using both MN and cortisol SIs. To establish a MN lateralisation index (LI), we excluded 9 patients who did not have contralateral suppression. ROC analysis of the remaining 117 identified an optimal AM LI cut-off of >4, yielding 93% sensitivity, 95% specificity, and an AUC of 0.95, indicating unilateral disease in those confirmed by AC criteria (AC LI >2, AC CSI <0.5). Concordant results were observed in 94% of cases. Among 14 patients with cortisol co-secretion, 5 had discordant AVS results, including 1 additional patient with a post-dexamethasone cortisol level of 36 nmol/l. Four of these five patients underwent adrenalectomy, confirming adenomas, while one opted for medical therapy. All surgically treated patients achieved complete remission.
Conclusion
While not the first study to describe this approach, our findings support that incorporating aldosterone/metanephrines improves diagnostic accuracy in primary aldosteronism with cortisol co-secretion, enhancing clinical decision-making and potentially improving patients' outcomes.

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OP3.4

Pregnancy outcomes in women with primary adrenal insufficiency: data from a multicentre cohort study

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Objective
To determine characteristics and outcomes of pregnancy in women with Primary Adrenal Insufficiency (PAI)
Design
Retrospective multicentre cohort study
Setting
23 maternity units; UK and Ireland
Sample
79 women with Primary Adrenal insufficiency (PAI) with 101 pregnancies
Main outcome measures
Adrenal crisis, pregnancy outcome
Results
Date were obtained on 101 pregnancies in 79 women with PAI. Most (51, 64.1%) had autoimmune disease, eight (10.3%) had prior adrenal infarction/surgery/haemorrhage, two had (2.6%) congenital adrenal hyperplasia and 18 were (21.3%) unclassified. 19 (24%) experienced adrenal crisis during pregnancy (18.8% of pregnancies). One woman died postpartum. Although all had recorded endocrinology input during pregnancy, steroid alert cards were documented to be carried in 40 (39.6%) pregnancies and only 9/19 (47.4%) of those with an adrenal crisis in pregnancy. Compared with pre-pregnancy dose, only 41% of women received increased hydrocortisone dose in pregnancy. Caesarean section rate was higher than UK average 62/97 (63.9%). Preterm birth rate was 21.2% (21/99) and 12.8% (12/94) of neonates had birthweight $< 10^{th}$centile.
Conclusion
Whilst the obstetric outcome of pregnancy with PAI is generally favourable, there are high rates of caesarean birth and prematurity. However, a high number of women experienced adrenal crisis yet the minority carried steroid alert cards. Recommendations regarding third trimester increases in hydrocortisone should be reviewed and potentially strengthened, in light of further evidence. All pregnant women with adrenal insufficiency should carry an NHS steroid warning card; this should be reinforced both by endocrine and obstetric teams because of the increased risk of life-threatening adrenal crisis.

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Thyroid and Reproduction

OP4.1

Use of 5α-reductase inhibitors and risk of major adverse cardiovascular diseases in people with benign prostatic hyperplasia and type 2 diabetes: a cohort study of two uk databases

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Introduction
5α-Reductase inhibitors are used in the long-term treatment of benign prostatic hyperplasia (BPH) to reduce androgen-dependent prostate growth. Their use has been associated with increased risk for type 2 diabetes mellitus. This study aimed to assess the cardiometabolic effects of 5α-reductase inhibitors in comparison with tamsulosin in patients with coexisting BPH and type 2 diabetes.
Methods
This study included all patients with BPH and type 2 diabetes receiving ≥ 2 prescriptions of 5α-reductase inhibitors or tamsulosin (control) in Scottish Diabetes Research Network National Diabetes Dataset (SDRN-NDS) and IQVIA Medical Research Data (IMRD-UK) between 2006-2021. Cardiometabolic outcomes included composite major adverse cardiovascular events (MACE), defined as myocardial infarction (MI), stroke, and cardiovascular death in SDRN-NDS, and MI and stroke in IMRD-UK; peripheral vascular diseases, diabetic retinopathy, nephropathy, neuropathy, and receipt of insulin-based medications. Hazard ratios (HR) were computed using the Cox proportional-hazard model after propensity score matching conditioned on baseline covariates.
Results
A total of 14,687 patients were included in SDRN-NDS and 17,289 in IMRD-UK with median follow-up durations of 3.8 years (IQR: 1.7-6.8) and 4.8 years (2.0-8.3), respectively. In SDRN-NDS, the HR of MACE in patients receiving 5α-reductase inhibitors relative to tamsulosin was 1.15 (95% CI 1.03-1.30), primarily driven by MI (1.20, 1.03-1.40). This was replicated in IMRD-UK, where the HR was 1.26 (1.07-1.47) for MACE and 1.33 (1.10-1.60) for MI. A moderate increase in risk compared to tamsulosin was found for peripheral vascular diseases (HR 1.20, 1.00-1.43). We did not observe any increased risk in stroke, other microvascular endpoints, or faster progression to insulin.

Conclusions
Among patients with co-existing BPH and type 2 diabetes, the risk of MACE is increased in users of 5α-reductase inhibitors, primarily driven by increased risk of MI. This suggests the need for careful monitoring of macrovascular outcomes when prescribing 5α-reductase inhibitors in this population.

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OP4.2

Differential response of gonadotropin-releasing hormone (GNRH1 and GNRH2) expressing cells to estrogen feedback

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Gonadotropin-releasing hormone (GNRH) represents the primary hypothalamic component of the reproductive neuroendocrine axis. It plays a key role in stimulating the pulsatile release of luteinizing hormone (LH) as well as the preovulatory LH surge. However, it remains enigmatic how hypothalamic GNRH neurons are capable of differentially responding to ovarian estrogen feedback (i.e., in a negative manner during the early follicular phase of the menstrual cycle but in a positive manner at the time of the mid-cycle LH surge). In the present study we show: (**1**) that female rhesus macaques, like women, express not one but two different molecular forms of GNRH (i.e., GNRH1 and GNRH2), (**2**) that *GNRH1* and *GNRH2* mRNAs are expressed by two completely distinct neuronal populations in the hypothalamus, and (**3**) that *GNRH2* mRNA is also expressed within the anterior pituitary gland itself. Moreover, we show that estrogen differentially affects GNRH1 and GNRH2 peptide concentrations in the pituitary gland, causing a significant increase in GNRH2 but not in GNRH1. Taken together, these findings suggest that different aspects of reproductive function in humans and nonhuman primates are likely to be controlled by two separate populations of GNRH producing cells, with GNRH1 peptide being responsible for maintaining tonic pulsatile LH release and GNRH2 peptide playing a primary role in triggering the estrogen-induced preovulatory LH surge. Consequently, it may be possible to block ovulation by selectively targeting GNRH2 expressing cells pharmacologically without negatively impacting the rest of the neuroendocrine reproductive axis, thus opening a novel approach to contraception. The findings may also shed new light on possible causes of idiopathic infertility and help with the development of effective therapies.

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OP4.3

A content analysis of the reliability and quality of information provided on social media for hypothyroidism

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Background
The increasing popularity of social media has made it a significant resource for sharing health-related information, including insights on medical conditions such as Hashimoto's thyroiditis and hypothyroidism. This study aims to assess the quality and reliability of these videos.
Methods
The social media platforms TikTok, Instagram (reels), and YouTube were explored using the search terms 'Hypothyroidism,' 'Hashimoto's,' and 'TPO antibody.' The top 50 videos for each search term (450 total) were screened between 30th September 2024 and 28th October 2024. Relevant videos were assessed for reliability and quality using the modified DISCERN score and Global Quality Score (GQS) by two doctors whose scores were averaged. Additional data, such as video length, upload date, and user engagement via likes, comments and shares, was also collected.
Results
A total of 379 videos were included in this study. The average number of likes, views, shares and comments for all the videos were 95231.76, 339253.73, 2792.57 and 490.22 respectively. The median for the modified-DISCERN scores and GQS was 1.7 (1.4-2.3) and 2 (1.5-2.5) respectively. 90.2% (342) of the videos had a score of less than 3 on the modified DISCERN while 75.7% of scores were less than 3 on the GQS.

	Median Modified-Discern (IQR)	Median GQS (IQR)
Reels	1.5 (1.2-1.8)	2 (1.5-2)
TikTok	1.5 (1.2-1.8)	2 (1.5-2)
Youtube	2.5 (2-3.1)	3 (2-4)
	Median Modified-Discern (IQR)	**Median GQS (IQR)**
Hypothyroidism	1.5 (1.2-2.3)	2 (1.5-3)
Hashimotos	1.6 (1.4-2.3)	2 (1.5-2.5)
Anti-TPO antibody	1.9 (1.6-2.3)	2 (2-2.5)

Conclusion
In conclusion, the modified-DISCERN and GQS scores were poor through the different social media sites. Thus, individuals should be cautious whilst attaining medical information about hypothyroidism and hashimotos from these sites. Health care professionals need to engage more with social media and promote evidence-based information to the public.

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OP4.4

Factors at first presentation and outcome in patients with graves' disease (GD) – a retrospective database analysis

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Objectives
To identify clinical features, biochemical thyroid function and thyrotrophin receptor antibody (TRAb) concentrations at first presentation of Graves' disease (GD), and their relationship to outcome (relapse, REl; remission, REM) after stopping anti-thyroid drug (ATD) treatment.
Methods
A retrospective analysis of the Thyroid Clinic electronic database was carried out, of all subjects at first presentation of GD between 2006-2012. TRAb concentrations, clinical and biochemical parameters were compared between the REL and REM groups after stopping ATD therapy. The follow up period was 11-17 years.
Results
Data from 399 subjects (322 women and 77 men) were available for analysis. During the follow up period, 205 (51%) had a relapse (77.5% females) and 194 (49%) remained in remission (84% females). In the REL group, TRAb concentrations (7.9 vs. 5.85 IU/l, $P = 0.03$) and goitre prevalence (58.4 vs. 46.4%, $P = 0.02$) were significantly higher compared to the REM group. Demographic and biochemical features were not significantly different between the groups.
Furthermore, in the REL group –
(i) 70% of subjects relapsed within one year of stopping ATD
(ii) median TRAb concentrations were significantly higher in those who relapsed within one year compared to those who relapsed later (10 vs. 6.25 IU/l, $P = 0.005$)
(iii) time to normalization was 11 vs. 8 weeks ($P < 0.001$) compared to REM group
(iii) however, sex, the presence of a family history, age, smoking and orbitopathy were not significantly different ($P = 0.1$-0.54)
Conclusion
We conclude that GD subjects who relapsed–
1. Had significantly higher TRAb concentrations and goitre prevalence at presentation ($P < 0.03$)
2. 70% of them did so in the first year after stopping ATD (TRAb concentration significantly higher compared to those who relapsed later, $P < 0.005$)
3. Took a significantly longer time to normalization of thyroid function ($P < 0.001$)
4. Did not show any significant association with other demographic, biochemical or clinical features

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Endocrine Cancer and Late Effects

OP5.1

PBF-mediated focal adhesion dynamics: a key driver of thyroid cancer cell motility

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Thyroid cancer progression is intricately linked to cell motility, a complex process that relies on the coordination of multiple signalling pathways, cell adhesion mechanisms, and actin dynamics. The proto-oncogene pituitary tumor-transforming gene (PTTG)-binding factor (PBF/PTTG1IP) significantly enhances thyroid cancer cell migration and invasion through Y174 phosphorylation by Src kinase. Phosphoproteomic and RNA-Seq analyses showed that PBF upregulation in Nthy-ori 3-1 thyroid cells altered expression and phosphorylation of adhesion and cytoskeletal proteins. We hypothesised that PBF is a physiological regulator of cell adhesion, and oncogenic expression promotes motility by altering adhesion dynamics. CRISPR/Cas9-mediated PBF-knockout (KO) TPC-1 papillary thyroid carcinoma cells exhibited significantly decreased adhesion on fibronectin compared with control TPC-1 cells. Immunofluorescence staining revealed altered structure and distribution of focal adhesions (FAs), which connect the cytoskeleton and extracellular matrix. PBF-depleted TPC-1 cells had markedly reduced focal adhesion kinase (FAK), vinculin and paxillin staining with fewer, shorter FAs predominantly around the cell periphery, whereas control cells displayed numerous, elongated FAs along actin fibers. Pbf-KO mouse embryonic fibroblasts (MEFs) also demonstrated decreased cell-substrate adhesion and altered FAs. Early adhesion assays (15-30 min) demonstrated reduced phosphorylated FAK-Y397 and fewer FAK-associated early FA structures at the Pbf-KO MEF peripheral membrane, while wild-type MEFs formed early FAK/paxillin adhesions that gradually matured over time. Live-cell LifeAct-GFP imaging indicated impaired spreading, lamellipodia formation and lack of directionality in PBF-KO TPC-1 and MEF cells. During migration, Pbf-KO MEF cells displayed disorganised Golgi lacking orientation towards the leading edge, suggesting impaired polarity. These findings provide important insights into FA dynamics in PBF-induced thyroid cancer cell motility, revealing a critical role for PBF in regulating early adhesion assembly. Further investigations are required to elucidate the precise interactions of PBF with cell adhesion protein complexes, which may ultimately reveal new therapeutic targets in thyroid cancer progression.

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OP5.2

Integrated, multi-omics liquid biopsy approach for disease monitoring in adrenocortical carcinoma: a preliminary study

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Background
Adrenocortical carcinoma (ACC) is a rare cancer with heterogeneous clinical outcome (5-year survival 10% to 60%). Close disease monitoring is essential but relies on radiological imaging that is challenging and associated with significant radiation exposure. Circulating cell-free DNA (ccfDNA) isolated from plasma can contain tumour-derived somatic variants, which potentially serves as a non-invasive tool for monitoring cancer patients. Similarly, tumour-derived steroid hormone precursors can be detected in urine from ACC patients.
Aim
Evaluate the role of combined ccfDNA sequencing and urine steroid metabolomics (USM) to monitor disease recurrence in ACC patients.
Methods
We investigated 7 patients with histologically confirmed ACC. Plasma and 24h urine samples were collected before primary tumour resection (baseline), early post-operation (28-42 days) and follow-ups at 3, 9 and 12 months. ccfDNA and germline DNA (gDNA) were isolated with commercially available kits. Tumour DNA (tDNA) was isolated from paraffin-embedded tissue. ccfDNA/gDNA/tDNA were sequenced using a customized ACC- specific panel and by shallow (0.1x) whole genome sequencing (sWGS). Somatic variants were called following standard bioinformatic protocols. 34 distinct adrenocortical steroid metabolites were quantified using gas chromatography/mass spectrometry.
Results
tDNA-derived somatic variants were detected in ccfDNA at baseline from 5/7 (71%) patients. Baseline steroid profiles were consistent with ACC diagnosis in 6/7 (86%) patients. No somatic variants or ACC-relevant steroids could be identified early post-operation. 4/7 patients developed radiological recurrence at 3 months, coinciding with detection of somatic variants and steroids in follow-up ccfDNA and USM samples in 3/4 (75%) and 4/4 (100%) cases, respectively. In two cases, sWGS gave a clear signal for recurrence that would otherwise be missed by targeted sequencing alone. 3/7 patients remain tumour free to date without somatic variants or steroids being detected in follow-ups.
Conclusion
Integrating molecular signatures from ccfDNA and USM can be used for monitoring ACC patients.

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OP5.3

Development of a sensitive gas chromatography mass spectrometry method for quantifying low concentrations of oestrogens in urine

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Oestrogen analysis presents a significant challenge due to the low concentrations of these hormones, especially in the case of oestradiol, the most potent oestrogen which plays a crucial role in fertility, bone health, and various endocrine disorders. Traditional methods of measuring oestrogens, immunoassays, are unreliable at low concentrations, and have high cross-reactivity, leading to inaccurate results and potential misdiagnosis. Mass spectrometry offers a more selective and sensitive alternative, with less cross-reactivity. However, even with MS, the quantification of oestradiol remains difficult due to its poor ionisation efficiency, necessitating the use of highly sensitive liquid chromatography tandem-mass spectrometers (LC-MS/MS) and large sample volumes, particularly when measuring in post-menopausal women, men, and children. In this study, we aimed to develop a method capable of quantifying very low concentrations of oestrogens. We collected 24-hour urine from 51 healthy females aged 22-73 years. To increase sensitivity beyond that typically achieved with LC-MS/MS, we optimised a gas chromatography-mass spectrometry (GC-MS) method for detection of 11 oestrogens, including oestradiol, oestrone, and their hydroxy and methoxy derivatives. Steroids were extracted from 2mL of 24hr-urine, deconjugated, and derivatised into methyloxime-trimethylsilyl ethers. The oestrogens were quantified relative to an internal standard and calibration series. Our method successfully quantified low concentrations of oestrogens in both pre- and postmenopausal women. The most predominant forms of oestrogens found in the urine were oestradiol 41.6μg/24hr (10.4-53.1) and 2-methoxy-oestrone 26.8μg/24hr (16.0-46.4), less predominant were oestrone 2.2μg/24hr (1.3-5.0) and oestriol 2.2μg/24hr (0.8-6.2), all others oestrogen concentrations ranged 0.1-17.7μg/24hr. This approach demonstrated the sensitivity required for clinical applications where measuring low oestrogen levels is essential, such as in studies evaluating the efficacy of treatments like tamoxifen that aim to reduce total oestrogen load.

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OP5.4

Phenome-centered multiomics in ovarian cancer for 3P medical approach

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Ovarian cancer (OC) seriously impacts on female health with high incidence and mortality, which is involved in a series of changes at the levels of genome, transcriptome, proteome, metabolome, and interactome. Among those

multiomics, proteome and metabolome are the important elements of phenome. We carried out the phenome-centered multiomics in OCs for 3P medical approach, including quantitative proteomics (205 differentially expressed proteins, DEPs) between OC tissues and control ovaries, quantitative proteomics (1198 mtDEPs) and phosphoproteomics (58 phosphoproteins) of mitochondria isolated from OC and control ovarian tissues, quantitative proteomics (390 DEPs) in OC cell or animal model treated with and without ivermectin, and transcriptomics data (20115 genes) from 419 OC samples. Comprehensive analysis of these omics data found energy metabolism pathway was significantly changed: (i) the upregulations of rate-limiting enzymes PKM2 in glycolysis, IDH2 in Kreb's cycle, and UQCRH in oxidative phosphorylation (OXPHOS) pathways, (ii) the upregulation of PDHB that converts pyruvate from glycolysis into acetyl-CoA in Kreb's cycle, and (iii) the binding sites between miRNA (hsa-miR-186-5p) and RNA-binding protein (EIF4AIII) in those key proteins in energy metabolism pathways. Furthermore, lncRNA SNHG3 interacted with hsa-miR-186-5p and EIF4AIII. Ivermectin regulated the rate-limiting enzymes and other proteins in glycolysis, Kreb's cycle, and OXPHOS pathways, and inhibited cell proliferation and promoted apoptosis of OC. Those results were further confirmed in the OC cell models, animal models, and clinical tissue samples, with energy metabolism and enzyme activity experiments. It clearly concluded that SNHG3 regulated energy metabolism through hsa-miR-186-5p and EIF4AIII to regulate the key proteins in the energy metabolism pathways; SNHG3 inhibitor can interfere with the energy metabolism to treat OCs; and ivermectin has new potential for OC treatment through regulating energy metabolism pathways. These findings provide more accurate understanding of molecular mechanisms of OCs and discovery of effective energy-metabolism-heterogeneity-based therapeutic drugs for OCs.

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Innovation in Teaching and Assessment

OP6.1

The hyponatraemia escape room: innovative endocrinology teaching to foundation doctors

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Background
Electrolyte disturbances are common in the hospital setting, often identified and managed initially by Foundation Doctors. Whilst some electrolyte disturbances are relatively straightforward to treat, Foundation Doctors can find the hyponatraemia more challenging. To address this, our trust's medical education department developed an interactive teaching session focussing on hyponatraemia, utilising gamification methods to maximise impact on clinical reasoning and decision-making skills.
Methods
A forty-five minute near-peer session was delivered by Clinical Teaching Fellows to 47 Foundation Year 2 Doctors (group size 8-12). It comprised of an introductory presentation on electrolyte disturbance, a 'Hyponatraemia Escape Room' where attendees completed a series of tasks to recognise and manage a patient in Addisonian crisis, concluded by facilitated group discussion. The escape room challenged the participants' knowledge of identifying true hyponatraemia, assessing the severity of hyponatraemia, assessing a hyponatraemic patients fluid status and correlating it to differential diagnoses, interpreting serum and urine osmolality and sodium levels, and treating an underlying cause. Participants completed anonymised pre- and post-session questionnaires, collecting mixed-methods data.
Outcome
Attendee-assessed confidence in diagnosis of hyponatraemia increased from a pre-session rating of 2.74/5 to 4.09/5 post-session. Confidence in management increased from 4.09/5 to 4.13/5. Following the session, 96% of attendees felt they knew how to differentiate severity of hyponatraemia, 98% knew how to investigate hyponatraemia, and 91% knew how to manage different types of hyponatraemia. All the participants found the session helped to develop teamworking skills. Feedback demonstrated the novel format provided an opportunity to consolidate and apply knowledge of a challenging topic in a fun, interactive way.
Take Home Messages
Gamifying hyponatraemia teaching using an escape room improved doctors' confidence in its diagnosis and management. The escape room format encouraged teamworking, peer-learning and communication skills, through an innovative teaching session.

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OP6.2

Endocrine emergencies course: use of simulation in novel specialty-based teaching programme for doctors in training in a district general hospital

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One of the key skills doctors in training need to develop is the ability to recognise and manage the acutely deteriorating patient and this is incorporated into the curriculum of *Foundation* and *Internal Medicine Training* Programmes. Simulation is an effective methodology to achieve this aim, with trainees encouraged to attend programmes such as *Advanced Life Support*. Opportunities for specialty-specific emergencies teaching is limited, which can lead to reduced confidence in managing endocrine and diabetic emergencies which may be less frequently encountered in clinical practice in a district general hospital setting. The *Endocrine Emergencies* course was therefore created to meet this demand, with use of endocrinology-specific simulation not previously encountered by any of the resident doctors who participated. The programme was delivered over 6 sessions and covered 12 emergencies including: diabetic ketoacidosis, hypoglycaemia, hyponatraemia, hyperglycaemic hyperosmolar state, adrenal crisis, thyroid storm, hypercalcaemia, myxedema coma, diabetic foot attack, euglycaemic ketoacidosis, pituitary apoplexy and phaeochromocytoma crisis. Pre- and post-course data enhanced teaching methods including a combination of case-based discussions of real clinical encounters and emergencies in the simulation suite. A total of 106 learners attended 2 cycles of the programme (13 sessions) ranging from healthcare students, clinical fellows, foundation and internal medicine trainees working in medical and non-medical specialties. Recommendation of 4.96 [out of possible 5] was given as an average score by resident doctors of various grades who attended the course. Rise of 1.58 in confidence rating in managing diabetic emergencies was seen [3.3 out of 5 pre-course, 4.88 out of 5 post-course] and 2.18 increased confidence rating in managing endocrine emergencies [2.7 out of 5 pre-course, 4.88 out of 5 post-course]. Further cycles are planned locally with endocrinology-specific simulation demonstrated as an effective and easily replicable method of postgraduate training in endocrinology and diabetes in other settings.

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OP6.3

Neurophobia vs neuroendocrinophobia - the dictionary ain't big enough for the both of us! using near-peer teaching to deliver neuroendocrine teaching to year 4 medical students in a world of established neurophobia

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Background
The term '*neurophobia*' reflects the difficulties and anxieties medical students experience when learning neurology. Neuroendocrinology, a complex component of the neurosurgical workload, may induce similar fears. Near Peer Teaching (NPT) – a pedagogical approach where students teach their juniors – has been shown to be as effective as faculty-led instruction and improves understanding of complex concepts. In the hope of preventing it from joining neurology in the medical student's list of phobias, this study explores whether NPT is effective for teaching neuroendocrinology.
Method
A Year 5 medical student, under Clinical Teaching Fellow supervision, designed and delivered a tutorial focused on diabetes insipidus (DI) and syndrome of inappropriate antidiuretic hormone (SIADH). Pre- and post-session feedback was collected via Microsoft Forms, using a 5-point Likert scale to evaluate students' self-rated knowledge and confidence regarding DI and SIADH. SPSS was used for statistical analysis; thematic analysis assessed qualitative feedback.
Results
85 Year 4 medical students participated, with 81 completing the survey. Pre-session, the median self-rated knowledge score for both DI and SIADH was 3.0 (neutral) (IQR 2.0-3.0), significantly increasing to 4.0 (good) (DI IQR 4.0-5.0; SIADH IQR 4.0-4.0) post-session (DI: U-statistic = 498.0, $p < 0.001$; SIADH: U-statistic = 616.5, $p < 0.001$). Confidence in answering general neuroendocrine SBAs improved significantly (U-statistic = 813.5, $p < 0.001$), as it did for DI (U-statistic = 700.0, $p < 0.001$) and SIADH (U-statistic = 795.0, $p < 0.001$). Thematic

analysis indicated that students found NPT helpful but desired greater variety and interaction.
Conclusion
NPT statistically significantly improves medical students' self-rated knowledge of general neuroendocrinology, specifically DI and SIADH. Importantly, it also statistically significantly improves student confidence in answering SBAs on these topics. Supported by the positive qualitative feedback, along with clear suggestions for development, the results of this study highlight the current and potential value of NPT in addressing the challenges of teaching neuroendocrinology and avoiding the coining of a new term: '*neuroendocrinophobia'*.

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OP6.4

Understanding the biochemistry of hormones, by thinking of a message in a bottle

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Students in professional health care programmes fear biochemical structures, terms and concepts. Some teachers use storytelling and // or anthropomorphisms subconsciously. I, however, am exploring their wider use. Outside of regulated curricula, I developed outreach formats for A-level students. These formats ran with great success from 2014 until Corona. Subsequently, I expanded them to an introductory textbook material in endocrine biochemistry. This way of communicating scientific content may help to organize knowledge. Within Legitimation Code Theory, it would specifically be the Autonomy and the Semantics dimensions, mainly supporting this storytelling approach. This abstract is to share experience and best practice of innovative teaching, and to explore the pedagogic theory behind anthropomorphic storytelling. Starting off with the famous quote by George Box – 'All analogies are wrong, but some are useful' – certain scientific content is paired with dedicated, but unorthodox visualizations. At times, endocrine topics are related to everyday objects. There are useful analogies, that allow some sort of reasoning within the realm of the analogy. Some topics require complex and // or mixed analogies. Here, I explore the journey of a hormone. Starting with hormone biosynthesis and regulated release from secreting cell, we will look at different stages of the whole hormone signaling process: the distribution of the hormonal 'message-in-a-bottle' throughout the body, the passing of some hormones through membranes, and pre-receptor metabolism. Binding to different classes of receptors is not the end of hormone signaling, but the beginning of a second phase of signaling via second messengers, before hormonal messages are switched off again.
Further readings
Dominic LAI, Jonathan Wolf MUELLER. Understanding the Biochemistry of Hormones – Message in a Bottle. Review article. In peer review at Essays in Biochemistry, submitted 22nd Sep 2024. Jonathan Wolf MUELLER. 2023. Ultimately Understanding Biochemistry. German edition. Springer Nature. Book. doi. 10.1007/978-3-662-66194-9.

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Bone and Calcium

OP7.1

Impact of Intraoperative PTH measurement during Parathyroidectomy for Primary Hyperparathyroidism

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Background
Intraoperative PTH (IOPTH) measurement during surgery for primary hyperparathyroidism (PHPT) predicts post-operative cure and provides important information during surgery. In 2017, we set-up IOPTH measurement on a laboratory-based mainline immunoassay analyser. Samples collected are – pre-incision(S1), pre-excision(S2) and 20mins post-excision(S3). A drop of $>50\%$ in S3 from either S1 or S2 is considered to be indicative of cure.
Patients and Methods
We reviewed the records of patients with PHPT who had parathyroidectomy between 2017-2024 and recorded demographic, biochemical, surgical and histological details to assess the predictive accuracy of IOPTH measurement and its impact on the surgical procedure.
Results
We had full biochemical and IOPTH details on 157 patients. Mean age 61 years, 78% females, mean serum calcium 2.93mmol/L. 142 patients had $>50\%$ drop in PTH and of these 140(99%) patients were cured. One of the two patients who was not cured was subsequently confirmed to have MEN-1. 15 patients had $<50\%$ drop and in all 15 patients, surgery was extended with further IOPTH measurement. In 10/15 patients IOPTH values dropped by >50% and all were cured, while in 5 patients PTH fall remained $<50\%$ and none was cured. The time taken to receive IOPTH result was comparable to the time taken for frozen section result.
Summary
$>50\%$ fall in IOPTH accurately predicted cure in 98.5% patients allowing the surgeon to undertake limited surgery with lower risk of local complications. $<50\%$ fall predicted absence of cure in 100% of patients allowing the surgeon to extend surgery. Following the extension once again IOPTH predicted cure or its absence with 100% accuracy.
Conclusions
IOPTH as measured in our centre accurately predicted the surgical outcome, thereby (a) reducing surgical time and local complications and (b) guiding the surgeon to extend surgery with reduction in frequency of surgical failure.

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OP7.2

Case detection of inherited primary hyperparathyroidism in 35 to 50 year olds

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Background
Approximately 10% of primary hyperparathyroidism (PHPT) cases are due to inherited germline pathogenic variants. Historically, genetic testing was recommended for people developing PHPT under 35 years, or for individuals under 45 with other risk factors for inherited disease (family history of PHPT, multigland disease or hyperplasia, presence of other syndromic features). The NHS England National Genomic Test Directory testing criteria have been updated to extend genetic testing to individuals developing PHPT under 50 years without additional risk factors for inherited disease.
Aim
To determine the yield of additional syndromic PHPT diagnoses in individuals with PHPT between 35-50 years where FHH (familial hypocalciuric hypercalcaemia) had been excluded biochemically (urinary fractional calcium excretion of >0.01).
Method
We identified individuals age 35-50 years, who had had surgery for PHPT in the past 5 years and identified those who had not been offered genetic testing at the time of their surgery. We contacted them by letter with the option to 'opt in' to genetic testing. Individuals opting in had a telephone consultation to discuss genetic testing and to obtain informed consent. Blood samples were sent for genetic testing and results obtained.
Results
61 individuals age 35 to 50 had undergone parathyroidectomy for PHPT. 9 had undergone genetic testing on clinical grounds (1 case of MEN-1 identified). 52 individuals were sent an opt in letter. 26 (50%) responded to the invitation (21/26 (81%) by email and 5/26 (19%) by post). Following a telephone consultation, all 26 consented for genetic testing and 26/26 (100%) genetic test results were negative.
Conclusions
We did not identify any pathogenic variants in 26 individuals undergoing genetic testing for PHPT age 35-50 years, where FHH had been excluded and other risk factors were not present. The yield of genetic testing in this age group is likely to be low.

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OP7.3

Utility of repeat ultrasonography in preoperative localization of parathyroid adenoma

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Background
Effective preoperative localization is crucial for successful surgical outcome in primary hyperparathyroidism. Ultrasonography (US) and radionuclide (RN) scan are requested, either concurrently or sequentially. At our centre, we also request a second US scan by an experienced radiologist to enhance localization accuracy in patients with negative first US scan irrespective of the outcome of RN scan.
Study Aim
To identify the diagnostic accuracy and impact on surgical outcome of a second US, performed by a specialist head and neck radiologist prior to surgery following the US and RN scans.
Patients and Methods
Records of patients undergoing parathyroidectomy for primary hyperparathyroidism from 2016-2023 were reviewed and demographic, biochemical, imaging, surgical and histological findings were recorded. Patients who had a second US scan after the initial US and RN scan were identified and their indications were studied along with cure rate following surgery. Cure was defined by postoperative normocalcaemia and histological confirmation.
Results
157 patients had parathyroid surgery (78% female; mean age 68 years). 36 were operated after the initial US without further imaging while 121 patients had both US and RN scans. 87/121 patients had conclusive RN findings although in 28/87 with negative initial US, a second US was requested for better anatomical localisation (group A). 34/121 had inconclusive findings and in 16/34 a second US scan was requested (group B). Overall, 44 patients (groups A + B) had second US scan with a cure rate of 90% while in group B alone it was 98%. These figures were comparable to cure rate in the overall cohort (92%).
Conclusion
Repeat US performed by a specialist radiologist demonstrated a high success rate. It can be usefully considered especially in patients with inconclusive imaging. It has the added advantage of being cost-effective with no radiation exposure while improving diagnostic accuracy.

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OP7.4

Interpretable ('explainable') machine learning in osteoporosis case finding: using SHAP values in clinical decision-support for the $FREM_{ML}$ fracture prediction algorithm

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Background
Machine Learning (ML) may improve case finding finding accuracy in comparison to standard regression modelling identifying subjects at high imminent (one-year) risk of major osteoporotic fractures (MOF). However, healthcare providers need to justify treatment decisions through observable risk factors.
Methods
$FREM_{ML}$ was trained and validated using complete registry data for the Danish population aged ≥45 years without prior osteoporosis diagnoses or treatment (n = 2,472,912). Predictors of fractures (15-year lookback) included diagnoses, filled prescriptions, days since last redemption of fall- and osteoporosis-risk medication, and polypharmacy and multi-morbidity. Risk outputs were backed by SHapley Additive exPlanations (SHAP) values to facilitate clinical interpretation.
Findings
$FREM_{ML}$ displayed an overall area under the curve of 0.77. To exemplify the clinical implications and interpretation, we show two hypothetical cases: In a 67-year old woman, a relative fracture risk of 1.67 was estimated. Using SHAP values, we identified the ten strongest personalized risk factors, including several previous fractures (combined SHAP: +1.41), multi-morbidity (SHAP: +0.29) and alcohol (SHAP: +0.19). While electronic health records (eHR) may be inspected further based on highlighted factors, dual x-ray absorptiometry (DXA) assessment is likely warranted. In contrast, Case 2, a 91-year old woman, was assigned a relative risk of 0.86. The majority of the absolute MOF probability was explained by age (SHAP: +1.36) and sex (SHAP: +0.28), while other predictors lowered the risk estimate (e.g., recent redemption of cardiac glycosides, no history of any MOF; cox-arthritis). Here, clinicians must decide whether an essentially age-motivated DXA scan is warranted. To translate SHAP values into interpretable insights, we suggest visual inspection of personalized scatterplots integrated into eHRs.
Conclusion
We propose to evaluate the $FREM_{ML}$-based relative risk estimates to promote osteoporosis case-finding in general practice. Importantly this alerts practitioners not only to the level of risk but also to the personalized factors driving the risk assessment.

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Reproductive Endocrinology

OP8.1

Gonadotropin response following intranasal kisspeptin administration is heightened in women with hypothalamic amenorrhoea compared to healthy women

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Background
Kisspeptin administration by intravenous/subcutaneous routes activates hypothalamic GnRH neurons to stimulate reproductive hormones and is under rapid development for treating common reproductive disorders, including hypothalamic amenorrhoea (HA). However, these invasive routes limit patient acceptability. Intranasal offers a novel non-invasive delivery route, which would be clinically preferable. Herein, we compare the reproductive endocrine responses after intranasal kisspeptin administration in healthy women to women with HA.
Methods
Randomised, double-blinded, placebo-controlled, crossover study in 12 healthy women during the follicular phase (mean age 22.1 ± 0.9yrs, BMI 22.1 ± 0.8 kg/m^2) and 10 women with HA (age 25.8 ± 2.7yrs, BMI 19.9 ± 1.3 kg/m^2). After intranasal delivery of kisspeptin-54 (12.8nmol/kg) or 0.9%-saline (placebo), reproductive hormones were measured every 15minutes for 4hours. Mean ± SEM presented.
Results
Intranasal kisspeptin-54 administration rapidly and robustly stimulated gonadotropin release in both cohorts. However, LH and FSH release were significantly augmented in women with HA, compared to healthy women: mean area under the curve (AUC) for the change in LH across 4hours 96.0 ± 45.8h•IU/litre (healthy women) vs. 600.6 ± 146.7h•IU/litre (women with HA) (P = 0.002). Consistently, mean AUC for the change in FSH was -36.1 ± 23.4h•IU/litre (healthy women) vs. 474.9 ± 237.3h•IU/litre (women with HA) (P = 0.02). The mean maximal LH change following kisspeptin-54 was >3fold greater in women with HA at 4.4 ± 0.7IU/L vs. 1.4 ± 0.3IU/L in healthy women (P < 0.001). Similarly, the mean maximal FSH change was >10-fold greater in women with HA at 3.1 ± 1.3IU/L vs. 0.3 ± 0.1IU/L in healthy women (P = 0.03).
Summary
Intranasal kisspeptin robustly stimulates reproductive hormone release in healthy women, with an even greater stimulation in women with HA. Therefore, intranasal kisspeptin offers not only a novel, effective, safe, and non-invasive route of administration for the management of reproductive disorders but also a potential simple diagnostic test to identify women with HA.

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OP8.2

Discordance of worldwide clinical practice with guidelines for treating male hypogonadism: results of an international content analysis

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Background
Worldwide testosterone prescribing has increased markedly within the last 20 years; this is partly due to increased testosterone seeking behaviour among men with age-related co-morbidities, obesity, and type 2 diabetes. Healthcare websites are the major source of information on male hypogonadism for the male population. A growing number of private 'men's health clinics' have emerged specialising in male hypogonadism treatment. It is not known how closely publicly available information on male hypogonadism mirrors clinical guidelines.
Methods
Virtual private networks were used to conduct localised web-searches within Australia, Brazil, India, South Africa, United Kingdom and the United States using pre-defined terms. Searches were conducted in English, Hindi, Spanish and Arabic using three major platforms (Google, Yahoo and Bing). After duplicate removal, a coding frame was developed using a validated methodology. Identified themes were graded by concordance with consensus from international guidelines on male hypogonadism.
Results
Data were extracted from 176 websites (USA 59.7%; UK 16.5%); 86/176 (48.9%) were advertised as 'Men's Health Clinics'. 141/176 (80.1%) websites advertised at least one clinical practice discordant with male hypogonadism clinical guidelines. Specific discordant claims were as follows: testosterone treatment with a serum total testosterone >12nmol/l (19/176, 10.8%); recommending unlicenced drugs e.g. selective oestrogen receptor modulators or gonadotrophins (32/176, 18.2%) or non-testosterone androgens (11/176, 6.3%); recommending testosterone micro-dosing (18/176, 10.2%); claiming testosterone improves psychological symptoms despite lack of evidence consensus (99/176, 56.3%).
Conclusions
We utilised validated content analysis methodology with approaches mitigating geographical and linguistic bias to provide an unbiased appraisal of information accessible to symptomatic men in different geographical regions. We identified several areas where men are being encouraged to seek non-evidence-based treatment for their symptoms. Addressing the accuracy of publicly assessable data may offer a simple approach to improve the quality of healthcare for symptomatic men and restrict inappropriate testosterone treatment globally.

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OP8.3

Prevalence and factors associated with increased obstructive sleep apnoea risk in women with polycystic ovary syndrome: results from the DAISy-PCOS study

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Introduction
Population-based studies have suggested that women with polycystic ovary syndrome (PCOS) are at increased risk of obstructive sleep apnoea (OSA). We report the prevalence of high risk of OSA in a prospectively recruited cohort of women with PCOS and identified factors associated with increased OSA risk.
Methods
Women with PCOS diagnosed according to the Rotterdam criteria were prospectively recruited in a multi-centre study in 10 centres in the UK & Ireland. The Berlin and Epworth questionnaires were completed to screen participants for risk of OSA, The Berlin questionnaire stratifies the response into high-risk and low-risk categories. The Epworth utilises a cut-off of >7 to classify high-risk category. Logistic regression models were used to identify factors that are associated with increased risks of sleep disturbances in women with PCOS.
Results
A total of 726 women with PCOS were included in our analysis [Age 30 (26-34), BMI (31.1 (25.1-38.4)]. Prevalence of increased risk of OSA were 47.3% (n = 325/687) and 48.9% (n = 355/726) with Berlin and Epworth questionnaires, respectively. Independent of BMI, hyperandrogenism [aOR: 1.97 (1.0-3.8)], and alopecia [aOR: 1.7 (1.1-2.6)] were associated with increased odds of abnormal Berlin score. With Epworth score, hyperandrogenism [aOR: 1.8 (1.0-3.0)] and having irregular periods [aOR: 1.6 (1.0-2.7)] were associated with an abnormal score, also after adjustment for BMI.
Conclusion
Independent of BMI, women with PCOS score highly on Epworth and Berlin scores, indicating increased risk of OSA. These results highlight the importance of screening for OSA in women with PCOS, regardless of BMI. Hyperandrogenism increased the odds of OSA. Thus, the role of androgens in the pathogenesis of OSA requires further study.

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OP8.4

Understanding the functional and physiological impact of modulating luteinizing hormone receptor (LHR) oligomerisation in the murine ovary

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The gonadotrophin hormone receptor, LHR, is essential for reproductive functions, mediating ovarian follicle development, ovulation, steroidogenesis and corpus luteum functions. As a G protein-coupled receptor (GPCR), LHR primarily signals through the Gαs recruitment/adenylyl cyclase/cAMP canonical pathway, however, it has been shown that under conditions of heightened LH concentration and LHR expression, the LHR can activate Gαq/11, triggering intracellular calcium release. A wide array of evidence has demonstrated that GPCRs exist and function as dimers and higher-order oligomers (homomers and heteromers), which diversify signal specificity, selectivity and diversifies receptor function. Our studies have shown that the LHR primarily forms and functions as homomers, but how LHR mediates this functional and physiological diversity remains unknown. Our previous work has also shown that LHR forms and functions as homomers and with FSHR as heteromers, providing a means to fine-tune signal specificity and magnitude of response. The aim of this study was therefore to determine the effect of modulating LHR homomerisation on LH/LHR ovarian functions. Synthetic peptides were designed to target specific receptor transmembrane domains (TM1, TM2, TM4, TM5 and TM6) were used to disrupt receptor oligomerisation. Disrupting peptides were shown to inhibit LH-dependent cAMP production. Culture of mouse ovarian fragments in the presence of the disrupting peptides highlighted trends for modulating LH-dependent regulation of EGF mediated pathways, steroidogenesis and inflammatory ovulatory pathways. Additional open follicle cultures demonstrated a shorter time to germinal vesicle breakdown (GVBD), in follicles treated with the disrupting peptides, suggesting a shift towards Gq-mediated activity. Together these data suggest that different LHR homomeric forms can distinctly modulate LH-dependent functions within the ovary fine tuning the response.

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Featured Clinical Case Posters

CC1

Prevalence of hypophosphatasia in a primary care setting

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A 51 year old male presented for an NHS healthcheck and was noted to have an alkaline phosphatase (ALP) level of 16iu/L (normal range 30-100). Review of his records revealed similar low readings. He had a recent third metatarsal fracture following an inversion injury and on xray was noted to have previous second and fourth metatarsal fractures. He had a fifth metatarsal fracture four years prior. He was of short stature as were his sister, father and grandmother. He reported having poor dentition as a child and adult. After further investigations in Primary Care, genetic testing confirmed a diagnosis of Hypophosphatasia (HPP). Having identified the diagnosis of HPP in the above patient, an audit was undertaken of all patients in the practice with a list size of 11,518 for low alkaline phosphatase within the previous five years. 23 patients were identified of which 14 were excluded due to a previous or subsequent normal ALP. 4 patients either declined or failed to respond to a request to repeat their ALP. 5 patients were referred for further genetic testing and in total 3 patients were confirmed to have HPP. On comparing this to the expected UK prevalence of 1 in 6,370, this practice had a prevalence of 1 in 3,839 which may suggest that milder forms of HPP may be underdiagnosed. A retrospective cohort study has been approved by CPRD to be undertaken by Alexion Pharmaceuticals to 'provide an updated estimate of the prevalence of HPP in the UK'. This is expected to confer a public health benefit by establishing an up-to-date overview of HPP in the UK; with a view to increase rates of detection and potential treatment.

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CC2

Pregnancy and lactation-associated osteoporosis: insight into this rare but challenging condition

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Background
Pregnancy and lactation-associated osteoporosis (PLO) is a rare condition that can often be missed by physicians, leading to delayed diagnosis and fractures in young patients. Treatment options include anti-resorptive therapy (bisphosphonates), anabolic therapy (teriparatide), and monoclonal antibody therapy (denosumab), but there is no clear consensus on the best treatment approach. We present two cases outlining the management of PLO.
Case 1
A 28-year-old woman sought medical attention for back pain 4 months postpartum, which she initially attributed to her pregnancy. She had severe hyperemesis gravidarum, requiring high dose prednisolone in second trimester, and was on a vegetarian diet. Although her bone mineral density (BMD) was normal, chest CT that she had for breathlessness showed multi-level compression fractures (T8-T12). The metabolic workup showed 25-OH vitamin D deficiency, 29 (N-50-120nmol/l) and elevated bone turnover markers, CTX, 0.56 (N-0.10-0.50µg/l) and P1NP, 151 (N-19-69µg/l). Following vitamin D replacement, a three-year course of zoledronate infusion was commenced.
Case 2
A 35-year-old woman, 11 months postpartum, sustained a low-trauma wrist fracture. She had been breastfeeding but had no other osteoporosis risk factors. BMD showed lumbar and hip T scores of -3.3 and -3.2, respectively, with elevated P1NP, 74 (N-19-69µg/l) and low oestradiol level, <92 pmol/l. She was advised to stop breastfeeding and was given a two-year course of teriparatide followed by a single zoledronate infusion. Post-treatment BMD showed significant improvement with no further fractures. The genetic test result for Osteogenesis Imperfecta is pending.
Conclusion
PLO has a complex pathophysiology, causing increased bone loss due to increased PTHrP, calcium secretion during breastfeeding, and suppression of the hypothalamic-pituitary-ovarian axis, leading to low oestrogen. Although BMD may recover in 12-18 months, early diagnosis and ruling out secondary causes are crucial for reducing fracture risk.
Discussion
Further evaluation of PLO treatment effectiveness, duration, and long-term outcomes is needed.

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CC3

A decade without a pancreas or exogenous insulin. a case report

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Background
Congenital Hyperinsulinism is a common cause of medically refractory hyperinsulinism in infants. Hence, surgical intervention is considered the gold standard treatment (1). We present a case of congenital hyperinsulinism in which the patient remained hypoglycaemic despite total pancreatectomy and remained independent of exogenous insulin subsequently for eleven years.
Case report
We present the case of a 24-year-old male who remained insulin-free 11 years after undergoing a total pancreatectomy for congenital hyperinsulinism. He presented with hypoglycaemia and hyperinsulinemia shortly after birth. He was treated initially with octreotide, diazoxide, and hydrocortisone, but these were ineffective. At one month of age, he underwent a 95% pancreatectomy; however, hypoglycaemia persisted. He was subsequently trialled on further medical treatment, which also failed. He continued on glucose/glucagon infusion and had a second pancreatectomy one month later, during which 98% of pancreas was removed but, hypoglycaemia continued. A week later, the remaining part of the pancreas was removed, and the entire duodenum was meticulously scraped. Histology revealed abnormal beta cells invading the wall of the duodenum. His hypoglycaemia persisted. A PET CT scan showed focal FDG uptake around the bed of the pancreatic head, suggesting that some abnormal pancreatic cells had adhered to the duodenal wall. Duodenectomy was not considered due to the high mortality risk. A PEG tube was inserted, and he was started on subcutaneous octreotide QDS and glucagon infusion. After two months, the glucagon infusion was stopped, oral feeding resumed and octreotide was continued. The patient experienced no further episodes of hypoglycaemia, and octreotide was continued until he was 10-year-old. A year later, HbA1c rose to 7.1%, and exogenous insulin was initiated. Initially, only rapid-acting insulin was used due to concerns about night-time hypoglycaemia. After four years, a multiple-dose insulin regimen was started.
References
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CC4

Severe hyponatremia in anti-LGI1 encephalitis: a rare presentation and management challenge

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Severe acute hyponatremia, if untreated, can be life-threatening, leading to cerebral oedema, seizures, coma and even death. Treatment with hypertonic saline is the standard approach in acute cases, with many guidelines suggesting intravenous boluses and repeating as needed. However, no consensus exists on the use of continuous infusion of hypertonic saline for managing refractory hyponatremia, and data is limited to inform the choice between slow continuous infusion and intermittent boluses. We present a challenging case of a 61-year-old woman admitted with acute confusion, disorientation and seizures. She had past medical history of autoimmune hepatitis, hypertension and pre-diabetes. Examination revealed facial contortion. Her initial serum sodium was critically low at 115 mmol/l. Despite aggressive management with repeated hypertonic saline boluses, her hyponatremia remained refractory, necessitating continuous slow infusion of hypertonic saline in intensive care unit. Biochemical workup indicated SIADH, yet her neuropsychiatric symptoms persisted even after correction of sodium to 136 mmol/l. Further neurological evaluation revealed subtle changes in the left medial temporal lobe on MRI, suggesting limbic encephalitis. CSF analysis showed slight increase in protein (0.55 g/l) and serology later confirmed positive anti-LGI1 antibodies, leading to a diagnosis of autoimmune limbic anti-LGI1 (anti-leucine-rich glioma inactivated 1) encephalitis. Treatment with IV methylprednisolone followed by oral steroids resulted in significant neurologic improvement and normalisation of sodium. This case underscores the potential utility of continuous slow hypertonic saline infusion in managing refractory severe hyponatremia and highlights the importance of thorough investigation into the etiology of SIADH, particularly when hyponatremia is severe and resistant to standard treatment. It also suggests that

the presence of autoimmune disorders should heighten suspicion for autoimmune encephalitis as a potential underlying cause of persistent encephalopathy.

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CC5

Acquired generalised lipodystrophy- a rare adverse effect of immune check-point inhibitors

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We present the case of 60 year old male with acquired generalised lipodystrophy secondary to nivolumab therapy (immune checkpoint inhibitor) which he received for two years following relapse of treated renal clear cell cancer (nephrectomy; pazopanib treatment on initial relapse). He had excellent response to nivolumab and completed treatment, but a month later he developed significant weight loss, starting with fat loss from his face. His wife identified some case reports of lipodystrophy as rare side-effect of nivolumab. He was referred to the nationally commissioned, highly specialised insulin resistance/lipodystrophy service at Addenbrooke's Hospital who confirmed the diagnosis of acquired generalised lipodystrophy. He had low subcutaneous fat mass, low leptin concentration, hypertriglyceridaemia, hyperinsulinaemia, hyperglycaemia and hepatic steatosis on serial MRI imaging (but no hepatic fibrosis). He was initially managed with metformin, fenofibrate and specialist dietitian input (low fat diet), along with increased physical activity. He declined starting a statin despite increased cardiovascular risk. It was later advised that he start metreleptin replacement therapy but he has currently declined this. Acquired generalized lipodystrophy is a very rare disorder and hence under-recognised. It is difficult to recognise initially as the clinical appearance overlaps with other causes of weight loss and the changes in fat distribution can easily be missed. In patients with acquired lipodystrophy, metabolic abnormalities associated with severe insulin resistance include hypertriglyceridemia, diabetes mellitus, hepatic steatosis and acanthosis nigricans may develop soon after the onset of subcutaneous fat loss. Immune checkpoint inhibitor (nivolumab, pemrozulimab) induced acquired generalized lipodystrophy has been reported in few case reports only and it is important to highlight to health care professionals to consider this as a differential diagnosis in patients losing weight after receiving these therapies, due to increasing use of these agents and the rarity of this syndrome.

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CC6

The challenge of identifying the correct surgical target in cushing's disease

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Cushing's disease, caused by an ACTH-secreting pituitary adenoma, accounts for up to 80% of endogenous Cushing's syndrome cases. While trans-sphenoidal surgery is the standard treatment, pituitary MRI identifies surgical targets in only about 60% of patients. We report a 63-year-old woman with a 12-month history of central weight gain, easy bruising, worsening hypertension, recent diagnoses of type 2 diabetes and obstructive sleep apnoea, who was diagnosed with ACTH-dependent Cushing's syndrome. Laboratory tests revealed a 10-hour post-1 mg dexamethasone cortisol level of 570 nmol/l (< 50 nmol/l), ACTH of 112 ng/L (10-30 ng/l), and a 24-hour urinary free cortisol (UFC) of 236 nmol/l (0-164 nmol/l). Inferior petrosal sinus sampling indicated a central source of ACTH excess. Initial pituitary MRI identified two potential areas of interest. An initial 11C-methionine PET/CT demonstrated tracer uptake within both areas and did not favour one over the other. Medical treatment was initiated to normalise cortisol and enhance ACTH signalling, aiming to better delineate a surgical target on repeat imaging. Initially treated with metyrapone, the patient switched to osilodrostat due to intolerable side effects. After 3 months of eucortisolaemia, her ACTH levels rose to 1091 ng/L (from 353 ng/l), prompting a repeat 11C-methionine PET/CT, which now identified a clear focus of increased tracer uptake in the left inferior pituitary gland. The patient subsequently underwent endoscopic trans-sphenoidal resection of the lesion. Postoperatively, cortisol levels were 51 nmol/l on day 3 and 34 nmol/l on day 11. She is currently on a stable dose of prednisolone (4 mg once daily) and feels well. Histological analysis confirmed a corticotroph pituitary adenoma. This case is the first to utilise 11C-methionine PET/CT before and after cortisol-lowering treatment, suggesting that blocking steroidogenesis may enhance the visibility of corticotroph adenomas through functional imaging.

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CC7

Mini case series to highlight the importance of remembering association between graves' disease and thymic enlargement

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Introduction
Thymic enlargement (TE) due to thymic hyperplasia is known to be associated with Graves' Disease (GD) and other autoimmune conditions. The incidence is not known. Increasingly, it is identified incidentally on imaging investigating unrelated symptoms. There is no consensus on TE management or follow-up.
Cases
We present three cases of TE and GD.
Case 1
25-year-old male. Diagnosed with GD after experiencing sweating and tachycardia, biochemistry confirmed thyrotoxicosis, TSH <0.01 Free T4 56.3 (9 – 19 pmol/l), Free T3 >30.72 (3 – 5.4 pmol/l), and TSH Receptor antibodies (TRABs) 28.7 U/l. Treated with Carbimazole. Two months prior, a CT Aortogram performed for chest pain revealed TE. Six-month interval imaging is planned.
Case 2
51-year-old female, diagnosed with GD was managed with Carbimazole. TSH < 0.01, Free T4 38.2, Free T3 20.1, and TRABs 10.1 U/l. Presenting with chest pain, investigations identified an anterior mediastinal mass on CT Aortogram. CT Thorax confirmed radiologic features in keeping with benign TE.
Case 3
27-year-old female, presented with palpitations, shortness of breath and haemoptysis underwent CT Pulmonary Angiogram revealing a 4.5 x 3.3 cm anterior mediastinal soft tissue mass representing TE. Biochemistry then confirmed GD; TSH <0.01, Free T4 42.6, Free T3 >30.72, and TRABs 17.1 U/l. Managed with Carbimazole and Propranolol. The thymus reduced in size (3.5 x 2.2 cm) on MRI Thorax four months later.
Conclusion
TE associated with GD is thought to be related to thyrotoxicosis and autoimmunity. We recommend undertaking thyroid function and TRABs to exclude GD as a potential cause when TE is identified incidentally on imaging, this will avoid inappropriate invasive procedures (biopsy or surgery). If the initial imaging did not reveal worrying thymic features including irregular borders, local invasion, heterogenicity or cystic changes, conservative management and interval thoracic imaging is recommended once thyrotoxicosis is controlled.

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CC8

Severe refractory hypocalcaemia in metastatic breast cancer in patient with concurrent primary hypoparathyroidism

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68y female with a history of autoimmune hypoparathyroidism and metastatic breast cancer with liver, lung and breast metastases developed severe refractory hypocalcaemia twice during introduction of different antitumour therapies for her metastatic disease in context of mixed type bone metastases and very stable calcium control on Alfacalcidol 1 mg and Adcal D3 (1500/400) once daily. She was diagnosed with breast cancer in 2015 and treated with wide local excision, adjuvant radiotherapy, tamoxifen and anastrozole. In 2020, developed predominantly sclerotic bone metastases. One month after commencing Fulvestrant in combination with Abemaciclib, her calcium dipped to 1.42 mmol/l (2.2-2.6) presumably due to high volume of sclerotic breast metastases. Hypocalcaemia responded to intavenous calcium, increase in oral calcium and alfacalcidol to 3 mg od for several months. In March 2024 there was progression in lytic metastases associated with significant ALP rise but stable calcium between 2.33-2.53 mmol/l on Alfacalcidol 1 mg od and Adcal D3 1 tbl od. Two weeks after commencing Paclitaxel, she was admitted with symptomatic hypocalcemia of 1.45 mmol/l requiring prolonged iv calcium infusions, doubling in alfacalcidol,

Adcal dose and eventually conversion to more potent calcitriol 2 mg am and 1 mg pm. There was no concurrent administration of biphoshonates or denosumab. Magnesium was mildly reduced at 0.61 mmol/l (0.7-1) and corrected intravenously.

Discussion

Breast cancer bone metastases are typically osteolytic or mixed type. Introduction of antitumour therapies can cause rapid shift in bone metabolism from osteolytic to osteoblastic, causing significant calcium absorption into the bone. This can cause severe hypocalcemia similar to 'hungry bone syndrome'. This effect can be profound and prolonged in patients with concurrent hypoparathyroidism unable to mount PTH response and where calcium and activated vitamin D doses are not adjusted in anticipation of this effect. Careful calcium monitoring throughout the treatment is recommended.

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CC9

Late diagnosis of digeorge syndrome in a 41-year-old male presenting with recurrent hypocalcemia and background of learning disability-a case report

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Background

DiGeorge syndrome also known as Velo-Cardio-Facial syndrome is associated with microdeletion at chromosome 22q11.2. Its main features include dysmorphia, hypoparathyroidism, hypocalcemia, hypoplasia or aplasia of the thymus, cardiac anomalies, renal anomalies, and behavioral/ psychiatric issues. This incurable syndrome could be treated for its complications to increase the quality of life. We present a case report of 41-year-old male with background of learning disability who presented with recurrent hypocalcemia secondary to hypoparathyroidism and was diagnosed with DiGeorge syndrome.

Case summary

A 41-year-old male was referred due to recurrent hypocalcemia, during recurrent presentations to hospital he was treated for pseudo-obstruction of small bowel, long QT syndrome and hypocalcemia secondary to hypoparathyroidism. Bone density scan was normal. Echocardiogram showed preserved left ventricular systolic dysfunction. On examination he had BMI of 39.5, plethoric complexion, short neck, short stature, coarse facial features, high arched palate and enamel hypoplasia. He had no goiter and Chvostek's sign was negative. He was born 4 weeks early but did not require any prolonged admission or special care. However, he had childhood history of tetanic spasms of hands which resolved with calcium supplements and also had known diagnosis of dyspraxia and learning disability. To find out cause of hypoparathyroidism microarray genetic testing was requested and diagnosis of DiGeorge syndrome was confirmed. Calcium substitution was initiated appropriately.

Discussion

An atypical disease course may delay the diagnosis and appropriate management of affected patients. In this case, confirmation of the diagnosis allowed the initiation of appropriate treatment and reducing the risk for further events. This case report demonstrates that DiGeorge syndrome should be considered as a differential diagnosis while investigating hypocalcemia and hypoparathyroidism in adulthood as this syndrome has very important implications on patient's health and future family planning.

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CC10

Hyperparathyroidism-jaw tumour syndrome, a case presentation

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Introduction

Hyperparathyroidism-Jaw Tumour syndrome is a rare autosomal dominant disorder involving parathyroid tumors, ossifying jaw fibromas, renal abnormalities, and uterine hyperplasia or neoplasia. This condition is linked to inactivating mutations in the CDC73 gene, which encodes Parafibromin, a protein with anti-proliferative functions. Patients often present with hyperparathyroidism symptoms like hypercalcemia, as well as jaw tumors.

Case History

A 38-year-old man was referred to his GP for depression. Routine blood tests showed hypercalcemia (corrected Ca 3.21 mmol/l), high parathyroid hormone (PTH) at 38.1 pmol/l, low phosphate (0.62 mmol/l), and low vitamin D (26.2 nmol/l). He had a history of parathyroidectomy age 13, of a 2 cm left parathyroid adenoma. Genetic testing at that time ruled out MEN1, His father had undergone parathyroidectomy at 27 for nodular hyperplasia. The patient was admitted, treated with IV fluids and cinacalcet. Ultrasound showed a 14x12x16mm hypoechoic nodule by the right thyroid gland, later confirmed on Parathyroid MIBI. Post-parathyroidectomy, PTH and calcium levels normalized. Histology confirmed an adenoma and residual scar tissue. Genetic testing diagnosed HPT-JT syndrome.

Discussion

In familial primary hyperparathyroidism (PHPT), it is essential to recognize the genetic variants implicated in its pathogenesis, including those in the CDC73, CDKN1B, GCM2, MEN1, RET, and CASR genes. Current guidelines recommend genetic testing for familial PHPT in individuals under 50, those with significant family history, or cases involving parathyroid carcinoma. Overlapping indications for testing include neonatal hyperparathyroidism and features of multiple endocrine neoplasia, emphasizing the need for a thorough evaluation in suspected cases. This case identified the need to retest those with likely familial PHPT diagnosis despite previously negative genetics given the evolution of genetic testing. This enables appropriate holistic follow-up to be established.

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Poster Presentations

Adrenal and Cardiovascular

P1

Adrenal adenoma to carcinoma transformation is possible – a case series of three patients who would have been discharged under ESE guidelines

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Incidental adrenal lesions are a common finding on radiological studies with a prevalence of 3-10% depending on the age of the population. The investigation, risk stratification and surveillance of adrenal incidentalomas has an opportunity cost in resource-finite healthcare systems. The current approach advocated in the 2023 European Society for Endocrinology (ESE) clinical practice guidelines relies on the doctrine that adrenal adenomas remain benign and do not transform to higher grade disease. The guidelines recommend characterisation with unenhanced adrenal protocol CT, or MRI, in addition to clinical and biochemical assessment for hormonal excess. Following this, patients with non-functioning homogenous adrenal lesions <4 cm that are ≤ 10HU can be discharged without further imaging or follow up. However, reports of patients developing adrenocortical carcinoma several years after initial diagnosis with an adrenal adenoma have been emerging. A retrospective review of adrenal nodules reviewed at Cambridge University Hospitals from 2018-2024 identified three patients seen with apparent transformation to adrenocortical carcinoma (ACC) several years after formal characterisation of a benign adrenocortical adenoma. These three cases account for 0.4% of all incidental adrenal nodule cases reviewed during this period. All three patients had non-functioning adenomas with size <4 cm and radiodensity <10HU at diagnosis, which showed stability on interval imaging performed for other reasons over a 7, 12 and 12 year period respectively prior to rapid transformation and subsequent histological confirmation of of ACC. These patients would have met the criteria for discharge under the existing ESE recommendations. Adenoma to carcinoma transition, with the progressive accumulation of driver mutations, is well described for other cancers such as colorectal carcinoma. The possibility of a similar scenario has been proposed in the adrenal, but remains unproven. These additional case reports give further credence to this hypothesis and validate the need for ongoing work to identify the underlying molecular mechanisms.

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P2

Prevalence of pheochromocytoma in incidentally discovered adrenal masses: a review from a large tertiary referral centre

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Introduction
Pheochromocytomas are often diagnosed incidentally through cross-sectional imaging tests conducted for other reasons. Biochemical confirmation can be achieved through plasma free metanephrines and normetanephrines or a 24-hour urine collection for both normetanephrine and metanephrine. Recent ESE guidelines suggest that testing may not be necessary for patients with clear radiological features of adrenal adenomas.
Methods
We conducted a retrospective analysis of radiological and biochemical data for patients with incidentally discovered adrenal nodules at Cambridge University Hospital from 2019 to October 2024. Only cases with formal radiological characterization through unenhanced CT, dedicated CT adrenal, or MRI were included. Data collected included age, gender, plasma metanephrines, laterality, tumour size, and follow-up.
Results
This study included 631 patients: 296 (47%) males and 335 (53%) females. Among them, 507 (80.34%) had an attenuation of <10 HU or signal dropout on MRI. Sixty-one patients (9.66%) had nodules with densities between 10-20 HU, and 63 (10%) had densities >20 HU. Most nodules (596 or 94.45%) were <4 cm. The mean patient age was 66 years (range 21-91). Only 2 patients (0.4%) with lipid-rich adenomas showed abnormal plasma metanephrines. One individual is on Venlafaxine, and both cases await further assessment with low clinical suspicion for pheochromocytoma. From our data, only 7 patients (1.10%) had confirmed biochemical and histological diagnoses of pheochromocytoma, all with unenhanced densities >20 HU. This also suggests that 11.4% of patients with unenhanced densities greater than 20 HU had pheochromocytoma.
Conclusion
This single-centre study identified a ~1% prevalence of pheochromocytoma in patients with incidentally discovered adrenal nodules, all with unenhanced densities >20 HU. Two patients with lipid-rich adenomas had equivocal plasma metanephrine levels and await further testing. This analysis supports ESE guidelines to exclude biochemical testing for pheochromocytoma in patients with radiologically characterized lipid-rich adenomas.

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P3

Exploring macrophage polarization in patients with non-functioning or cortisol-producing adrenocortical adenoma

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Background
In patients with overt Cushing's syndrome (CS) chronic endogenous excess of cortisol drives dysregulation of innate and adaptive immunity, characterised by increased monocyte and decreased lymphocyte counts. The impact of 'subclinical' CS in patients with cortisol-producing adenomas (CPA) and mild autonomous cortisol secretion (MACS) remain poorly defined. We hypothesise that macrophage polarisation and activation can be altered in both patients with CPA-CS and CPA-MACS leading to dysregulation of macrophage immune function.
Methods
Primary human macrophages were polarised into M1-like inflammatory type by adding TNFα (10ng/ml) and IFNγ (20ng/ml) and co-treated with 10% serum from 14 patients with adrenocortical adenomas, including 5 CPA-MACS, 4 CPA-CS, and 5 sex/age-matched endocrine inactive (EIA) controls, for 24 hours. Inflammatory and anti-inflammatory cytokine levels and corresponding gene expression were analysed by ELISA and RT-qPCR, respectively, and correlated to demographics and degree of steroid secretion.
Results
The marker of pro-inflammatory activation IL6 was decreased in M1-like polarised macrophages in response to CPA-MACS ($P = 0.0389$) and CPA-CS($P = 0.0283$) patients' serum when compared to EIA, while gene expression showed a non-significant decrease in CPA-MACS ($P = 0.0794$) and CPA-CS ($P = 0.1302$). GILZ (glucocorticoid-induced leucine zipper) gene expression was slightly increased in CPA-CS ($P = 0.2830$), but not in CPA-MACS ($P = 0.9921$) vs EIA. The pro-resolving M2-like macrophage marker CD163 gene expression was slightly increased in CPA-CS ($P = 0.1545$) and CPA-MACS ($P = 0.1761$) vs EIA. CD163 gene expression positively correlated with gene expression of GILZ ($P < 0.0001$) and anti-inflammatory marker CD64 ($P = 0.0038$). CD163 gene expression positively correlated with cortisol levels after overnight Dexamethasone suppression test ($P = 0.0153$) and tumour size ($P = 0.08$).
Conclusions
Both patients with CPA-MACS and CPA-CS showed suppression of M1-like inflammatory polarisation makers and a changing profile of pro-resolving M2-like polarisation. We plan to increase our patient cohorts and investigate M1 to M2 polarisation induced by the patient's serum to identify the mechanism of immune dysregulation.

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P4

The impact of lipoprotein(a) measurement on cardiovascular risk management post bariatric surgery – a case series

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Introduction
Elevated Lipoprotein(a) or Lp(a) is an independent major risk factor for atherosclerotic cardiovascular disease (ASCVD); an Lp(a) of ~250 nmol/l nearly doubles the risk of ASCVD irrespective of other risk factors. Roux-en-Y gastric bypass (RYGB), the most effective long-term treatment for obesity and weight-related comorbidities, does not have a clinically significant impact on Lp(a). Due to improvements in lipid profiles including cholesterol and triglycerides post-bariatric surgery, lipid-lowering treatment is sometimes discontinued. However, patients with elevated Lp(a) remain at higher risk of ASCVD post-surgery and should stay on lipid-lowering treatment to achieve the LDL-Cholesterol target of < 1.8 mmol/l. Nevertheless, in the UK, Lp(a) measurement is not routinely recommended in patients undergoing RYGB.
Methods
Lp(a) was measured in 36 patients as part of a prospective longitudinal study of participants with prediabetes or type 2 diabetes undergoing RYGB. Same-day renal and thyroid function tests were reviewed to exclude secondary causes of raised Lp(a).
Results
10 patients (27.8%) had elevated Lp(a) (> 90nmol/l). ASCVD risk factors were reassessed, and LDL-C was found to be suboptimal in 80% of patients with elevated Lp(a): Five patients were started on statin for the first time, statin was restarted in one patient where it was discontinued following RYGB, and two patients were started on combination therapy to achieve the LDL-C target. Patients with Lp(a) >200nmol/were advised to inform their first-degree relatives for cascade testing.
Conclusion
Lp(a) was elevated in a significant number of patients, when measured in post-RYGB cohort, resulting in the initiation or intensifying lipid-lowering treatment in a majority of these participants. Lp(a) measurement should be considered in patients undergoing RYGB as an essential tool to assess and manage ASCVD risk.

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P5

Primary or secondary hypoadrenalism. is this important?

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Introduction
Secondary adrenal insufficiency (AI) is commonly due to exogenous glucocorticoids, other causes being infection, tumour, surgery or radiation. Aldosterone production is usually unaffected. We present two cases of AI in patients with aspergillosis on itraconazole and steroids.
Case 1
A 35 year old lady with aspergillosis was referred with suboptimal response to short synacthen test (SST). She was on itraconazole and required 6 courses of prednisolone 30-40 mg over the past year. Clinically she was well. A second SST showed a cortisol of <20nmol/l (ACTH <5ng/l, Plasma renin 1.1nmol/L/h), 72nmol/l and 108 nmol/l respectively at 0, 30 and 60 minutes.
Case 2
A 57 year old lady with 8 year prednisolone use following previous ICU admission with swine flu, respiratory failure and aspergillosis. She was treated with posaconazole achieving dormant aspergillosis. SST showed cortisol of 55nmol/l, 199nmol/l and 265nmol/l respectively at 0, 30 and 60 minutes (ACTH 8ng/l, Renin 0.3ng/L/L/l).
Discussion
Prolonged exogenous glucocorticoid use is the commonest cause of secondary AI. With concurrent conazole this can be difficult to interpret as they can cause primary or secondary AI. Conazoles such as itraconazole and posaconazole inhibits hepatic enzyme CYP3A4, leading to reduction in metabolism of synthetic glucocorticoids, prolonging exposure causing pituitary suppression. Conazoles also inhibit the steroidogenesis pathway, and although useful in treating Cushing's syndrome, there is potential adverse effect of primary AI in patients with normal hypothalamo-pituitary-adrenal axis. Infective causes of primary or secondary AI should also be considered the context of active fungal infection thereby challenging conclusions of the cause. Thus imaging and biochemistry profile are important to assess.
Conclusion
There remains an ongoing debate on the cause of AI in aspergillosis patients with concurrent use of conazole and steroid therapy. Clinical history along with relevant investigations is key in determining the underlying pathology therefore guiding management.

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P6

Primary bilateral macronodular adrenocortical hyperplasia recurrence after unilateral adrenalactomy: a case report

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Introduction
Primary bilateral macronodular adrenocortical hyperplasia (PBMAH) is a rare cause of ACTH-independent Cushing's syndrome. The optimal treatment approach remains a topic of debate. We present a case of recurrent Cushing's syndrome following unilateral adrenalectomy for PBMAH.
Case report
A 57-year-old patient, under the care for an independent ACTH hypercorticism related to bilateral macronodular hyperplasia of the adrenal glands, was identified during a routine check-up in the presence of uncontrolled diabetes. A 19-noriodocholesterol scintigraphy was conducted, indicating a slightly higher degree of fixation on the left side (58% on the left vs 42% on the right). The patient underwent unilateral left adrenalectomy, with a favourable clinical and biological course. After seven years of remission, the patient presented with a recurrence of clinical Cushing's syndrome, an imbalance in his diabetes requiring insulin therapy and in his hypertension requiring three medications. The 24-hour urine free cortisol level was three times the normal range and adrenal CT scan revealed a 6x8x3 cm nodule of the right adrenal gland. The case was discussed and a right adrenalectomy with hormone replacement was recommended.
Discussion
The characteristic feature of PBMAH is the presence of adrenal nodules exceeding 1 cm in diameter. It is a diverse entity, and the underlying pathophysiological mechanisms remain unclear. It is a genetic disorder caused by the inactivation of ARMC5, which is described in 20-25% of PBMAH cases, and KDM1A, which is responsible for >90% of PBMAH cases. The standard treatment is bilateral adrenalectomy, but unilateral adrenalectomy may be an alternative to avoid adrenal insufficiency. In our case, recurrence was noted after seven years of remission, and the decision to perform total adrenalectomy was taken in view of the frank nature of the Cushing's syndrome and the patient's cardiovascular risk.

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P7

Is primary aldosteronism underdiagnosed in patients with adrenal incidentalomas: review of data from a regional adrenal MDT

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Introduction
Primary hyperaldosteronism (PA) is known to be an underdiagnosed secondary cause of hypertension in the population, with an estimated prevalence of up to 29% in patients with resistant hypertension. In patients with adrenal incidentalomas (AI), PA is estimated to be 1.1-10% and is lower than rates seen for detection of cortisol hypersecretion and pheochromocytoma. The diagnostic pathway is complicated by factors including confounding medications, co-morbidities and scarcity of adrenal venous sampling (AVS) and functional imaging.
Methods
Retrospective review of data from patients with AI who undertook screening for PA (2018-2023) was conducted. Data were collected for demographics, comorbidities, imaging, biochemistry and management outcomes.
Results
833 patients with AI had biochemical screening for PA. 63 (7.6%) had aldosterone: renin ratio (ARR) results potentially indicative of PA and required further investigation. Of those with ARR < 1000, 439 (57.0%) were on medications that could cause a false negative. 8 (1.8%) had medications stopped prior to initial testing. Of the 63 with possible PA, 49 (77.8%) were on confounding medications. 15 (30.6%) were on medications which could cause a false positive. 28 (44.4%) had further testing with saline infusion, AVS or both. Of those with ARR >2000, 51.9% had hypokalemia and 96.3% had hypertension versus 27.8% and 77.8% respectively for those with ARR between 1000-2000. 37 (58.7%) were subsequently diagnosed with PA, representing 4.4% of the entire cohort, and received either medical or surgical intervention or both. 35 (55.6%) with indicative ARR results, did not have further investigations for various reasons.

Conclusions
In this real-world cohort, we identified a significant proportion of AI patients with biochemical suspicion of PA on confounding medications, potentially resulting in missed diagnoses. Additionally, several patients did not undergo further testing. Therefore, our study suggests multiple possible causes leading to underdiagnosis of PA in patients with AI.

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P8

Supposed suprarenal sepsis

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A 22 year old man with no medical history presented to the hospital with weight loss, abdominal pain, fever, drenching night sweats and flank pain. His inflammatory markers were elevated, multiple cultures were sent all of which were negative. A CT pulmonary angiogram was requested for a new oxygen requirement. This revealed multiple bilateral lung nodules, mediastinal lymphadenopathy and a 46mm left sided adrenal gland. A follow up CT reported a 7 cm left adrenal necrotic mass and recommended an MRI. The MRI findings were consistent with a soft tissue mass. He was discussed at adrenal MDT as there were concerns that this may be malignant. Consensus was for an adrenal biopsy as the images and biochemistry were not consistent with an adrenocortical carcinoma (normal metanephrines, androgens, cortisol, renin and aldosterone). Adrenal biopsy was normal however a psoas sample was collected which grew staphylococcus aureus and treated with antibiotics. He was reviewed by the respiratory team and had a bronchoscopy/endobronchial ultrasound/lymph node biopsy which ruled out malignancy and tuberculosis. Of note this gentleman's HIV and hepatitis serology was negative. The MDT plan was for repeat imaging and to drain this collection, however, on serial imaging the mass decreased in size and eventually resolved. His symptoms have resolved, and he has now returned to work. Adrenal abscesses are uncommon but more frequently found in immunocompromised patients (1,2). Patients present with fever, back pain, weight loss and tachycardia (1,3,4). The most common pathogens are fungal (5). It is important to consider this as a differential in patients presenting with suspicious adrenal masses (often bilateral) with systemic symptoms supporting an underlying infection to prevent unnecessary adrenalectomies as well as to follow up after resolution to investigate for adrenal insufficiency (6). Our case is interesting in that he appeared to have spontaneous resolution.

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P9

Abstract Unavailable

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P10

Characterising primary aldosteronism outcomes using PAMO and PASO criteria: experience of a UK regional adrenal MDT

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Background
Primary aldosteronism (PA) is a treatable cause of secondary hypertension, associated with significant cardiovascular morbidity. Whilst up to 25% of patients with hypertension have underlying PA, it remains underdiagnosed. Management approaches comprise medical (mineralocorticoid receptor antagonists, (MRA)) and/or surgical (adrenalectomy). Our study aimed to evaluate medical and surgical outcomes of treated PA in patients with adrenal incidentalomas (AI) in a UK cohort using established criteria.

Methods
Retrospective data were collected from unselected patients with AI assessed for possible PA between August 2018 and March 2023. Data included demographics, biochemistry, radiological characteristics and management. Further outcomes such as post-treatment blood pressure, biochemistry and relevant medications were also collected. Outcomes were assessed using the PA medical (PAMO) and surgical outcome (PASO) scoring criteria at 3- and 12-months following treatment for both biochemical and clinical outcomes.
Results
Of 833 patients (46.1% male) with incidentalomas, 42 patients (5.0%) were diagnosed with PA. Of these, 37 (88.1%) received MRAs and 20 (47.6%) underwent unilateral adrenalectomy. Of available outcomes, 10 (91%) achieved partial or complete clinical success and 11 (85%) biochemical success at 12 months post-adrenalectomy as per PASO. After 12 months of medication only, 21 (87.5%) and 17 (77.2%) achieved partial or complete clinical and biochemical success, respectively. Higher proportions of both cohorts had partial or complete clinical and biochemical success at 12 months compared to outcomes at 3 months though these were not statistically significant.
Conclusions
Our results demonstrate that most patients had partial or complete clinical and biochemical success following treatment. More patients achieved successful outcomes when managed with surgery, compared to medication alone, with preferable outcomes at 12 versus 3 months in both groups. PASO and PAMO criteria are useful standardised tools for assessing PA-related outcomes and should facilitate better post-intervention follow-up to help identify patients potentially requiring further intervention.

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P11

Impact of diagnosis and targeted interventions on the quality of life and cognition of patients with adrenal tumours: a systematic review

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Introduction
Adrenal hormone excess and malignancy are associated with clinical manifestations which can affect health-related quality of life (HRQoL) and cognition in patients with adrenal tumours. However, this has not been assessed systematically.
Methods
We conducted a systematic review of original research articles published between January 1990 and December 2023 in the MEDLINE, Embase, Cochrane, and CINAHL databases. Abstract screening, full-text review, and data extraction were conducted in parallel by authors working in pairs. Disagreements and data inconsistencies were resolved through consensus. The 2013 CONSORT-PRO extension statement was used for quality assessment.
Results
After screening 17,601 abstracts, 88 studies were included, which reported on 14,161 adults with adrenal tumours: 7102 had primary aldosteronism (PA), 3062 incidentalomas with or without mild autonomous cortisol secretion (MACS), 2287 adrenal Cushing's syndrome (CS), 1016 phaeochromocytoma (PHAEO), and 694 adrenocortical cancer (ACC). PA was associated with decreased HRQoL with impaired scores in both physical and mental components, as well as an increased prevalence of depression and anxiety, which improved with targeted interventions (adrenalectomy was more effective than mineralocorticoid receptor antagonists). HRQoL was compromised and fragility was more prevalent in patients with non-aldosterone producing adenomas on a spectrum of increased severity across non-functioning tumours, MACS, and CS, and were ameliorated by adrenalectomy. Decreased cognitive function was also observed in MACS and CS prior to treatment. PHAEO presented with impaired HRQoL and numerous cognitive-inhibiting symptoms, with one study showing improvement 3 months after adrenalectomy. Targeted interventions of ACC were associated with treatment-emergent adverse events negatively affecting HRQoL and cognition.

Studies were of moderate-to-high quality, with significant variability in the tools employed to assess the outcomes of interest and the use of adrenal tumour-specific tools was limited.
Conclusions
Adrenal tumours and related treatments affect HRQoL and cognition, which has implications for patient management and long-term follow-up.

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P12

An audit of steroid biomarkers in patients with adrenal lesions

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Background
Several steroids have been reported as possible biomarkers for differentiation of adrenal adenomas from adrenal cortical carcinomas (ACC). These include serum 11-deoxycortisol, urine tetrahydro-11-deoxycortisol (THS) and pregnenetriol. Simplification of testing is important due to identification of increasing numbers of adrenal lesions.
Methods
All Scottish urine steroid profile (USP) requests with clinical details of adrenal lesion from July 2017 until April 2024 were included. One request per patient was included. Clinical details were collated from the electronic patient record to include where available size of lesion, Hounsfield units, serum androgen profile and diagnosis. Patients were excluded if no diagnosis available.
Results
Three hundred and thirty patient samples were included, 58% female, 42% male with median age 63 years, range 24-91. Patients were classified into benign adenoma (75%), ACC (6%) and other (19%). Of those with ACC, 70% were female, 30% male, median age 58 years. All ACC patients had a lesion >4 cm and 75% had abnormal USP. THS was quantifiable in 75% (15/20) of the ACC group (median 2354 µg/24hr, range 219-35286 µg/24hr) compared with 1% (3/247) of the adenoma group (range 265-610 µg /24hr). Pregnenetriol was quantifiable in 65% (13/20) of the ACC group (median 2101 µg/24hr, range 222-8373 µg/24hr) compared with 5% (13/247) of the adenoma group (range 150-806 µg/24hr). Serum androgen profile was measured in 34% patients, 60% ACC group, 34% adenoma group. The median 11-deoxycortisol result was 30.6 nmol/l, range 2.5-$>$43.4 nmol/l in the ACC group, and 0.7 nmol/l, range $<$0.5-5.4 nmol/l in the adenoma group. The ACC patients with normal USP did not have serum androgen profiles measured.
Conclusion
THS, pregnenetriol and 11-deoxycortisol show promise as biomarkers, but a significant proportion of ACC are non-secretory. Serum 11-deoxycortisol is a simpler, cheaper test than USP and more appropriate for high throughput testing.

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P13

From fall to diagnosis: unraveling a rare case of pheochromocytoma

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We present a 62-year-old woman admitted after a fall that caused a severe head injury. During her hospitalization, she exhibited persistent leukocytosis despite negative inflammatory markers and cultures. Notably, she experienced episodes of delirium, which required intervention. Her medical history included palpitations, a normal sinus rhythm on ECG, treated ductal breast cancer, and tachycardia managed with beta-blockers. Her systolic blood pressure peaked at 249 mmHg, and she suffered a syncopal episode that led to shallow subgaleal hemorrhage observed on CT imaging. Given the unusual presentation and abnormal biochemistry, including hypokalemia and leukocytosis, we investigated potential endocrine causes rather than attributing her symptoms to sepsis. Laboratory tests revealed significantly elevated plasma metanephrine levels of 5686 pmol/l (normal: 51-358) and normetanephrine levels of 1959 pmol/l (normal: 137-1047). Urinary tests confirmed increased metadrenaline (25.3 µmol/24h; normal: 0-1.4) and normetadrenaline (5.03 µmol/24h; normal: 0-3). Cortisol levels were also elevated at 3300 nmol/l (normal: 140-700), with partial suppression after an overnight dexamethasone test (79 nmol/l; normal: $<$50) and unsuppressed ACTH at 22 pmol/l (normal 1.3-16.7). A diagnosis of pheochromocytoma, possibly with ectopic corticotropin-releasing hormone secretion, was made, and the patient was started on doxazosin. A CT scan revealed a 48mm left adrenal mass, suggesting characteristics of an adenoma rather than pheochromocytoma. Subsequent MRI and MIBG scans indicated a reduction in the mass size to 3.7 cm. The patient underwent laparoscopic left adrenalectomy, with histopathological findings confirming pheochromocytoma with central infarction. Following surgery, she experienced significant symptom relief, and her catecholamine, cortisol, and white blood cell counts normalized. This case highlights the need to recognize classic symptoms of pheochromocytoma, even when imaging results are inconclusive. This case underscores the importance of recognizing pheochromocytoma's classic symptoms, even in the presence of conflicting imaging results, highlighting the complexities involved in managing such cases.

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P14

Assessment of an oral corticosteroid withdrawal pathway for severe asthma patients receiving biologic therapies

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Background
The optimal approach for weaning maintenance oral corticosteroids (mOCS) in severe asthma patients receiving biologics remains unclear. Previous studies assessed hypothalamic-pituitary-adrenal function at 5 mg daily prednisolone, a supraphysiologic dose for many, necessitating further mOCS reduction for adrenal recovery.
Aim
We evaluated a protocol-driven nurse-led mOCS withdrawal pathway for severe asthma patients receiving biologics.
Methods
Severe asthma patients receiving biologics and mOCS, who had reduced mOCS to 5 mg prednisolone daily and maintained good asthma control, entered the withdrawal pathway. Prednisolone was decreased to 4 mg daily for 6 weeks then 3 mg daily for 6 weeks, followed by 09.00 serum cortisol measurement. Patients with cortisol $>$ 25 nmol/l followed a 20-week weaning protocol. Serum cortisol was re-checked 12 weeks after stopping mOCS.
Results
Of 102 patients, 92 had cortisol $>$ 25 nmol/l on 3 mg prednisolone and continued weaning. Seventy-three (72%) successfully discontinued mOCS with median [IQR] cortisol increasing from 192 [88-299] nmol/l on 3 mg prednisolone to 314 [248-437] nmol/l 12 weeks after discontinuation ($P < 0.0001$). Twenty-nine patients (28%) paused weaning due to adrenal insufficiency symptoms ($n = 22$), worse asthma control ($n = 1$), anxiety ($n = 2$) and other reasons ($n = 4$). The baseline cortisol in this group was 53 [25-166] nmol/l, and they are currently well receiving median 3 [3-3.9] mg prednisolone. Duration of prior OCS use was significantly shorter in the successfully weaned group compared to those who failed ($P = 0.003$). No serious adverse events occurred.
Conclusion
The majority of clinically stable asthma patients receiving biologics successfully withdrew mOCS without requiring dynamic adrenal function testing. This confirms that referral to Endocrinology is not helpful in patients who need withdrawal from prednisolone.

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P15

The benefits and pitfalls of wider hormone testing for incidental adrenal nodules prior to clinical review

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Introduction
Biochemical assessment of incidental adrenal nodules is increasingly performed prior to clinical review. Occasionally, serendipitous diagnoses can result. Here we

discuss two patients with adrenal nodules where additional endocrine testing both helped and hindered diagnosis, respectively.
Case details
Case 1 A 52-year-old man was referred following incidental detection of bilateral adrenal nodules. There were no clinical examination features of endocrinopathy. Biochemical evaluation demonstrated a non-suppressed cortisol level following dexamethasone administration (53 nmol/l); Opportunistic urine steroid profile testing revealed increase metabolites of 17-hydroxyprogesterone (17-OHP) in-keeping with congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency. Diagnosis was confirmed with Synacthen stimulated 17-hydroxyprogesterone and the patient was counselled and offered genetic testing. The adrenal lesions were deemed representative of underlying adrenal hyperplasia. Case 2 A 55-year-old lady was referred with incidental bilateral adrenal. Clinical examination revealed elevated body mass index but no definite stigmata of Cushing's syndrome. Baseline biochemical evaluation (plasma metanephrines, aldosterone, plasma renin activity, androgen profile and overnight dexamethasone suppression test) were normal but ACTH was markedly elevated at 282 ng/L (0-46) . Low dose dexamethasone suppression and urine cortisol were normal. Assay interference was considered and alternative assay testing revealed normal ACTH levels of 27 ng/L (7.2-63.3). Follow-up 6-month interval imaging revealed stable appearances of the adrenal nodules, and the patient was discharged from follow-up.
Discussion
Wider hormone testing for incidental adrenal nodules may identify rare conditions early. However, managing unexpected findings can be challenging. Careful test selection is advisable and knowledge of the relative strengths and limitations of tests used is essential. Including an androgen profile or urine steroid profile can be beneficial but requires caution due to potential false positives.

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P16

Novel medications inducing adrenal insufficiency – case report of suspected Adalimumab induced secondary adrenal suppression

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Adrenal insufficiency can arise from a primary adrenal disorder, secondary to adrenocorticotropic hormone deficiency, or by suppression of adrenocorticotropic hormone by exogenous glucocorticoid or opioid medications. Immune check point inhibitors (ICI) are reported to cause adrenal insufficiency, but this phenomenon has never been seen with ant-TNF inhibitors. We present a case of a 42-year-old female known to have severe Rheumatoid Arthritis resistant to traditional therapies who was started on Adalimumab (anti-TNF inhibitor) and one week later, presented to hospital with headaches and neck stiffness. She was initially treated as presumed meningoencephalitis but later on had a normal MRI Brain and normal CSF analysis. Due to ongoing dizziness, postural hypotension and episodes of vomiting, a 9 a.m cortisol was requested which came back low at 117 nmol/l (reference 133-537 nmol/l). A Short Synacthen test confirmed adrenal insufficiency (cortisol at 0 mins 40 nmol/l, at 30 mins 228 nmol/l, at 60 min 332 nmol/l). ACTH was found to be low at 2.0 ng/L (reference 10-50 ng/l) but rest of pituitary hormone profile was normal. She was started on oral hydrocortisone and her symptoms and later on biochemical markers improved drastically. This case was discussed in our local Pituitary MDT and with Rheumatology team, and they advocated the concurrent use of hydrocortisone and adalimumab. This case is unique as this phenomenon was never observed with monoclonal antibodies and this is the first ever case of suspected anti-TNF inhibitor induced secondary adrenal insufficiency. The likely explanations are either Adalimumab directly suppressed hypothalamic-hypophysial adrenal axis or caused an infection which resulted in indirect suppression of hypothalamic-hypophysial adrenal axis which ultimately caused secondary adrenal insufficiency. It is unclear how this patient developed secondary adrenal insufficiency, more research is needed in this area.

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P17

Characteristics of familial glucocorticoid deficiency (FGD) type-1 and 2: an update

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Introduction
FGD is a rare autosomal recessive disorder, characterised by isolated glucocorticoid deficiency. Loss-of-function mutations in *MC2R* (ACTH receptor) cause FGD type-1 (FGD1) and mutations in *Melancortin-2-receptor accessory protein (MRAP)* cause FGD type-2 (FGD2). Here, we describe characteristics of FGD1 and FGD2.
Methods
Retrospective analysis of our FGD international database. Statistical analysis performed on SPSS-Version-29. Significance defined as $P < 0.05$.
Results and discussion
Our database includes 70 patients with FGD1 (F=29, M=40, unknown $n = 1$) and 56 with FGD2 (F=17, M=27, unknown $n = 12$). Mean age of presentation for FGD1 was 2.21 +/- 3.13 yr (range 0.003-10.0 yr) compared to 1.90 +/- 4.01 y (range 0.003-18 yr) for FGD2, $P = 0.347$. There was no statistically significant difference in height, weight or BMI Z-scores between FGD1 and FGD2. Comparing FGD1 to FGD2, mean baseline serum cortisol and ACTH levels were similar (cortisol 25.0 vs 27.70 nmol/l, ACTH 238.45 vs 203.12 pmol/l). Hydrocortisone replacement was 15.2 +/- 4.0 vs 13.0 +/- 6 mg/m^2/day, higher than recommended dosages for primary adrenal insufficiency. Our database includes 26 different *MC2R* and 18 *MRAP* mutations. S74I is the commonest mutation for FGD1 (40%, $n = 28$) and M1I for FGD2 (21.2%, $n = 11$). *MC2R* missense mutations account for 78.6%, $n = 55$ of FGD1, whereas *MRAP* nonsense mutations (involving initiating methionine or causing truncating non-functional protein) account for 86.5%, $n = 45$ of FGD2. *MRAP* nonsense mutations present significantly earlier compared to missense *MRAP* mutations (mean age 0.538 +/- 0.914 yr, range 0.003-4.0 yr vs 7.528 +/- 7.142 yr, range 1.5 – 18.0 y), $P < 0.001$, and all *MC2R* mutations, $P = 0.006$.
Conclusions
MRAP nonsense mutations present clinically earlier compared to *MRAP* missense and *MC2R* mutations. There is no difference in anthropomorphic or biochemical markers between FGD1 and FGD2. Hydrocortisone replacement is higher compared to recommended dosages. Long-term follow-up data would help determine associated co-morbidities in FGD1 and 2.

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P18

A 24-weeks steroid weaning regimen is safe and effective in a patient with 20 years of chronic glucocorticoid use

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Introduction
Rapid withdrawal from chronic glucocorticoid (GC) treatment could precipitate adrenal insufficiency (AI), GC withdrawal symptoms (GWS) or recurrence of underlying inflammatory condition. Here we report a successful GC weaning case in clinical practice.
Case Report
A 52-year-old man was treated with oral prednisolone (5-20 mg/day) for atopic dermatitis for 20 years was commenced on Dupilumab resulting in remission. Chronic steroid had led to easy bruising and weight gain. He previously tried a 3-weeks steroid weaning regimen, starting with 5 mg daily in the first week followed by 5 mg every 2-days in the second week and 5 mg every 3-days in the third week. However, on the third week, he developed severe nausea and lightheadedness and prednisolone was resumed at 10 mg. Initial investigations revealed AI with 8am cortisol of <28nmol/l and serum adrenocorticotrophic hormone (ACTH) of 13.1 pmol/l (1.6-13.9 pmol/l). Initial Short Synacthen Test (SST) confirmed AI (0-minutes cortisol 34nmol/l, 30-minutes cortisol 74nmol/l, 60-minutes cortisol 77nmol/l). He was started on a NICE-approved steroid weaning regimen, with dose of prednisolone reduced from 5 mg to 0 mg over 24 weeks.[1] He also received 6 weekly telephone consult to assess for symptoms of GWS and AI. SST on 13th week of the regimen showed 0-minutes cortisol of 74nmol/l, 30 and 60-minutes cortisol of 121nmol/l and 134nmol/l, and on week 22 cortisols of 131nmol/l, 183nmol/l and 217nmol/l. Serum ACTH rose from 13.1 pmol/l to 24.3 pmol/l, suggesting slow corticotroph recovery[2]. The patient is currently at 22nd week of the regimen (1 mg three times weekly) and has not reported GWS or AI.
Conclusions
This 24-weeks GCs weaning process is safe and effective in allowing adrenal glands recovery without the adverse effects of AI or GWS. Larger studies are needed to confirm this.

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P19

Takutsubo cardiomyopathy secondary to phaeochromocytoma a unique presentation

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Background
Takotsubo cardiomyopathy (TTC) is a type of non-ischemic cardiomyopathy typically induced by emotional or physical stress. Patients commonly present with symptoms mimic those of acute coronary syndrome with normal coronary vessels. Characteristic findings include transient dilatation and dysfunction of left ventricle. TTC has recently been recognized to occur due to various physical stressors, including excess of catecholamine such as pheochromocytoma/paraganglioma. Cardiomyopathy was reported in 11% of cases of pheochromocytoma /paraganglioma (PGL).
Case description
Our case presents a unique scenario involving a 62-year-old woman with a history of well controlled hypertension (on ramipril) and newly type 2 diabetes. She presented to same day emergency care, with severe vomiting over four days without chest pain, initially diagnosed with acute kidney injury. Her ECG showed global T-wave inversions, and troponin levels raised to 1624 ng/l. A bedside echocardiogram revealed a dilated left ventricle with global dyskinesia, leading to a diagnosis of myocarditis and transfer to the cardiac unit. Subsequent cardiac angiography indicated normal coronary arteries. MRI cardiac revealed features of stress cardiomyopathy and incidental adrenal lesion measuring approximately 6.7 cm. Plasma metenaphrine was >25000 pmol/l Normetanephrine >25000 pml/l, raising the suspicion of pheochromocytoma-induced cardiomyopathy. She developed a hypertensive crisis due to unopposed beta-blockade after being started on carvedilol for left ventricular failure. Once transferred to the endocrinology ward, her symptoms resolved completely after discontinuing carvedilol and initiating doxazosin, which was gradually titrated up to 4 mg per day. She was later reintroduced to carvedilol at a dose of 12.5 mg. Her systolic blood pressure remained well-controlled, under 120 mmHg, with manageable postural hypotension. MIBG later showed appreciable uptake in left adrenal. A plan was made for a laparoscopic adrenalectomy.
Discussion
This case report highlights the importance of considering paheo/paraganglioma. As a cause of Tabkotsubo /stress cardiomyopathy even with atypical presentation.

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P20

An analysis of symptom scoring in a large cohort of patients with phaeochromocytoma and paragangliomas

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Background
Phaeochromocytomas and paragangliomas (PPGLs) often present incidentally and many patients are asymptomatic. Symptoms are often non-specific but can include palpitations, hyperhidrosis or headaches and are usually linked to catecholamine hypersecretion measured by plasma metanephrines. Patterns of secretion can vary based on underlying genetics and can be grouped according to defined clusters. Our study aimed to evaluate symptoms of patients with suspected PPGLs in a large UK cohort.
Methods
Retrospective data were collected on patients with probable PPGLs at Leeds Teaching Hospitals between 2018-2023. Data collected included demographics, symptom status, biochemistry, lesion characteristics and genetics.
Results
99 patients (56.1% male) were included, mean age was 55 ± 19 (SD) years. 43(43.4%) patients had at least 1 symptom, with the most common being palpitations in 39 (91.6%), hyperhidrosis in 27 (62.7%) and tachycardia in 25 (58.1%). Of symptomatic patients, 41(95.3%) had secretory lesions. Whilst both normetanephrine and metanephrine levels were higher in symptomatic patients compared with asymptomatic patients, these differences were non-significant. There were also no significant differences in lesion size between the two groups. Using a previously validated symptom scoring tool (Geroula *et al*) for PPGLs, a score ≥ 3 is suggestive of PPGl. 18 of the whole cohort (18.2%) had a score of ≥ 3. 45 lesions had cluster 1 characteristics, of these 25 (55.6%) were symptomatic. 46 lesions had cluster 2 characteristics and 16 (34.7%) of these were symptomatic. We found there was no clear difference in basic symptom score between cluster groups.
Conclusion
Our data suggest that the majority of patients with PPGLs may be asymptomatic, and many do not present with the hallmark symptoms of PPGl. We did not find any clear differences in symptoms between cluster 1 and cluster 2 lesions. Additionally, metanephrine levels and size of lesion did not correlate with symptom status nor scores.

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P21

A case of Addison's disease and dilated cardiomyopathy

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We present this case of 29-year old lady who presented 3 weeks post-partum with new onset dilated cardiomyopathy.
Case report
This lady was complaining of fatigue, dizziness and weight loss since 2019. She went to Turkey and felt that 'tan never went away'. She had her thyroid function done by GP in January, 2020, which showed sub-clinical hypothyroidism with positive TPO. She was started on Levothyroxine which she never tolerated. She lost 25 kg of weight in 2 years. She became pregnant in June 2020 and had hyperemesis which continued till end of pregnancy. Baby's growth stopped at end of term. She had uneventful delivery in Feb, 2021. She had an episode of black-out 3 weeks post-partum and presented to hospital. On admission, she was noted to have pigmentation on neck, shoulders and face. Her electrolytes showed hyponatremia and hyperkalaemia. She had short synacthen test which showed cortisol $<$ 30 at 0 and 30 minutes. Her ACTH was >2000. Her adrenal antibodies were positive. She was started on hydrocortisone replacement. As she had collapse and positive D- dimer, CTPA was done which showed pulmonary edema. She had ECG which showed global T-wave inversion. Her trop was elevated at 231 and BNP at 11,486. She had ECHO cardiogram which confirmed reduced ejection fraction of 38% and left ventricular hypokinesia. She was started on low dose beta blockers and ACEi. She had cardiac MRI 72 hours later which showed mildly dilated LV and normal ejection fraction. The changes were not suggestive of post-partum cardiomyopathy. A follow up cardiac MRI scan in 3 months showed complete resolution of changes. Her BNP returned to normal.
Conclusion
This case reflects a rare complication of Addison's disease with resolution of cardiomyopathy after hormonal replacement therapy.

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P22

A rare case of cushing's syndrome during pregnancy: diagnosis, management, and postoperative outcomes

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A 26-year-old-pregnant woman at 22 weeks presented with hypertension (155/94 mmHg), gestational diabetes (GDM), purple striae, and acne on her chest and back. Physical examination showed fat deposits in her interscapular and neck regions, emotional instability, and easy bruising, but without facial rounding or muscle wasting. She was started on Labetalol and Nifedipine for hypertension, and GDM was managed with dietary changes. Initial laboratory results revealed elevated morning serum cortisol of 1100 nmol/l, suppressed ACTH (<3 pg/mL), 24-hour urinary cortisol of 3510 nmol/L-eight times the normal value. At 24 weeks, hydrocortisone day-curve test indicated no diurnal cortisol variation. Dexamethasone suppression tests (DST) with 2 mg and 8 mg doses showed 0% suppression, with cortisol remaining at 1261 nmol/l and 1437 nmol/l, respectively. Plasma metanephrines were normal. MRI adrenal scan identified 3.8 cm heterogeneous left adrenal adenoma After multidisciplinary team consultation, laparoscopic left adrenalectomy performed at 28 weeks' gestation. Intraoperatively, she received hydrocortisone replacement (20/10/10 mg). Post-surgery, cortisol levels fell to 390 nmol/l, with marked improvements in mood, blood pressure, and glycemic control, negating the need for antihypertensive medication. She experienced steroid

withdrawal symptoms and continued hydrocortisone (10/5/5 mg) throughout the pregnancy. Histology confirmed adrenal adenoma. She delivered a healthy baby at 34 weeks + 6 days. Three months post-adrenalectomy, short Synacthen test (SST) showed inadequate adrenal response, with a peak cortisol of 203 nmol/l, necessitating continued hydrocortisone. At six months, SST results remained low, but by ten months, adrenal function improved with a peak cortisol of 552 nmol/l, reaching 609 nmol/l by eleven months, allowing for hydrocortisone discontinuation. Cushing's syndrome during pregnancy is rare, with 138 reported cases. Pregnancy-induced physiological changes can mimic Cushing's, complicating diagnosis. Elevated urinary/salivary cortisol and 8 mg DST are valuable for differentiating Cushing's from pregnancy-related changes.

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P23

Management of severe hyponatremia in a HDU/ITU setting

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Background
Hyponatremia is the most common electrolyte imbalance encountered in clinical practice. It is associated with increased morbidity and mortality. Despite this, it remains a diagnostic and therapeutic challenge and its management varies across different settings.
Aim
The aim of this study is to provide an overview of the management of severe hyponatremia in HDU and ITU settings of a District General Hospital and to determine whether patients with severe hyponatremia were managed in line with the trust's guidelines.
Method
A descriptive, retrospective hospital record study was performed using a bespoke audit tool (Snap). All patients with an episode of severe hyponatremia (sodium level $<$125mmol/l) managed in HDU and ITU during a calendar year (2023) were identified and audited (56 patients).
Results
42% of the patients were discussed with the ITU/Medical registrar on presentation. 27% were given a single bolus of hypertonic saline (2.7% Sodium Chloride) via peripheral venous access as per the local guidelines and indication. 27% of them received a second infusion of hypertonic saline and 30% required a third dose of hypertonic saline. Only 4% were monitored with hourly venous blood gases. None of them were monitored for phlebitis following the administration of hypertonic saline.11% had an endocrinology team consultation. 46% of patients achieved the desired sodium level rise of less than 8mmol in the first 24 hours of presentation.
Conclusion
No assurance was found and most of the key standards of care were found to be absent. Immediate action was implemented by the introduction of a proforma for management of severe hyponatremia. The findings were presented in the audit meeting and a re-audit will take place in order to test the implemented change.

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P24

Vaccine-induced thrombosis and thrombocytopaenia with bilateral adrenal haemorrhage

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Summary
Vaccine-induced thrombosis and thrombocytopaenia (VITT) is a rare complication associated with the ChAdOx1 (Astra Zeneca, University of Oxford) adenoviral vector vaccine against severe acute respiratory syndrome coronavirus (COVID-19). We herein present the case of a 47-year-old female who developed bilateral adrenal haemorrhage as a sequela to VITT following administration of this vaccine.
Background
A number of cases of unusual thrombosis and thrombocytopenia has been reported in individuals receiving the ChAdOx1 vaccine. This very rare prothrombotic syndrome was termed vaccine-induced thrombosis and thrombocytopaenia (VITT). Here, we present the case of a patient with VIIT complicated by bilateral adrenal haemorrhage.
Case Presentation
A 47-year-old female, presented a few days history of epigastric pain and vomiting. The patient had received her first dose of the AZ vaccine three days prior. During her admission, she developed shortness of breath, fatigue and postural dizziness. Observations were in the normal range. No palmar or buccal pigmentation was noted.
Investigations
Initial blood investigations were normal. Subsequently, the platelet count fell to 10 x 10^9/l. Blood lactate (6.07 mmol/l) and d-dimer (24,004 µg/l) were elevated. CT abdomen and pelvis with contrast showed bilateral adrenal haemorrhage most likely due to adrenal vein thrombosis. A right pulmonary embolus was also noted. Antiphospholipid syndrome antibodies and antinuclear antibodies (ANA) were negative. Heparin-induced thrombocytopaenia (HIT) screen was positive detecting antibodies against platelet factor 4. Short synacthen test showed suboptimal response.
Treatment
A diagnosis of VITT was made and treatment commenced with intravenous immunoglobulin, the direct thrombin inhibitor argatroban and IV hydrocortisone. Once the platelet count improved, treatment was changed to apixaban, oral fludrocortisone and hydrocortisone.
Discussion
On the backdrop of the vaccination programme against COVID-19, VITT has emerged as a rare but life-threatening complication following AZ vaccine administration. Bilateral adrenal haemorrhage is a potentially devastating complication of VITT.

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P25

'Unrevealing the mismatch: discrepancies between imaging and AVS results in primary hyperaldosteronism'

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Overview
Discrepancies between adrenal imaging and adrenal vein sampling (AVS) are relatively common in primary hyperaldosteronism, occurring in 20-40% of cases. AVS is considered the gold standard for determining whether aldosterone overproduction is unilateral or bilateral, whereas CT/MRI is better for anatomical localization.
Case presentation
Screening tests showed elevated aldosterone (462) and suppressed renin ($<$0.1), suggesting primary hyperaldosteronism. A saline infusion confirmatory test revealed increased aldosterone (240) with a high aldosterone-to-renin ratio (ARR) . Imaging showed a 4 cm left adrenal nodule without concerning features, and adrenal vein sampling indicated right-side dominance. A whole-body FDG PET CT confirmed no significant changes in size or activity of the left adrenal nodule. with a minimal cancer risk. Due to the challenges in obtaining a CETO PET scan and the absence of concerns from AVS (adrenal vein sampling) results, the patient underwent laparoscopic right adrenalectomy on November 13, 2024. All antihypertensive medications were discontinued postoperatively. The patient was discharged without complications and with follow-up arranged with the surgical team. Histological outcome showed a nodule measuring 8$\times$9$\times$6 mm, consistent with an adrenal cortical adenoma.
Discussion
Discrepancies between adrenal venous sampling (AVS) and imagines can complicate adrenal disorder diagnosis. AVS is more sensitive for localizing aldosterone production, while CT/MRI/ PET may miss hormonal activity due to metabolic factors. These differences can lead to conflicting results, highlighting the need to understand both methods to improve diagnostic accuracy and patient care.

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P26

Use of MIBG scanning in the diagnostic pathway for phaeochromocytoma and paragangliomas; experience of a uk tertiary centre

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Background
Phaeochromocytomas and paragangliomas (PPGLs) are often identified incidentally, with a high proportion being asymptomatic. Screening, typically with unenhanced CT scan, and biochemistry is often inconclusive. Therefore, many patients have additional I-123 metaiodobenzylguanidine scintigraphy (MIBG) which may help with diagnosis and staging. Sensitivity/specificity of MIBG in PPGLs vary depending on lesion characteristics and genetics. This study aimed to evaluate the role of MIBG in PPGL management in a large UK cohort.
Method
Retrospective data were collected on patients with probable PPGLs at Leeds Teaching Hospitals between 2018-2023. Data collected included demographics, lesion properties, screening biochemistry +/- MIBG and histological diagnosis.
Results
Of 99 patients (56.6% male), 90 (91.8%) had secretory biochemistry. 73 (91.2%) of those with available histology were consistent with PPGl. 72 (72.7%) underwent an MIBG scan. Patients who did not have MIBG scans tended to have larger lesions (mean 4.9 cm versus 3.7 cm). 66 (91.7%) of MIBG scans showed avidity. Of those with secretory biochemistry, 68 (75.6%) had MIBG, 63 of these (92.6%) showed avidity. Management changed as a result in only 3 cases. In the non-avid group, 4 (80.0%) were PPGL histologically. In 8 patients with non-secretory biochemistry, 4 (50.0%) had MIBG and 3 of these showed avidity. One case although MIBG-avid, histologically was not a PPGl. One case was a non-avid, non-secretory PPGl. Of 6 patients within the whole cohort who had non-avidity on MIBG, 3 had further imaging.
Conclusion
Use of MIBG in initial characterisation of PPGLs in patients with secretory biochemistry does not appear to alter diagnosis or management in the vast majority of cases. In patients with non-secretory biochemistry but radiological suspicion of PPGL, MIBG was useful in guiding diagnosis in 75% of cases. These data suggest that MIBG use should be targeted to patients with diagnostic uncertainty, particularly in those with non-secretory biochemistry.

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P27

A comparison between hydrocortisone and prednisolone in the treatment of adrenal insufficiency – HYPER-AID study interim results from a tertiary care center

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Background
Adrenal insufficiency (AI) is treated with lifelong glucocorticoid replacement historically with Hydrocortisone (2-3 divided doses per day) (1). Prednisolone is an alternative option with longer half-life up to 3.2 hours and requires once daily dosage. Currently there is no clear evidence indicating the superiority of one medication over the other (2).
Objectives
To investigate the effects of hydrocortisone and prednisolone on bone health, cardiovascular risk, blood glucose levels, and overall well-being in patients with AI.
Methods
A retrospective observational study was conducted at UHL, following the established protocol for the 'Hydrocortisone versus Prednisolone for the Treatment of Adrenal Insufficiency Disease' (HYPER-AID Study), IRAS ID: 234243. Baseline data, including anthropometric measurements, cardiovascular (CV) risk factors, and metabolic biochemistry, were collected before switching from HC to once-daily Prednisolone and followed-up after a minimum of four months.
Results
$n = 18$, 11 were male, with a mean age of 57.8 years and mean weight of 82.90 $\pm$ 15.2 kg. Hydrocortisone (HC) dosages, ranging from 20 to 30 mg/day, were replaced with 3 to 5 mg of prednisolone. The mean follow-up duration was 13 months. There were no significant changes in BMI (29.57 to 28.89 kg/m^2), mean waist circumference (100.9 cm to 100.5 cm), or HbA1c levels (5.98% to 5.92%). Additionally, no significant differences were observed in blood pressure, heart rate, FBC, bone profile, lipid profiles, serum electrolytes, renal and liver functions, or hormonal profiles. All patients opted to continue treatment with Prednisolone due to its convenience and general wellbeing reasons.
Conclusion
Prednisolone appears to be a safe alternative to hydrocortisone (HC) as replacement therapy in adrenal insufficiency (AI) patients. Patients showed a preference for prednisolone due to the convenience of once-daily dosing. Interim analysis suggests that prednisolone is non-inferior to HC, but further research with larger cohorts is needed to confirm these findings.

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P28

Hypoglycemic therapy in patients with type 2 diabetes mellitus after cardiovascular surgery

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Introduction
The prevalence of type 2 diabetes mellitus (T2DM) is rising, currently affecting over 9% of the adult population. Approximately 52% of these individuals suffer mortality due to cardiovascular disease, highlighting the need for effective surgical management strategies for high-risk patients. This study examines hypoglycemic therapy in T2DM patients undergoing cardiovascular surgery via percutaneous coronary intervention (PCI).
Materials and Methods
We analyzed data from 29 T2DM patients admitted to the Republican Specialized Scientific Practical Medical Centre of Endocrinology. Pre- and post-surgery metrics included fasting and postprandial glycemia, HbA1c, CRP levels, heart rate, and EchoECG findings. Patients were categorized based on hypoglycemic therapy: 12 received basal-bolus insulin therapy, while 8 were treated with SGLT2 inhibitors, with or without incretins (GLP1/GLP1R analogs or DPP4 inhibitors).
Results
Post-surgery, fasting glycemia decreased by 1.7 times ($P < 0.05$) and postprandial glycemia by 1.8 times ($P < 0.05$). HbA1c levels also fell significantly (1.4 times, $P < 0.05$) due to tighter control and adherence to therapy. While heart rates remained stable, both systolic and diastolic blood pressures showed significant reductions. Coagulation improved, evidenced by a 1.4-fold decrease in fibrinogen ($P < 0.05$) and a 40% reduction in CRP levels. EchoECG results indicated improvements in heart compartment size and function, with myocardial blood flow increasing by 45%. Patients on a combination of SGLT2 inhibitors and incretins exhibited superior biochemical and hemodynamic outcomes.
Conclusions
T2DM patients undergoing cardiovascular surgery demonstrated enhanced glycemic control, reduced CRP levels, and improved heart function, alongside increased cardiac blood flow. Initial findings suggest that combined therapy with SGLT2 inhibitors and incretins may lead to better outcomes. Further research with larger patient cohorts is warranted.

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P29

Perioperative steroid management for patients undergoing unilateral adrenalectomy for autonomous cortisol secreting adrenal adenoma

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Background and rationale
Autonomous cortisol secretion (ACS) has become a distinctive clinical condition without clinical feature of Cushing's syndrome but significantly associated with metabolic complications and adrenalectomy can improve biochemical and clinical parameters. Guidelines suggest prescribing steroid perioperatively until

'recovery of the HPA axis'. A dose of intravenous dexamethasone is also given routinely during general anaesthesia for post-operative nausea. However, short term steroid therapy was not without risk. In our centre, we have started adopting an MDT tailored approach and some treated without perioperative steroid. 9am serum cortisol was checked at day 1 post operative period for those cases. A close clinical monitoring for potential hypoadrenalism was observed.
Methods
Retrospectively, we reviewed our ACS management from 2016-2024. The terms 'autonomous cortisol secretion' and 'adrenalectomy' were searched. Detailed investigation for cortisol excess, cardiovascular disease risk factors, review of anaesthetic charts, post-operative adrenal function testing results were recorded.
Results
We identified 80 patients who failed dexamethasone suppression test (mean cortisol 112.8nmol/l). Among them, 13 patients ((hypertension(n = 10), diabetes(n = 10), Other CVD risk (6), osteoporosis(n = 7)) underwent adrenalectomy. With MDT approach, perioperative steroid therapy was not given in 8 patients (61%), 6 had cortisol >300nmol/l at 9am on day 1 post-op. 2 patients had lower cortisol (275 and 210nmol/l), subsequent same day short synacthen test(SST) excluded hypoadrenalism (peak cortisol 612 and 551nmol/l). 5 patients (87%) who were given steroid had normal SST at first post op follow-up. All patients were cured (Post-operative dexamethasone suppression test with cortisol of <50nmol/l).
Conclusions
We demonstrated that sparing use of steroid in ACS perioperatively was safe. Performing a 9am cortisol at day 1 post-op is essential to prevent potential adrenal insufficiency. We have reduced steroid burden especially for those with diabetes as well as the need for outpatient SST. Further validation with larger numbers is required.

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P30

Development and validation of salivary cortisol and cortisone quantitation by liquid chromatography-tandem mass spectrometry to evaluate hypothalamic pituitary adrenal axis function

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Introduction
Home cortisol testing in saliva is simple and cheap. Late-night salivary cortisol or cortisone and waking salivary cortisone show high diagnostic accuracy for Cushing's syndrome and adrenal insufficiency, respectively. This project aimed to develop a Liquid Chromatography-Tandem mass Spectrometry (LC-MS/MS) method to measure cortisol and cortisone in saliva in an NHS teaching hospital, which offers an accurate alternative for measurement of cortisol and cortisone that overcomes any assay interference issues in immunoassays.
Methods
Samples were collected using *Salivette*® devices. The method was developed using *Chromsystems*® - *MassChrom*® Cortisol, Cortisone in Saliva. Analysis was performed using LC-MS/MS.
Results
Validation of the assay revealed no significant effects from ion suppression or carryover. Lower limit of detection and quantitation were 0.77 and 1.40 nmol/l for cortisol, and 1.07 and 2.13 nmol/l for cortisone, respectively. The assay was linear from 2.83 to 267.04 nmol/l for cortisol and 25.96 to 506.75 nmol/l for cortisone, with r^2>0.999. Intra-assay precision was < 5% CV for cortisol and cortisone and inter-assay precision <10% across the analytical range of the assay. Uncertainty of Measurement was <10%. An assessment of bias for cortisol was performed by comparison to external quality control reference values, with all results falling within the interquartile range of the target reference values. Patient comparison (n = 50) gave regression equations using Passing-Bablok for cortisol and cortisone of $y=0.01919+0.9649x$ and $y=0.6382+0.9536x$, both with r^2= 0.99 (CI of 95%). The mean relative differences were 2.1% for cortisol and 2.6% for cortisone between methods.
Conclusion
We have developed an assay for the measurement of salivary cortisone and cortisol. The test will obviate the need to send samples to an external central laboratory, hence improving turnaround time and reducing costs. The validation and verification processes demonstrated that the assay is accurate and precise and suitable for routine clinical application.

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P31

Approach to adrenal Ganglioneuroma in adults, case series and review of literature

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Background
Ganglioneuromas are rare benign tumours that arise from neural crest cells including the adrenal medulla. Adrenal ganglioneuromas account for approximately 1% of all adrenal incidentalomas. Due to their rarity, the characterization of these lesions pre- operatively is challenging, with diagnosis typically being made post- operatively on histological assessment.
Method
A retrospective review was performed on the presentation and management of ganglioneuromas at a tertiary referral centre over a 5 year period.
Result
5 ganglioneuromas were treated, 4 males and 1 female patient. The median age was 23 years (range 16-51 years). The median size radiologically was 5.5 cm (range 3.5-14 cm) and pathologically was 5.8 cm (5-14 cm). All lesions were identified on CT, 3 as incidentalomas and 2 following presentations with abdominal pain. All patients had complete biochemical adrenal work up inclusive of plasma or urinary metanephrines, aldosterone- renin ratio and a 1 mg overnight dexamethasone suppression test. Three patients required additional biochemical assessment including tumour markers. A broad range of radiological investigations were performed to inform management including CT, MRI, MIBG, and MR Angiography. One patient proceeded to an image guided biopsy. All ganglioneuromas were resected with a surgical approach tailored to the lesion. Two underwent open resection, two transperitoneal laparoscopic and one retroperitoneal approach. Four patients had surveillance imaging (CT/ within a year of resection or longer if suspicious findings were identified.
Conclusion
Our experience with ganglioneuromas is of a heterogeneous group with a spectrum of presentations and a resource- intensive approach to reaching a diagnosis. This latter challenge reflects the rarity of the condition.

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P32

Weaning patients off long-term prednisolone: a survey of general physicians' practice

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Background
Prolonged glucocorticoid (GC) use is associated with significant morbidity and mortality, including the development of glucocorticoid-induced adrenal insufficiency (GI-AI). Recent NICE guidelines recommend a slow taper if patients are treated with GC for longer than 12 weeks. However, there is limited understanding into current practice across different medical specialties and the barriers to GC weaning.
Aim
To establish how GCs are weaned in patients across medical specialties.
Methods
An anonymous online survey was disseminated to internal medicine physicians at Imperial College Healthcare NHS Trust and the National University Hospital in Singapore between May - July 2024.
Results
Respondents were asked about their management of a patient no longer requiring 10 mg prednisolone for their underlying condition. Forty-eight responded to the survey from a broad range of medical specialties: 11.6% Rheumatology, 9.3% Respiratory, 11.6% Dermatology, 16.3% Gastroenterology, 20.9% Neurology, 4.6% Haematology, 2.3% Nephrology and 23.3% Acute Medicine. Approaches to discontinuing prednisolone were heterogeneous. 16.7% of respondents would stop prednisolone abruptly. In contrast, 47.9% said they would wean slowly (e.g. 1 mg per month) compared with 35.4% who said they would taper more rapidly (e.g. 1 mg over two weeks). 10.4% of respondents would refer to endocrinology to supervise weaning, whilst 12.5% would confirm with a random or early morning

cortisol. 14.6% of respondents would arrange an SST. Amongst the respondents, 71.7% reported relapse of the underlying condition, 8.7% reported symptoms of GC-AI and 8.7% reported symptoms of GC withdrawal.

Discussion

The guidelines correctly suggest that Endocrinologists should not be involved in therapeutic GC tapering. As reported here, relapse of the underlying condition is common, and endocrinology input may not be appropriate when this occurs. However, there is huge variation in the rate of GC weaning and evidence-based research establishing effective GC weaning protocols at physiological doses is indicated.

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P33

A complex case adrenocortical carcinoma requiring multi-dimensional approach: a clinical case report

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52 years old was admitted to the hospital following 2 weeks of lower limb pain and abdominal swelling. As part of her investigations, she had CT Pulmonary angiogram and CT AP which showed that she had right adrenal lesion with haemorrhage and necrosis in keeping with adrenal carcinoma and invasion of IVC and extension into the right atrium. MRI showed that she had malignant adrenal lesion of 8.8 X 7.6 cm with extension into the IVC and right atrium. She was referred to the MDT regarding the management options as it required multiple teams to be involved for its management. In the meanwhile, she had PET CT scan which showed the lesion to be hypermetabolic and infiltrative in nature. There was no distant metastasis but had extension into IVC and right atrium. She also had full hormonal workup that included 24-hour urine cortisol, ODST Aldosterone renin ratio, Plasma metanephrines, 17-OHP, DHEAS, Androstenedione, Testosterone and SHBG were negative, essentially meaning that lesion was non secretory. She was planned for combined de-bulking surgery involving Liver, Endocrine, Vascular and Cardiothoracic surgical teams as per recommendation from Adrenal MDT. The complex surgery was performed by doing cardiopulmonary bypass between SVC and CFA. She was in deep hypothermic cardiac arrest for 14 minutes and had atrial thrombectomy and tumour was removed from IVC. She also had excision of right adrenal gland. Hence, all macroscopic tumour was removed from the abdomen, IVC and right atrium. She also had required chest drain for pneumothorax. Post surgery she was started on Mitotane and is under oncology. The histology confirmed a non-secretory adrenocortical carcinoma and Ki-67 to be 15%. This case emphasizes the value of a team-based approach in tackling complicated cases. Moreover, an individualized treatment plan can lead to substantial improvements in quality of life.

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P34

Bilateral phaeochromocytoma in neurofibromatosis type 1 - a rare entity but not to be missed

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We present a 65-year-old gentleman with Neurofibromatosis Type 1 (NF-1), referred for assessment of adrenal nodularity. These were incidental findings on CT as he had imaging for obstructive defaecation and weight loss. Colonoscopy showed a proximal ascending colon lesion with histology keeping with inflammatory polyp. There were no clinical features indicative of catecholamine excess. The MDM considered carefully the comprehensive imaging. Although there was confidence that the right lesion was phaeochromocytoma, on balance bilateral adrenalectomy was recommended given the indeterminate nature of the left gland, with underlying NF-1.

Histology revealed bilateral pheochromocytoma:

Right nodule - Ki67 2.4%, PASS 9/20

Left nodule - Ki67 0.7%, PASS 3/20

Post-operative plasma metanephrines were unremarkable. Subsequently, he underwent an open right hemicolectomy and ileocolostomy. There were 56 polyps, but none were suggestive of moderate/high grade dysplasia. The genetic susceptibility and association between NF-1 and pheochromocytoma is known with incidence of 0.1-5.7%. Bilateral pheochromocytoma is even rarer. Screening for phaeochromocytoma should be considered in these patients with careful decision making, especially when bilateral adrenal lesions are present.

Biochemistry	Results (pmol/l)	Normal values (pmol/l)
Plasma metadrenaline	9;2,546	<510
Plasma normetadrenaline	1,800	<1180
Plasma 3-methoxytyramine	73	<180
Imaging		
CT Adrenals	2 cm right adrenal nodule with small cystic spaces: -Pre-contrast attenuation of 42HU -Absolute washout 55% -Relative washout 31% -Small cystic spaces shows persistent enhancement 1.7 cm left medial limb nodule: -Benign washout characteristics 1.1 cm left proximal medial limb nodule: -Pre-contrast attenuation of 32HU -Absolute washout 32% -Relative washout 19%	
MR Adrenals	2 cm well-circumscribed right adrenal body, suspicious for phaeochromocytoma Indeterminate left adrenal lesions, T2 hyperintensity	
MIBG Iodine 123 scan	Pathological high-grade increased uptake in right adrenal mass lesion No pathological activity in left adrenal gland	
FDG-PET CT	High-grade uptake caecal mass Moderate uptake in right adrenal nodule consistent with a pheochromocytoma Low-intensity update in 1.1 cm left nodule	

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P35

Evaluation of glucocorticoid weaning practices in a tertiary centre

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Background

Prolonged and increased cumulative use of glucocorticoids (GCs) suppress the hypothalamic-pituitary-adrenal axis (HPA) leading to glucocorticoid-induced adrenal insufficiency (GI-AI). There is limited evidence and no consensus as to whether thrice-daily shorter-acting hydrocortisone (HC) or once daily longer acting prednisolone is more effective in allowing recovery of the endogenous cortisol production whilst GCs are weaned.

Aim

To evaluate current GC weaning practices at our centre, including the rate of GC-dose reduction for recovery of the HPA axis.

Methods

One-year retrospective study for patients attending the endocrine clinic with GI-AI.

Results

Forty-five patients were referred for GI-AI, of which 39 were on HC and 6 were on prednisolone. 42.2% (19/45) were successfully weaned off GCs over an average of 9.2 months, requiring 2-3 clinic appointments. Twenty-six patients (57.7%) remained on GC after one year. Of those who were successfully weaned, 17/39 (43.5%) were on HC and 2/6 (33.3%) were on prednisolone. HC dose reduction occurred at an average of 2.8 mg reduction per month over a nine month period. All patients underwent an SST prior to being completed weaned, patients underwent an average of two SSTs during their GC wean. Mean baseline cortisol was 136nmol/l and no difference in baseline cortisol level between those who were successfully weaned and those who were not weaned off GC. Five patients (11.1%) had also used other forms of GCs – including inhaled (6.6%) and topical (4.4%) GCs. Seven patients had previously used herbal and traditional Chinese medicine, which was felt to be the cause of their HPA axis suppression. Fourteen (31.1%) patients experienced glucocorticoid-withdrawal symptoms (GWS). The symptoms reported included: dizziness (13.3%), hypotension (4.4%) and fatigue (15.6%).

Conclusion

Both HC and prednisolone can be used to successfully wean patients off long-term GCs, allowing for recovery of the HPA axis.

Keywords: Cortisol, adrenal insufficiency, weaning

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P36

Verification of LC-MS/MS analysis coupled with machine learning models for the identification and classification of primary aldosteronism

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Introduction
Primary aldosteronism (PA) is one of the most common causes of secondary hypertension, leading to a higher risk of patient morbidity and mortality. Through collaboration with the University of Dresden and New South Wales (NSW) Health Pathology, we have developed a LC-MS/MS method for measurement of aldosterone and various metabolites to streamline identification and subtype classification of PA utilising previously validated machine learning (ML) models. This has been shown to enable early identification of PA patients with KCNJ5 mutations to enable swifter adrenalectomy, without necessitating the need for adrenal vein sampling or other confirmation.
Methods
Analysis of 18-hydroxycortisol, 18-oxocortisol, DHEA, 17-hydroxyprogesterone, androstenedione, corticosterone, 11-deoxycortisol, 21-deoxycortisol, cortisone, cortisol, aldosterone, 11-deoxycorticosterone and 11-dehydrocorticosterone was performed in a single LC-MS/MS method after supported liquid extraction (SLE) of plasma samples. Analytical and ML comparisons were undertaken between MFT, Dresden and NSW using fully validated methods.
Results
Validation parameters were acceptable. There was clear numerical correlation for the analytes, analysis highlighted a negative bias for 18-hydroxycortisol which was minimised after a change in calibration material. Results were processed through ML programs and outcomes compared.
Discussion
We have developed an LC-MS/MS assay and proven the results generated are comparable with the groups in Dresden and NSW. To our knowledge, we are the only UK laboratory involved in this project and hope to develop our in-house method further, with a view to implementing this approach in the future for diagnostic work up of PA patients.

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P37

Secretory composite pheochromocytoma – ganglioneuroma of the adrenal gland: a case report

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Background
Composite pheochromocytoma (CP) is a rare condition with only about one hundred cases reported in the medical literature. The diagnosis is based solely on pathological findings, with most patients having manifestations of excess catecholamines with no distinctive pre-operative clinical or radiological features compared to usual pheochromocytoma (PCC) or paraganglioma (PGL). Prompt and accurate diagnosis of the neural and endocrine components is vital, as undifferentiated, or poorly differentiated tumours have prognostic implications if malignancy affects one or both components of the composite tumour.
Case report
A 43-year-old normotensive male was referred for evaluation of an incidentally detected heterogeneous left adrenal mass (46mm x 31mm x 29mm). The patient described adrenergic symptoms that included excessive sweating, anxiety, and headaches. Plasma metanephrine and normetanephrine levels were elevated (518 pmol/l and 3670 pmol/l respectively). MIBG Iodine 123 SPECT Scan showed marked focal tracer uptake within the left adrenal gland consistent with a phaeochromocytoma. Laparoscopic left adrenalectomy was undertaken after appropriate pre-operative alpha and beta blockade. Histology of the excised adrenal tumour showed composite pheochromocytoma, with a ganglioneuroma as the histological second component. On immunohistochemistry staining, both tumours stained positive for chromogranin and synaptophysin. The ganglioneuroma tissue component was highlighted by neurofilament, S100 and SOX-10 positivity. Plasma metanephrines normalised after surgery.
Discussion
While pheochromocytoma and paragangliomas are tumours that originate from the chromaffin cells, ganglioneuroma represents the mature spectrum of tumours from autonomic ganglion cells or their precursors. The vast majority of composite pheochromocytoma with ganglioneuroma are benign with malignant pheochromocytoma reported in about 3% of cases. Approximately 13% of composite pheochromocytoma/-ganglioneuromas are known to metastasise. Long term follow-up is vital to monitor for risk of recurrence and metastases.

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P38

The utility of precision radiotherapy in the management of a patient with a retroperitoneal paraganglioma

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Paragangliomas are rare neuroendocrine tumours that often pose significant diagnostic and management challenges. A 69-year-old male was referred to our hospital for investigation of an incidentally discovered retroperitoneal mass on a staging computed tomography (CT) scan after a recently diagnosed low-grade bladder cancer (biopsy proven). His other past medical history included severe ischaemic heart disease, hypertension, atrial fibrillation, type 2 diabetes and psoriasis. Symptomatically, the patient only reported occasional palpitations with a normal blood pressure on antihypertensive therapy (losartan, amlodipine). Initial biochemical testing revealed elevated plasma 3-methoxytyramine (7995 [0-180]) with normal metanephrine (344 [0-150]) and normetanephrine (878 [0-1180]) levels. Positive emission topography (PET)/CT scans with 18F-fluorodeoxyglucose and gallium-68 dotatoc supported the diagnosis of a localised retroperitoneal paraganglioma (5.6x5.6 cm). Germline mutational screening revealed a mutation in the succinate dehydrogenase B (SDHB) gene. Following anaesthetic assessment, surgery was deemed to carry excessive risk, and the patient was referred for precision radiation therapy (RT). He completed a dose attenuated course of RT of 30Gy delivered in 5 alternate-day treatments due to proximity of the small bowel. He did not have any CTCAE V 5.0 Grade 3 or above toxicities and demonstrated a radiological RECIST criteria partial response at his 3-month post treatment assessment scan. In the 33 months we have been following him up since RT, there has been both a biochemical (3-methoxytyramine 7995 pmol/l to 695 pmol/l) and radiological response (progressive reduction in tumour size to 50% of original). He has not had any evidence of new or metastatic paragangliomas on biochemical and imaging surveillance. This case highlights the importance of personalised multi-disciplinary management strategies in patients with paragangliomas. It demonstrates that precision RT is a promising palliative option for localised disease in patients who are unable to undergo potentially curative surgery.

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P39

Adrenal incidentaloma pathway: a review of clinical outcomes from 3-years of this formal service at derriford hospital, plymouth

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Plymouth Hospitals NHS Trust (PHNT) has provided a formal adrenal incidentaloma pathway for over 3 years. Clinical outcomes for patients referred to this pathway were reviewed and are presented here. 419 patients have been referred due to incidental adrenal lesion(s) on imaging requested for indications unrelated to the adrenals or cancer. Routine investigation for all patients accepted to the pathway includes biochemical assessment of autonomous cortisol secretion and catecholamine excess. Aldosterone over-secretion is only assessed if clinically indicated. Of 76 patients with aberrant cortisol measurements, 37 underwent repeat/alternative assessment and were subsequently discharged; since Feb'24 patients are no longer offered alternative testing and instead are diagnosed

with MACS (8 patients). 13 patients were offered endocrine clinical review, 10 of which were discharged and 3 await appointments. 7 were discharged without further testing or endocrine review. 11 are categorised as miscellaneous. Of 32 patients with elevated metanephrines, 8 underwent repeat/alternative assessment and were subsequently discharged. 10 patients were offered endocrine clinical review, 8 of whom were discharged and 2 await appointments. 4 had adrenalectomy (histologically 3 phaeochromocytomas, 1 mesothelial cyst) and 10 are categorised as miscellaneous. 43 patients were referred to urology, all on the basis of radiologic findings though 22 also had an aberrant metanephrine and/or cortisol finding. 7 underwent adrenalectomy (histologically 3 phaeochromocytomas), 18 remain under surveillance, 16 were discharged. 2 have phaeochromocytomas but are unfit for surgery. In summary, of 419 referred patients 97 (23%) had abnormal initial chemistry (64 (15%) cortisol, 19 (5%) metanephrines, 12 (3%) metanephrines and cortisol, 1 metanephrines and ARR, 1 ARR). 20 patients (5%) required endocrine clinical follow-up. 43 patients (10%) were referred to urology, with 7 patients (2%) undergoing adrenalectomy. 301 patients (72%) required no further investigation or follow-up. No adrenocortical carcinomas have been identified through this service.

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P40

Secretory adrenal medullary hyperplasia: a precursor pheochromocytoma mimic

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Introduction
Adrenal medullary hyperplasia (AMH) is a rare, benign disorder marked by overproduction of catecholamines. AMH shares clinical similarities with pheochromocytoma (PCC) but differs in cellular structure and lacks the polygonal cell proliferation typical of PCC. Information on AMH is sparse. We present this case to broaden understanding of AMH's role in endocrine hypertension.
Clinical Case
A 59-yr-old female with a history of treated hypertension and asthma was referred for investigation of possible carcinoid syndrome. Presenting symptoms included tachycardia, flushing, episodic anxiety, breathlessness and fatigue. On examination, the patient was hypertensive (BP 167/95 mmHg) and tachycardic (HR 127 bpm). Systemic examination was normal. ECG confirmed sinus tachycardia, and echocardiogram showed normal left ventricular function. 24-hour urine 5-HIAA excretion was normal, but plasma normetanephrine was mildly elevated (1510 pmol/l). The clinical history and biochemistry were indicative of PCC. Adrenal CT scan showed slight nodularity within the left adrenal nodule and MIBG SPECT scan confirmed unequivocal avidity in the left adrenal gland, consistent with a left PCC. Laparoscopic left adrenalectomy after adequate preoperative alpha-blockade and tachycardia management with a calcium antagonist (Diltiazem XL) was undertaken after MDT discussion. Histology of the excised adrenal gland showed adrenal medullary hyperplasia rather than classical PCC. Plasma normetanephrine remained elevated (1410 pmol/l) after surgery suggesting possible bilateral adrenal medullary hyperplasia. Genomic analysis was negative for PPGL predisposition genes.
Discussion
AMH is thought to represent a PCC precursor lesion and is more likely to be associated with a genetic condition compared to PCC. Metanephrine levels are reported to be lower in AMH compared to PCC. The presence of elevated metanephrines after adrenal surgery suggests the possibility of bilateral disease. AMH may evolve into classical PCC over time and lifelong follow up is mandatory to monitor hypertension and disease progression.

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P41

Pseudohyperkalaemia in thrombocytosis – a reminder

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Introduction
Pseudohyperkalaemia is defined as a raised serum potassium with concurrent plasma potassium levels within the normal range. There is usually a slight difference between serum and plasma potassium levels, owing to release of potassium from activated platelets during clotting; pseudohyperkalaemia occurs where there is a difference greater than 0.4mmol/L between the two values, in the absence of symptoms or ECG changes. While pseudohyperkalaemia occurs relatively frequently in primary care, owing to difficulties in storage and transportation of samples, it is far less common in the hospital setting.
Case
A gentleman with a background of ulcerative colitis, pancreatic cancer and diabetes mellitus was seen during a routine consultation while an inpatient for management of his diabetes. Routine blood tests showed a serum potassium of 6.0 mmol/l. There were no concerning ECG features; the hyperkalaemia was refractory to standard treatment. He did not take any medications that would predispose him to hyperkalaemia, and was adherent to a low-potassium diet as advised by a dietitian. Random cortisol was checked and was found to be 464 nmol/l, excluding Addison's disease. It was noted that he had significant thrombocytosis, with an apparent positive correlation between his platelet count and serum potassium levels. Repeat blood tests showed serum potassium of 5.6 mmol/l; the same sample was simultaneously run through a blood gas analyser, with a potassium of 4.8 mmol/l. Given all other causes of hyperkalaemia had been excluded, it would appear that this was a case of pseudohyperkalaemia secondary to thrombocytosis. He has since been referred onto a Haematologist for further investigation.
Conclusion
Pseudohyperkalaemia should always be considered in patients with unexplained, hyperkalaemia where the clinical context or progress is unusual. Identifying pseudohyperkalaemia may avoid subjecting patients to unnecessary investigations and potentially harmful treatments.

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P42

Development of a high sensitivity LC-MS/MS method to measure progesterone in serum and its application to derive a reference interval in a male cohort

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Introduction
Progesterone is a steroid hormone commonly measured during assessment of female ovarian function. However, there is a lack of validated methods with the sensitivity to quantitate progesterone at concentrations found in males, post-menopausal females or patients on steroid hormone lowering medications. Here, we aimed to develop a high sensitivity LC-MS/MS method for this purpose. We also applied this method to derive a reference interval in a male cohort.
Methods
The method was developed on a Waters TQ-XS mass spectrometer. Calibrators and quality controls were gravimetrically prepared from separate stocks of certified reference material. The method utilised a 96-well plate format, with a progesterone-2,3,4-$^{13}C_3$ internal standard. Extraction was performed using supported liquid extraction with MTBE. Male samples (n = 52), collected between 8 – 10 AM from patients aged 25 - 81, were retrieved prior to disposal, anonymised and analysed.
Results
Progesterone and its internal standard eluted with a symmetrical peak at 3.3 minutes. Concentrations ranging from 25 to 54000 pmol/l could be quantitated. The method demonstrated good recovery and minimal matrix effects. Male samples (n = 19) were excluded from the reference interval (n = 14 due to medications that may cause adrenal suppression, n = 5 due to outlying progesterone concentrations). Mean progesterone was 170 pmol/L, with 2nd and 97.5th percentiles were 71 and 316 pmol/L, respectively.
Conclusions
We present a high sensitivity LC-MS/MS method to measure serum progesterone. This may benefit clinical applications such as assessment of infertility or breast cancer risk in post-menopausal women. We have also applied this method to derive a male reference interval for progesterone.

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P43

Adrenalectomy cohort data at a tertiary centre: correlating pre-surgical diagnosis to histological diagnosis

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This study reviewed 322 adrenalectomies performed between April 2010 and April 2023 at a tertiary centre with specialist services, which excluded six due to incomplete records. The analysis focused on surgical indication, against the post-adrenalectomy histological results. Of the 322 cases, 182 (57%) were for functional adrenal diseases, and 140 (43%) were for malignancy associated reasoning. The most common single indication was carcinoma related ($n = 80$), confirmed subsequently as malignant in 86% of cases. For indications specific to an adrenal lesion $\geq$4 cm ($n = 41$); average size 6.2 cm, incidentally revealed in 70%; 93% were benign; all <9cm size ($n = 37$), whereas 3 of the 4 >9 cm showed malignant histological features (MHF) (based on histopathological scoring systems). Functional disease indications included pheochromocytomas ($n = 70$), with 40% showing MHF; MACS or Subclinical Cushing's ($n = 44$, 4.5% MHF), adrenal Cushing's syndrome ($n = 18$, 28% MHF), Cushing's disease ($n = 13$, 0% MHF), and Conn's syndrome ($n = 32$, 0% MHF). Histological reporting of prominent zona fasciculata occurred in 23% with MACS, 28% with adrenal Cushing's syndrome, and 16% with Conn's syndrome, none of which had MHF ($n = 27$). Six patients had confirmed genetic susceptibility factors, (4 x pheochromocytoma, 1 x large adenoma, 1 x Cushing's disease). This study data revealed an adrenal lesion size cutoff of 9 cms for size only concerns, predicted MHF with 75% sensitivity and 100% specificity, whereas below this threshold all were benign, suggesting an amended threshold for adrenalectomy would be appropriate. An unexpected 28% incidence of MHF in adrenal Cushing's syndrome specimens, and 40% in Phaeochromocytomas suggests concerns beyond functional disease impact in these patient groups warranting greater study. Overall, a low concordance (55%) between preoperative expectations of malignancy and actual MHF was revealed. A poor correlation between histological findings in the Cushing's groups was revealed, although when present was indicative of benign histology.

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P44

Adrenal incidentaloma audit from a single centre and proposed trust guidelines

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An adrenal incidentaloma (AI) is an adrenal mass $\geq$1 cm detected on imaging not performed for suspected adrenal disease. Our audit aims to formulate a safe protocol to reduce unnecessary testing, streamline appointments and minimise costs. Data was generated from our local Soliton radiology system. Search criteria included adult CT and MRI with adrenal adenoma (AA) between 2018-2023. 140 incidentalomas were identified and 123 were AA. Full data was obtained on 63 of the cases. Outcomes included size, radiological characteristics and biochemical testing for the functionality of the incidentaloma. In patients who had surgery, histology was also documented. 80% of adenomas were >1.5 cm and 86% were non-functional. 78% of functional adenomas were patients >65y/o. Further imaging was requested in only 21 patients after MDT discussion. 74% were discharged with stable adenomas, only 1% had follow-up appointments. Most AI's are adenomas and the majority are not functional.

Proposed guideline

- All AI's should first be discussed in MDT with radiologists to reduce re-imaging.
- If AA <1.5 cm, with no concerning radiological features and age >30y/o, arrange functional work-up. If non-functional, no radiological follow-up and discharge.
- If AA >1.5 cm and age <30y/o, discuss in Endocrine MDT.
- MDT should consider surgery or specific treatment for incidentalomas causing hormone excess or >4 cm size.
- If cortisol <138nmol/l, monitor for comorbidities or discuss surgery.
- If cortisol >138nmol/l with comorbidities or hypertension, hypokalaemia with high aldosterone/ renin ratio and a unilateral adenoma or metanephrine secreting tumours, offer surgery.
- If patient is not for surgery, undertake annual follow-up for 2-4y. If no changes or improves, discharge to GP to monitor annually for hypertension and diabetes. Alert for new concerns.

This approach will streamline referrals for AA, reduce unnecessary imaging, decreases the likelihood of missing sinister pathology and makes a comprehensive management plan. This will save the Trust costs.

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P45

Cushing's syndrome: a significant modifier of outcomes in lymphoma patients - a national inpatient sample analysis 2016-2020

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Background

Cushing's syndrome, characterised by elevated cortisol, weakens immune system and trigger chronic inflammation, potentially promoting lymphoma development. Previous studies indicate that adrenal tumours and pituitary adenomas can lead to both Cushing's syndrome and lymphoma, suggesting a shared pathophysiology. Despite this, the link between cortisol excess and its effects on hospitalised lymphoma patients remains underexplored. This study aims to analyse the impact of Cushing's syndrome on mortality, bleeding, and resource utilisation in lymphoma hospitalizations.

Methods

The National-Inpatient-Sample-database (2016-2020) was analyzed to identify adult lymphoma hospitalisations with Cushing's syndrome, using ICD-10 codes. Chi-square tests assessed categorical variables, while t-tests evaluated continuous variables, with significance set at $P < 0.05$. Multivariate regression analysis examined the impact of Cushing's disease on hospitalization outcomes in lymphoma, controlling for confounders, demographics, and hospital characteristics.

Results

1,485,770 lymphoma hospitalizations were observed, 530 cases had Cushing's syndrome. Average age of patients with Cushing's was 59.13 years, vs 64.48 years for those without. Among Cushing's patients, 61.54% were female. 65.69% were whites, 11.76% black, and 10.78% Hispanic ($P = 0.05$). Those with Cushing's experienced higher resource utilisation, with an average increased length of stay by 3.75 days (10.61 vs 6.86) and costs by $46,451 (134,765$ vs 88,314$). Multivariate regression analysis showed that lymphoma hospitalizations with Cushing's syndrome were linked to poorer outcomes, as detailed in the table.

Table 1. Impact of Cushing's syndrome on lymphoma hospitalisations

	% with and without Cushing's (p-value)	Adjusted-Odds-Ratio for confounders (95%-Confidence-Interval)	P-value
Mortality	10.37, 4.88 ($P = 0.02$)	2.90 (1.37-6.17)	0.005
Bleeding	13.20, 3.12 ($P < 0.001$)	4.91 (2.27-10.63)	<0.001

Conclusion

This study shows that Cushing's syndrome negatively impacts hospitalisation outcomes in lymphoma patients, resulting in increased resource utilisation and higher mortality rates. Elevated risk of complications, like bleeding, highlights the need for effective management of Cushing's. Further prospective studies should explore strategies to improve healthcare results in this population.

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P46

Once daily low dose prednisolone vs. hydrocortisone in treating adrenal insufficiency (HYPER-AID Study)

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Background
Low dose once daily prednisolone is an easier and cheaper steroid option than multiple dose hydrocortisone. Prednisolone is noted to be seven times more potent than hydrocortisone.
Methods
A cross-over study of patients with adrenal insufficiency (AI) treated at the National Hospital Kandy, Sri Lanka were switched over from hydrocortisone to equivalent doses of low dose Prednisolone (3.75 – 5 mg). An analysis was performed comparing means of outcomes by the paired t-test.
Results
117 patients were recruited and 101 continued Prednisolone for the study period, while 6 lost to follow up and 9 switched back to hydrocortisone within 2 to 8 weeks of changing to prednisolone. 89 were on 3.75 mg prednisolone and 12 on 5 mg daily. Male:female ratio was 1.19:1 and mean age was 48.4 years (SD = 16.7). 76 and 25 patients had secondary (pituitary) and primary AI respectively. Those with primary AI were administered Fludrocortisone in addition to Prednisolone. There was no difference in weight, BMI and waist:hip ratio ($P = 0.059$) while on either of the drugs. Mean HDL was higher on prednisolone than on hydrocortisone being 54.7 mg/dl vs 51.3 mg/dl respectively ($P = 0.017$). Total cholesterol, LDL, triglyceride levels were non-significantly lower on prednisolone compared to on hydrocortisone. Mean HbA1c on hydrocortisone was 6.5% and 6.3% on prednisolone ($P = 0.2$). ALT ($P = 0.005$) and AST ($P = 0.011$) were lower on prednisolone than on hydrocortisone. There was no significant difference on sodium, potassium, creatinine and bilirubin level. There was no difference in quality of life assessed by the separate SF36 9 domains while on either prednisolone or hydrocortisone. There was no difference in outcomes if prednisolone was used in primary or secondary AI.
Conclusion
Once daily Prednisolone is a non-inferior alternative to multiple dose hydrocortisone in treating primary and secondary AI and has metabolic benefits.

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P47

A case of cyclical cushing's disease: a diagnostic conundrum of investigations and management

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Cyclical Cushing's syndrome is a rare condition marked by intermittent episodes of cortisol excess (peaks) followed by normal cortisol levels (troughs). We report a 51-year-old woman admitted to the University Hospitals of Leicester for urgent plastic surgery following deliberate self-harm. She presented with severe myopathy, a Cushingoid appearance, and psychosis. Laboratory tests showed urine cortisol > 1000 nmol/l, serum cortisol 1656 nmol/l, potassium 2.4 mmol/l, and ACTH 200 pmol/l. Treatment with metyrapone resulted in significant symptom resolution within a month. A review of laboratory results from the referring hospital showed the patient's cortisol levels followed a cyclical pattern (1749, 489, 925, 178 nmol/l). In May 2024, before transferring to UHL, she was admitted to her local hospital with an acute abdomen requiring a colectomy, likely due to pseudo-obstruction from the severe hypokalaemia. Her cortisol level was 1749 nmol/l, and ACTH was 211 pmol/l, indicating ACTH-dependent Cushing's syndrome. The patient underwent CT whole body, MRI pituitary, FDG-PET, octreotide scan, and 68-Ga-DOTATAE PET scans. Aside from bilateral adrenal hyperplasia, consistent with ACTH-depended Cushing's, no significant focal uptake to suggest a primary lesion was observed. She went on to have inferior petrosal sinus catheter sampling (IPSS) which showed no significant central versus peripheral gradient after desmopressin stimulation of ACTH. The patient continues to do well off metyrapone. As part of a multi-centre cyclical Cushing's study, she is collecting twice-weekly late night salivary cortisol and having weekly post 1 mg dexamethasone suppression salivary cortisol levels assessed, as well as hair cortisol. Overt cyclical Cushing's syndrome is a rare and difficult clinical problem. It is likely that in Cushing's syndrome per se there is some cyclicity of cortisol. The need to investigate this condition has led to a multi-centre study and we hope to publish on this in due course.

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P48

A case of adrenocortical carcinoma- time is of the essence in this aggressive tumor

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Introduction
Adrenocortical carcinomas (ACC) are rare and aggressive, with a mean five-year survival rate ranging between 20% and 50%. These tumours often lead to excessive hormone production further complicating management. We report a patient with abdominal pain who was eventually diagnosed with adrenocortical carcinoma.
Case report
A 53 year old man presented to primary care with 1 month history of abdominal pain. A community ultrasound revealed adverse findings, which prompted admission to our tertiary hospital. Computed tomography of abdomen in hospital showed large right sided mass (21 cm maximum diameter) reported as probable adrenocortical carcinoma with hepatic and pulmonary metastases, and thrombus in IVC. There was biochemical evidence of cortisol and androgen hypersecretion, although patient was not overtly Cushingoid. Biopsy was performed, patient was started on metyrapone and referred to the local adrenal MDT, then discharged 12 days after admission. Local MDT deemed patient inoperable and he was referred to the regional neuroendocrine MDT, subsequent plan was to schedule an FDG PET-CT scan, this showed metastatic right adrenal malignancy. Histology and immunohistochemistry confirmed adrenocortical carcinoma. On the next MDT, patient was re-admitted to our centre with new respiratory compromise and malignant hypercalcaemia (unusual in ACC). The MDT decision was for mitotane therapy, however patient was no longer fit for transfer to the quaternary centre. Local oncology teams reviewed but felt as performance status had declined from 1 to 3, he was not fit for any other chemotherapy either. He was subsequently placed on palliative care 6 weeks after first hospital admission and died a few days later.
Learning points
1. ACC is often diagnosed late and requires prompt treatment due to its aggressive nature. 2. Increasing the availability of chemotherapy outside quaternary centres may allow for treatment to be initiated in the narrow time window that patients with ACC have.

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P49

CRISPR-Cas9 MRAP knockout H295R clones as a tool to study familial glucocorticoid deficiency type 2 (FGD2)

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Melanocortin-2-receptor (MC2R) accessory protein (MRAP) is a small single transmembrane protein, highly expressed in adrenal glands and essential for MC2R expression and function. ACTH binds to the MRAP-MC2R complex and activates the adenylyl cyclase cascade, leading to cAMP production, phosphorylation of cAMP-dependent PKA, activation of the steroidogenesis pathway and production of adrenal glucocorticoids (GC). Loss-of-function mutations in MRAP give rise to isolated GC deficiency aka FGD2. FGD2 presents early in childhood with symptoms and signs of hypocortisolaemia and excessive ACTH: hyperpigmentation, failure-to-thrive, hypoglycaemic attacks or coma and death. Mutations of MRAP account for 20% of FGD. In 2005, Metherell *et al* reported patients carried mutations either in exon 3 (c.3G > A, c.106 + 1G > A, c.106 + 1G > T, c.106 + 1G > C, c.106 + 1delG, c.106 + 3insT) or exon 4 V44X (c.128delG) of MRAP, leading to non-existent or non-functional protein. Since then, more than ten other MRAP mutations have been reported. However, like many conditions variants of uncertain significance (VUS) remains the bottleneck to diagnosis and reporting back to patients. To be able to study FGD2 and test the functionality of novel variants, we used CRISPR-Cas9 to remove MRAP expression at the genomic level in adrenocortical carcinoma cell-line NCI-H295R. Targeted cells were single cell sorted and single clones of MRAP-KO H295R cells were assessed. Genomic DNA of the KO clones were purified and the locus of MRAP were amplified by PCR. KO of MRAP at the genomic level was confirmed by Sanger sequencing of three successfully created MRAP-KO clones. MRAP-KO clones showed decreased cAMP level when stimulated by

ACTH by a pGlo assay (CLARIOstar®), which confirmed the lack of MRAP. The established MRAP-KO H295R cells will be a new tool for us to test novel variants and seek drugs and therapeutics to treat FGD2.

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P50

An annual mortality rate of 42% is noted in profound hyponatraemia (Na <120 mmol/l) patients

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Background
Profound hyponatraemia is associated with considerable morbidity and mortality. There is a lack of mortality rate estimation in severe hyponatraemia patients.
Objective
We explore calculating mortality rates in patients admitted with severe hyponatraemia of Serum sodium (Na) <120 mmol/l.
Methodology
Retrospective case notes & electronic records' review were undertaken to identify hyponatraemia patients admitted to University Hospitals of Leicester (UHL) from 1st January 2022 to 31st December 2022 (UHL QIP No:11408). All consecutive patients of Na <120 were identified based on UHL lab & electronic mortality records.
Results
n = 622 patients with a Na <120 mmol/L included; mean Na = 115 mmol/l. Total deaths = 329 occurred as of 16th October 2024. 260/622 (42%) of profound hyponatraemia patients died within a year of Na <120 reading. Out of 329 deaths, 79/329 (24%) of deaths occurred within 7 days, 131/329 (40%) deaths occurred within 30 days & 260/329 (79%) deaths occurred within 365 days. Mean = 173 days, the duration from time of least Na value to death; Median = 55 days.
Discussion
The degree of hyponatraemia is a marker of severity of the underlying aetiology. In our study, 1 in 5 hyponatraemia patients (21%) died within a month of Na < 120 & 2 in 5 (42%) died within a year. In comparison, pancreatic cancer has a 1-year mortality rate of 74%. Further explorative analysis of non-cancer mortality rates & various aetiologies are currently being undertaken.
Learning points
1. Profound hyponatraemia patients with Na <120 mmol/L have very poor prognosis with an estimated mortality of >40% at 1 year irrespective of the aetiology.
2. Aggressive management is imperative to identify the underlying aetiology and appropriate treatment strategies placed.
3. To educate patients & families about the poor prognosis in such cohort of patients if irreversible causes are identified such as malignancy, end-stage organ failure etc.

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P51

Phaeochromocytoma or not? an adrenal haemorrhage conundrum

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A 57 year old lady was admitted to hospital with right flank pain radiating to the right shoulder. Subsequent work-up revealed an acute right adrenal haemorrhage of size 82 x 53 x 56 mm on CT abdomen and pelvis, with CT angiogram confirming no ongoing haemorrhage. Biochemistry showed significantly elevated plasma metanephrines and normetanephrines, with unremarkable adrenal profile otherwise. She had been experiencing palpitations, excessive diaphoresis and headaches on a background of hypertension, for which she was on lercanidipine. Some of the symptoms were attributed to the menopause, for which she was taking HRT prior to hospital admission, albeit without complete symptom relief. At 6 weeks follow-up following discharge, plasma metanephrines had normalised but normetanephrines remained elevated, albeit significantly improved, as shown in the table below. Due to ongoing palpitations and hot flushes, Lercanidipine was switched to Doxazosin, which provided symptom relief and improved blood pressure. A repeat CT adrenal at 2 months follow-up, showed significant size reduction in the haematoma to 47 x 29 mm. However, plasma normetanephrine remained elevated at 4 months post admission. A subsequent MIBG scan revealed increased uptake within the right adrenal nodule suggestive of phaeochromocytoma. The case highlights the difficulty in distinguishing between elevated plasma metadrenalines secondary to haemorrhage in a normal adrenal gland or a nonfunctional adrenal tumour and haemorrhage associated with an underlying pheochromocytoma. The presence of pre-existing adrenergic symptoms and a positive functional scan helped distinguish between the 2 scenarios in our case.

Component	On admission	At 6 weeks	At 4 months
3-methoxytyramine 0 - 180 pmol/L	<75	<75	<75
Plasma Metanephrines 0 - 510 pmol/L	3212	269	310
Plasma Normetanephrine 0 - 1,180 pmol/L	19,166	2275	2550
Cortisol (nmol/l)	924 (at 14:48); 527 (9 am)	-	-
Aldosterone: renin ratio (0-1000)	-	160	-

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P52

The impact of a nurse-led preparation protocol for saline infusion testing in suspected primary aldosteronism

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Introduction
Primary aldosteronism is a clinically significant and treatable cause of hypertension. Diagnosis relies on accurate assessment of the renin-aldosterone axis: both hypokalemia and interfering agents need consideration. In ensuring the necessary conditions are met prior to confirming the diagnosis with a Saline Infusion Test (SIT: gold standard), multiple clinic attendances are often required. Our investigative unit sought to implement a nurse-led protocol to streamline the process.
Protocol
The protocol was implemented in September 2022 for patients undergoing SIT following confirmation of an elevated aldosterone:renin ratio. The following steps are included:
1. Review of baseline renal function and electrolytes.
2. Ensuring interfering agents had been stopped for sufficient time (6 weeks for aldosterone antagonists, 2 weeks for beta blockers, diuretics, angiotensin receptor/ACE inhibitors) and patients changed to doxazosin, verapamil, and/or hydralazine.
3. Blood pressure monitoring 3, 2 and 1 week prior to the test with serum potassium two weeks prior.
Results
We assessed 15 patients prior to implementing the protocol, and 10 patients after (mean age 51 years; 64% male). 32% were prescribed potassium replacement. The average number of day unit visits prior to SIT increased from 1.7 to 2.6. Slightly more patients had sufficient time off polluting agents before the protocol (93% vs 80%). Implementation of the protocol improved the proportion of patients with hypokalemia (<3.5mmol/l) at the time of SIT (22% vs 60%), and significant hypertension (>160/100mmHg) on the day of SIT (10% vs 20%). It also reduced cancellations due to hypertension, hypokalemia or pulmonary oedema (13% vs 20%).
Conclusion
Our nurse-led protocol led to fewer cancellations and more accurate salt load tests, with less hypokalemia. An average of one extra visit per patient was required to achieve this. Overall this creates a safer and more efficient service with appropriately performed and readily interpretable SITs.

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P53

Retrospective study to determine 9am cortisol level for primary care to refer for short synacthen test to secondary care against recent NICE guideline NG 243 cut off of serum cortisol of 300nmol/L

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Background
The NICE guideline Adrenal insufficiency: identification and management [NG243] was published in August 2024. It states an 8-9 am cortisol concentration of >300 nmol/l suggests that adrenal insufficiency is very unlikely. Until now, we have made the same assertion only for random samples >430 nmol/l, which is the recommended cut-off for our assay post-Synacthen. Patients with 9 am cortisol <430 nmol/l may require a Synacthen test to demonstrate adequate adrenal reserve.
Aim
To assess local data and collect evidence for an assay and population specific concentration at which adrenal insufficiency is very unlikely.
Method
In line with other published studies, retrospective Synacthen test data was examined. Three years of data from Doncaster and Bassetlaw NHS FT was gathered, and Receiver Operated Characteristics (ROC) analysis performed to determine baseline cortisol concentrations that predict a pass outcome for a Synacthen test at 0.95 and 0.99 sensitivity. Data was assessed in three groups (a) all data, (b) baselines taken between 8-10 am and (c) baselines not taken between 8-10 am.
Results
1231 SST data sets were analysed, of which 128 (10.4%) already had a baseline cortisol >430 nmol/l. Of the remaining 1103 patients, 205 (18.6%) did not have cortisol >430 nmol/l at 30 minutes post-Synacthen. ROC analysis suggested baseline results ranging from 306-372 nmol/l could predict a post-Synacthen cortisol of >430 nmol/l, depending on the data group and sensitivity chosen.
Conclusion
The concentration at which NICE states adrenal insufficiency is very unlikely is lower than all cut-offs modelled here. Not requiring a Synacthen test in patients with cortisol above 306-372 nmol/l could reduce the Synacthen test workload by 11.1-32.5%. Local guidance for primary care has been created between the Endocrine and Biochemistry departments to maximise efficiency and patient safety.

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P54

Excellent response to DHEA treatment in a male with post orgasmic illness syndrome

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A 51-year-old man presented with a plethora of symptoms that affected him soon after ejaculation and often lasted for a few days afterwards. These symptoms were characterised by debilitating fatigue, palpitations, muscle aches, possible phonophobia, reduced concentration, irritability, headaches and blurred vision. He had reduced libido, erections, reduction in spontaneous early morning erection and his muscular strength was affected leaving him unable to perform in the gym as he had in the past. The history was suggestive of post ejaculation illness syndrome (POIS). He had been taking testosterone, but he had elevated haematocrit, so testosterone therapy was discontinued which he tolerated, and he subsequently had unequivocally normal total and free testosterone readings at follow-up. He also had low-normal salivary DHEA level: 0.34nmol/l [0.25 – 2.22nmol/L]. Dietary supplements, stress management strategies and Melatonin had little noticeable effect. Treatment with DHEA (50 mg daily), although unlicensed, produced a substantial improvement of POIS related symptoms. As a result, the patient was able to drop many other supplements. Reducing the dose of DHEA to 25 mg saw a return of symptoms. POIS is rare but could be underreported and can cause intrusive symptoms in affected men. There is poor understanding of the causes which include, but are not limited to, autoimmune phenomenon, allergic disorder, and micronutrient deficiencies. As a result, there are no recognised treatments for this disorder. However, various treatments have been tried including antihistamines, selective serotonin reuptake inhibitors, non-steroidal anti-inflammatory drugs, glucocorticoid steroids and benzodiazepines. In this abstract we present a case that responded quickly and dramatically to DHEA treatment. It is known exactly why it helped but DHEA is known to have immunomodulatory effects which might be helpful in autoimmune pathologies.

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P55

A rare case of hypokalaemia, hypomagnesaemia and metabolic alkalosis

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Background
Hypokalaemia is frequently encountered in endocrinology practice; yet it is important to be aware of rarer causes, their investigation and management. Gitelman's syndrome is an extremely rare cause of hypokalaemia, with prevalence estimated at 25 cases per one million population. We report a case of likely Gitelman's syndrome, presenting with hypokalaemia, metabolic alkalosis and secondary hyperaldosteronism.
Case
A 30-year-old gentleman was referred by his family physician with tiredness and hypokalaemia (serum potassium - 2.6 mmol/L [3.5-5.3]). Admission bloods confirmed hypokalaemia and hypomagnesaemia (2.4 mmol/L and 0.49 mmol/L (0.70-1.00) respectively). Given his young age, absence of comorbidities or malnutrition, he was assessed for renal tubulopathies. Further investigations showed metabolic alkalosis (serum bicarbonate 33 mmol/L [22-29]), raised aldosterone (710 pmol/l [>631]) and renin (11.0 nmol/L/h [03 -2.2]), with high urinary output of magnesium (10.9 mmol [2.5-6.5]), potassium (169 mmol [25 -125]), and low 24-hour urinary calcium (1.5 mol [2.5-7.5]). These all suggest a thiazide-sensitive NaCl cotransporter (NCC) channelopathy; with likely diagnosis of Gitelman's Syndrome. On intravenous potassium chloride followed by oral Sando-K (600 milligrams potassium chloride and 400 milligrams potassium bicarbonate - two tablets three times a day) and Spironolactone (50 milligrams a day), his hypokalaemia improved. His serum magnesium levels were more resistant to treatment, remaining low on intravenous or oral magnesium aspartate (0.42 - 0.45 mmol/l). After reviewing the latest guidelines and liaising with international experts, his treatment was switched to magnesium lactate (Magnalac 84 milligrams), and potassium chloride (PotaChlor MR 600milligrams), which thus improved his electrolyte levels. His genetic analysis for renal tubulopathies is awaited.
Conclusion
It is important to have a broad clinical suspicion when coming across common electrolyte disturbances. Our case of likely Gitelman's Syndrome raises awareness of this rare condition and highlights the challenges incurred in its assessment and treatment.

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P56

Establishing new cortisol thresholds for short synacthen testing (SST) in the diagnosis of adrenal insufficiency (AI) using the beckman access cortisol immunoassay

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Background
Beckman Access Cortisol immunoassays, utilising monoclonal antibodies, produce more accurate serum cortisol concentrations but approximately 20% lower compared with older assays necessitating reduction in thresholds to maintain diagnostic accuracy of SST. Cortisol thresholds were lowered from 550 nmol/l to 460 nmol/l at 30- or 60-minutes at the Great Western Hospital in 2016, and to 410 and 460 nmol/l at 30- and 60-minutes respectively in 2022. We reassessed the effectiveness of newly established SST (250 mg ACTH) thresholds and 8-10 am cortisol which may negate the need for dynamic tests.
Methods
A retrospective analysis included 101 patients who underwent SST from June to September 2022.
Results
Of the steroid-naïve patients ($n = 74$), 92% passed the SST and 8% failed who later were diagnosed with AI. One test result was indeterminate. Of the steroid-exposed patients ($n = 27$), 34.6% passed and 65.4% failed the SST and among them, 4 patients had suboptimal cortisol response (between 350 – 459). Threshold concordance between 30- and 60-minutes was 99%. 4 patients (5.1%) with false negative results had further testing with Insulin Tolerance test (ITT) and received a final diagnosis of secondary AI. Average morning cortisol in steroid-naïve patients, who passed the SST and did not end up with a diagnosis of AI, was 283 nmol/l (106-565), and in those who failed SST, 42.8 nmol/l (11-77).

Conclusion
The high concordance between 30- and 60-minute thresholds suggests that 30-minute sampling alone may be sufficient to maintain diagnostic accuracy. The revised SST thresholds effectively eliminated false positives, but false negatives still occurred. Therefore, if there is high clinical suspicion of secondary AI, ITT should be considered. In steroid-naïve patients morning cortisol <100 nmol/l measured by Beckman Access warrants starting management for AI, cortisol $>$ 210 nmol/l likely indicates low pretest probability of AI.

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P57

Significant reduction in AVS waiting time for primary aldosteronism in a district general hospital (DGH) in the UK from the provision of direct access in requesting adrenal vein sampling

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Background
Primary aldosteronism (PA) is a common cause of hypertension, with a 5% - 22% prevalence and is associated with a higher incidence of co-morbidities. Unilateral PA can be curable, and treatment improves quality of life. Yet, $<$ 1% of PA are diagnosed. Subtyping PA with adrenal vein sampling (AVS) is time-consuming. The AVS waiting time for our DGH was nearly 2 years following the Tertiary Endocrinology service referral pathway. The direct AVS requesting access reduced our waiting time to 7 weeks.
Aim
We aimed to investigate the waiting time from referral to completion of adrenal vein sampling. As a secondary objective, we analysed the correlation of AVS (unilateral or bilateral) to age, sex, ethnicity and BMI.
Methods
Retrospective analysis of 25 patients referred directly for AVS between December 2022 and June 2024.
Results
The mean waiting time for AVS was 7 weeks ($n = 23$, 2 withdrawn), with a reduction in waiting time ~ 98 weeks. Results showed 14 bilateral disease, 6 unilateral. 2 bilateral with a unilateral predominance, and 1 sampling error. 3/6 unilateral PA were offered adrenal ablation (WAVE trial), 2 received ablation,1 declined. In total, 5/8 unilateral or bilateral with predominance underwent adrenalectomy, and 1 opted for medical treatment. There was no significant correlation between unilateral (U) or bilateral (B) disease and age (mean B $=$ 47.7, mean U $= 45.6$, $P = 0.66$), BMI (Mean B $= 32.1$; U $= 30.6$, $P = 0.53$), or ethnicity (black U $=$ 4/8, white U $=$ 4/14, $P = 0.31$) but significant sex difference (Men U $=$ 8/14, women 0/8, $P = 0.0074$).
Discussion
We have shown that direct access to AVS has significantly reduced the waiting time. We did not find any association between age, ethnicity, BMI, and subtype of PA. In our cohort females had more bilateral PA. However, our cohort was too small for statistical confidence.

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P58

SIADH as first presentation of adrenal insufficiency due to abrupt discontinuation of potent topical corticosteroids with successful treatment with dupilumab in a patient with severe, difficult to treat atopic dermatitis

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Background
Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is characterized by hyponatremia and hypoosmolality due to excessive ADH release. It is an uncommon initial presentation of adrenal insufficiency, particularly after abrupt cessation of potent topical corticosteroids. This case report describes a patient with severe atopic dermatitis (AD) who developed SIADH as a first sign of adrenal insufficiency after stopping clobetasol propionate, subsequently managed with dupilumab.
Case Presentation
A 40-year-old female with a longstanding history of severe atopic dermatitis unresponsive to conventional treatments presented with new-onset confusion, nausea, and generalized weakness. The patient had been applying clobetasol propionate 0.05% cream extensively for over three years and had recently discontinued it abruptly upon starting dupilumab therapy. On physical examination, the patient appeared disoriented and lethargic. Vital signs showed hypotension (BP 88/54 mmHg) and bradycardia (HR 60 bpm). Laboratory tests revealed severe hyponatremia (serum sodium: 118 mmol/l), low serum osmolality (250 mOsm/kg), and inappropriately high urine osmolality (550 mOsm/kg), consistent with SIADH. Further endocrine evaluation showed a significantly low serum cortisol level (240 mol/l) and subsequent Short Synacthen Test showed a blunted response with stimulated cortisol of 310 nmol/l and low ACTH (5.8 ng/l) confirming secondary adrenal insufficiency. Immediate management included 1.8% hypertonic saline for hyponatremia and fluid restriction. Clobetasol was reintroduced at a lower dose and tapered gradually, along with oral hydrocortisone. Dupilumab was continued, resulting in significant AD symptom improvement.
Discussion
This case underscores the need to recognise SIADH as a potential presentation of adrenal insufficiency following abrupt discontinuation of potent topical corticosteroids. Healthcare providers should be aware of the risks associated with HPA axis suppression in patients undergoing long-term potent topical corticosteroid therapy and ensure gradual tapering of these medications. Dupilumab is effective for severe AD but requires careful management of prior corticosteroid use.

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P59

Management of autonomous cortisol secreting incidental adrenal adenoma: evolving clinical pathway

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Background
Autonomous cortisol secretion (ACS) is the most common (up to 40%) functioning adrenal incidentaloma. Active management of ACS become increasingly important due to emerging evidence of its associated cardiometabolic risk and osteoporosis. Aim: We aim to evaluate our service of ACS from 2016-2024.
Method
We retrospectively collected data from patients with ACS with the search term Autonomous Cortisol Secretion' and/or 'failed to suppress overnight dexamethasone suppression test (ODS)'. Demographic data, investigations to assess cortisol excess, cardiovascular comorbidities were analysed descriptively. Our clinical pathway was evaluated.
Result
We identified 80 cases of patients with a failed ODS (cortisol $>$50nmol/L- mean cortisol 123nmol/l). The demographic showed mean age 69.2yrs (SD$\pm$ 13.1), female (57%), with established comorbidities (hypertension (76%), diabetes (39%), other CVD risks (51%), and osteoporosis (21%). 76 (95%) underwent Low dose dexamethasone suppression test (LDDST) and 50 (63%) had a paired plasma ACTH. Only 9 (12%) LDDST was normal (cortisol $<$50nmol/l) excluded ACS diagnosis. In remaining 71 cases (mean cortisol post LDDS 109nmol/l), assessment of cortisol burden was carried out. 38 (54%) cases had serum cortisol day curve (mean cortisol 310nmol/l), 23:00 salivary cortisol (mean 2.77nmol/l) and cortisone. 55 (77%) had DEXA scan (mean T score –1.7). 13 patients (18%) underwent laparoscopic robotic adrenalectomy with cure of ACS and improved CVD risks.
Discussion
ACS is a complex entity which needs thorough work-up to determine treatment course. It is reassuring that ODS is still a good screening tool with an 89% specificity comparing with LDDS. We recommend development of a standardised more detailed investigation pathway allowing for multiparametric assessment of cortisol burden and comorbid status to help inform decision-making, particularly surrounding curative (surgical) management. Further evaluation of our data is needed for outcomes of those who were currently under observation, deem not fit for surgery or those who declined surgery.

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P60

Incidental pheochromocytomas: a case series from a single-centre experience

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Introduction
Pheochromocytomas/paragangliomas (PPGL) are rare tumours derived from chromaffin cells of the adrenal medulla or autonomic nervous system. In the past, most cases had imaging triggered by symptoms suggestive of phaeochromocytoma. We present 11 cases of incidentally found pheochromocytomas and paragangliomas diagnosed in the last 5 years.
Methods
We reviewed hospital records of all patients who were diagnosed with PPGL in Birmingham Heartlands Hospital from 2019 to present date. The reason for the scan, clinical and biochemical features as well as the management was analysed.
Results
The cohort included 11 patients (7 males, 4 females) with the median age of 66 (44-85) years who underwent imaging for abdominal pain on contralateral side, lung health check, staging scans for cancer, suspected pulmonary embolism or weight loss. Nine patients were diagnosed with phaeochromocytomas and 2 with paragangliomas of which 1 was non-secretory. All were found incidentally. The median size of the adrenal/paraganglioma lesions was 6.3 (2.5 to 10) cm. Elevated nor metadrenaline levels were observed in all secretory PPGLs, with a median of 12,197 (2342 to $>$30,000) pg/ml. Metadrenaline was also elevated in 3 cases with mean level of 876 pg/ml. All patients were blocked with doxazosin (total daily dose of 8-24 mg) in preparation for surgery. Surgical intervention was performed in 9 cases, all but 1 adrenalectomies, with 2 cases managed conservatively with alpha-blockade as not suitable for surgery due to frailty. Two patients had a small residual or recurrent disease treated with alpha-blockade.
Conclusion
This series emphasizes the importance of recognizing incidental pheochromocytomas during imaging. Timely biochemical evaluation, alpha-blockade and surgical intervention can lead to favorable outcomes, although ongoing monitoring is essential to manage recurrent disease.

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P61

Adrenal haemorrhage: bilateral versus unilateral

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Adrenal haemorrhage is a rare but clinically significant condition, presenting as unilateral or bilateral. Common underlying causes are trauma, sepsis, anticoagulation, and adrenal tumours. This condition is critical and can precipitate adrenal insufficiencies/crisis. Here, we compare cases of bilateral versus unilateral presentations of adrenal haemorrhage; highlighting differences in their aetiology, clinical presentation, and management strategies. Case 1: 70-year-old male with known previous stroke, hypertension, AF (not on anticoagulation) and COPD, presented with flank pain, urinary sepsis and refractory hypotension. Abdominal CT imaging revealed bilateral adrenal thickening. Dedicated CT adrenal confirmed bilateral adrenal haemorrhages. 9am cortisol 61nmol/l, ACTH 14ng/l, low aldosterone $<$60 pmol/l, high renin 16.8nmol/L/h - suggesting primary adrenal insufficiency, with normal sodium (144mmol/l) and potassium (5.0mmol/l). The 1 mg overnight-dexamethasone suppression cortisol was normal (35nmol/l). He was commenced on hydrocortisone cover. Repeat imaging in five months showed resolution of the adrenal haemorrhage. Currently, he is being reviewed in the endocrine clinic and has persistently low aldosterone levels. He continues hydrocortisone and fludrocortisone therapy and is scheduled for further tests to assess his adrenal reserve. Case 2: 82-year-old male on anticoagulation therapy and heart failure medications, presented with a fall and hypotension. He was found to have unilateral adrenal haemorrhage on CT abdomen. CT adrenal showed an adrenal lesion consistent with hematoma. 9am cortisol was 319nmol/l, sodium 140mmol/L and potassium 4.4mmol/l, i.e. adequate adrenal function. Although clinically stable, this patient requires close endocrine monitoring to assess lesion functionality and exclude malignancy, with follow-up imaging scheduled to confirm resolution 3 months after diagnosis. Both cases explore the challenges in diagnosing adrenal haemorrhage due to its nonspecific symptoms and emphasise the need for targeted imaging and endocrine evaluation. Unilateral haemorrhage with no adrenal insufficiency often stabilises with conservative management; whereas bilateral haemorrhage needs vigilant monitoring and potential lifelong adrenal steroid cover.

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Bone and Calcium

P62

Acute calcium-alkali syndrome associated with severe hypercalcemia following postsurgical hypoparathyroidism: a case report

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Background
Calcium-Alkali Syndrome (CAS) characterized by the triad of hypercalcemia, renal impairment, and metabolic alkalosis often occurred in patients receiving calcium and vitamin D supplementation for bone health. Here, we present a case of acute CAS following postsurgical hypocalcemia.
Clinical case
A 52-year-old female presented with a 3-day history of vomiting and abdominal discomfort. Her recent medical history included postsurgical hypoparathyroidism following thyroidectomy due to huge thyroid goiter in the previous week. Pathology of thyroid gland revealed oncocytic adenoma of thyroid. She was prescribed 5,400 mg of elemental calcium carbonate and 1.5 µg of calcitriol per day at the time of discharge after switching from intravenous calcium gluconate. Her latest plasma calcium was 8.3 mg/dL with low plasma intact parathyroid hormone (iPTH) level at 4.2 pg/ml. She denied intake of diuretics, other supplements, antacids, or NSAIDs. Initial investigations showed severe hypercalcemia, metabolic alkalosis, slightly impaired renal function but normal plasma potassium and phosphate levels (plasma calcium 18.6 mg/dL). Plasma iPTH was still low at 3.5 pg/mL and plasma 25-OH vitamin D level was 61 ng/ml. Calcium and vitamin D supplements were suspended and hypercalcemia resolved within 3 days after aggressive intravenous fluids and subcutaneous calcitonin injection. However, hypocalcemia with ongoing hypoparathyroidism developed and intravenous calcium gluconate was required. The plasma calcium levels normalized, and the renal function improved to the baseline. At 1 month later, she was asymptomatic with a normal plasma calcium and recovery of parathyroid function. Finally, she was diagnosed with acute CAS as a consequence of oral calcium carbonate and transient hypoparathyroidism following total thyroidectomy.
Conclusions
Individuals with postsurgical hypoparathyroidism requiring calcium and active vitamin D supplementation could develop CAS at any stage of hypoparathyroidism. Close monitoring of calcium levels are required, especially when high doses of active vitamin D are administered.

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P63

Giant cystic parathyroid adenoma: a rare culprit of anterior compressive neck swelling, primary hyperparathyroidism, and hypercalcemia

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A palpable neck lump secondary to cystic parathyroid lesions is an exceptionally uncommon occurrence, accounting for only 0.01% of all neck masses. Cystic parathyroid adenomas can be asymptomatic, can cause compression to the nearby structures, or can rarely lead to hypercalcemia due to primary hyperparathyroidism (PHPT), which accounts for less than 2% of PHPT cases in the literature. Our case was a 75-year-old woman who presented with an acutely enlarging anterior neck swelling causing dysphagia, odynophagia, and hoarseness. Due to the acute onset of compressive symptoms, she was taken for surgical drainage on the suspicion of the swelling being an abscess or infected cyst. A biopsy was taken, and it was later confirmed that the swelling was a parathyroid cystadenoma. Her admission serum biochemistry showed hypercalcemia, hypophosphatemia, and hyperparathyroidism which were consistent with the biopsy results. Fatigue and polydipsia secondary to hypercalcemia showed up later, at which point she underwent surgery for the removal of the parathyroid cystadenoma with hemithyroidectomy. Intraoperative parathyroid monitoring showed a drop in parathyroid hormone levels, confirming a successful surgery. This case alerts clinicians about the rare presentation of parathyroid cystadenoma as an acutely

enlarging neck swelling and it being a causative source of PHPT and hypercalcemia to prevent its accidental rupture during surgery leading to a potentially life-threatening hypercalcemic crisis.

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P64

Coexistence of PTH dependent and independent hypercalcaemia in the same patient: a case report

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Sarcoidosis is rare cause for hypercalcaemia, where PTH is suppressed. Primary Hyperparathyroidism is a common disorder where high Parathyroid Hormone (PTH) causes hypercalcaemia leading to renal and skeletal complications. We describe a patient where PTH hypersecretion worsened hypercalcaemia from sarcoidosis. A 69-year-old gentleman on long -term Prednisolone (10-20 mg/d) for sarcoidosis with lung nodules and mediastinal lymphadenopathy had moderate hypercalcaemia of 2.4-2.6 mmol/L (2.1-2.55) for around ten years but presented acutely with symptomatic increase in corrected calcium to 3.07 mmol/L (2.1- 2.55), normal phosphate 1.0 mmol/L (0.8-1.5), high PTH 19.3 pmol/l (1.6-7.2). He had mild chronic kidney disease with serum creatinine of 119 umol/L (63-111), and vitamin D 93 nmol/l (50-150). He was diagnosed with primary hyperparathyroidism, but parathyroid adenoma was not identified on ultrasound or sestamibi scans. After neck exploration three normal parathyroid glands were removed. The left inferior parathyroid was not found. Although left thyroid lobectomy was performed for suspected intrathyroidal parathyroid adenoma, this was ruled out on histology. Post operative calcium remained mildly high (2.5 – 2.65 mmol/l), although PTH level normalised (6.5 pmol/l). Post operatively low dose steroids was continued for sarcoidosis. As steroids were weaned, he presented again with hypertensive seizures and confusion. His corrected calcium was 3.44 mmol/L with suppressed PTH of 2.9 pmol/l. His creatinine was 186 umol/L and vitamin D 82.8 nmol/l. He was diagnosed with Posterior Reversible Encephalopathy Syndrome and treated with antihypertensives, intravenous fluids, and bisphosphonate infusion. Prednisolone (10 – 20 mg/d) was restarted for progression of lung nodules and rising serum ACE levels. He remains clinically stable with calcium in reference range on Prednisolone. Our case demonstrates diagnostic and management conundrum when high calcium is from co-existence of PTH-dependent and PTH-independent causes in the same patient.

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P65

Bone health assessment and management are suboptimal in endogenous cushing's syndrome: a large tertiary centre experience

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Background
Skeletal impairment and fragility fractures are frequent complications of endogenous Cushing's Syndrome (CS). Despite this, specific guidelines for managing bone health are lacking, and little is known about clinicians' engagement with bone health in this high-risk population. Therefore, I aimed to assess engagement with bone health assessment and management in endogenous CS using real-world data from a tertiary referral centre. I hypothesised that bone health would be assessed and managed in less than 50% of patients with endogenous CS.
Methods
79 patients with endogenous CS were retrospectively investigated. The frequency of bone health assessment, indicated by vitamin D measurement, and bone health management were recorded as primary outcomes. Changes in bone mineral density (BMD), fracture risk using FRAX, and fracture prevalence were assessed before and after CS treatment. A sub-group analysis compared BMD changes in patients treated with bone-protective agents to those not treated.
Results
Vitamin D was measured in only 34 patients (43%). Bone health was managed in only 31 patients (39.2%) with either calcium, vitamin D, or bone-protective agents. Improved BMD was observed after CS treatment. BMD was measured in only 35 patients (44.3%) during active CS; of these, 22.9% had osteoporosis. 14 patients (17.7%) had fractures within two years of CS diagnosis, and 12 fractures occurred during follow-up, despite CS remission. Treatment with bone-protective agents significantly improved lumbar spine BMD compared to those not treated.
Conclusion
These data demonstrate that skeletal impairment and fragility fractures are highly prevalent during active endogenous CS, and fracture risk may persist despite CS remission. However, bone health assessment and management were inadequate. These results indicate specific practice guidelines are needed to improve the assessment and management of skeletal complications in endogenous CS. Long-term prospective studies are needed to evaluate the efficacy of bone-protective agents on skeletal recovery in endogenous CS.

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Curious case of calcium - cutaneous sarcoidosis presenting as asymptomatic PTH-independent hypercalcemia

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Introduction
Sarcoidosis is a rare disease primarily affecting the pulmonary system in approximately 90% of cases with skin being second most commonly affected organ. Cutaneous involvement occurs in 20-35% of sarcoidosis patients and can present without systemic manifestations.
Clinical Case
We report a unique case of cutaneous sarcoidosis presenting with asymptomatic hypercalcemia. An 81-year-old White British woman with a medical history of type 2 diabetes mellitus, anaemia, hypertension, and polymyalgia rheumatica (PMR) was managed for left leg cellulitis. Examination revealed a systolic murmur, clear chest, bilateral erythema and pitting oedema at the infection site. An admission chest x-ray showed a known large hiatus hernia. Routine blood tests revealed adjusted calcium levels of 3.52 mmol/l, and PTH levels were low at 0.9 pmol/l (1.6-6.9 pmol/l), indicating PTH-independent hypercalcemia. Further blood tests showed normal vitamin D (129nmol/l), ACE levels (<5 IU/l), and TFTs with negative Myeloma and autoimmune screens. Elevated 1,25-dihydroxy vitamin D (calcitriol) was noted at 246 pmol/l. Occult malignancy was ruled out via normal CT chest, abdomen, and pelvis, gastroscopy with biopsy, and CT head scans. Initial PET CT results were reported as normal. Hypercalcemia management included intravenous fluids, zoledronic acid, denosumab and steroids. Subsequent detailed PET CT report revealed extensive moderate FDG uptake in the subcutaneous tissue of both arms. Physical examination identified subcutaneous nodules, and histology confirmed a florid dermal non-necrotizing granulomatous reaction, diagnosing extra-pulmonary cutaneous sarcoidosis. Interestingly, the patient had been on long-term prednisolone (10 mg) for PMR, recently reduced to 4 mg prior to admission. Her calcium levels normalized (2.57 mmol/l) after weaning off prednisolone.
Conclusion
Hypercalcemia in cutaneous sarcoidosis without pulmonary involvement is rare. Long-term follow-up is essential, as patients with cutaneous sarcoidosis may develop systemic involvement. She was referred to pulmonary and dermatology specialists for further evaluation.

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P67

Tertiary hyperparathyroidism in X linked hypophosphatemia: challenges and emerging therapeutic strategies

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Background
X-linked hypophosphatemia is a captivating yet challenging disorder that leads to rickets, skeletal deformities, osteomalacia, and impaired growth due to elevated

levels of fibroblast growth factor 23 and subsequent hypophosphatemia. Traditionally, managing this condition has involved high doses of phosphate salts and vitamin D.
Case Report
Startlingly, we document a case presenting X-linked hypophosphatemic rickets caused tertiary hyperparathyroidism, in a patient, regardless of phosphate and vitamin D replacement. X-linked dominant hypophosphatemic rickets (XLHR) is a metabolic bone syndrome, hereditary in nature, relatively infrequent with progression to developing irreversible tertiary hyperparathyroidism. Tertiary hyperparathyroidism (TH) is recognized as an unusual complication associated with XLHR observed in patients undergoing the treatment of phosphate and calcitriol. In 2019, an MIBI scan and 4D CT parathyroid excluded the presence of adenoma or parathyroid hyperplasia, prompting the surgical removal of all four parathyroid glands to address tertiary hyperparathyroidism, which subsequently normalized calcium levels. Histological analysis confirmed parathyroid hyperplasia. However, in 2022, the patient again developed hypercalcemia and elevated PTH levels. A follow-up MIBI scan identified a rare 12 mm hyperplastic parathyroid nodule within the soft tissues of the neck. This raised a serious concern in parathyroid multidisciplinary team meetings regarding surgery, as its execution might not work again and the patient would develop parathyroid nodules, again. Currently, Burosumab, a human anti-FGF23 monoclonal antibody is in consideration to be administered with calcimimetic like cinacalcet - that will be licensed in the UK from August 7, 2024 – to manage the complications.
Conclusion
This case highlights the urgent necessity for alternative treatments for XLHR patients who have had minimal success or adverse reactions to phosphate/calcitriol therapy. We advocate for more comprehensive research to help the scientific community reach a consensus on whether surgical intervention or the use of various effective agents, such as Burosumab, should be prioritized for managing tertiary hyperparathyroidism.

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P68

Hypocalcaemia unveiled: the impact of institutional protocols on patient safety

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Introduction
Hypocalcaemia is a complication post-thyroidectomy which requires close monitoring and is treated with oral calcium supplementation. We present a case of iatrogenic hypocalcaemia due to incorrect dosing of calcium supplementation because of an institutional protocol, leading to inadvertent patient harm.
Case Report
A 28-year-old female with Graves' Disease (on methimazole) undergoes a total thyroidectomy. Her post-operative course is complicated by recurrent hypocalcaemia, which resolves with titration of calcium carbonate to 1,500 mg four-times daily, calcitriol 1.5g daily, and 50,000 units of vitamin D weekly. She is subsequently discharged on this regimen, however, represented to the hospital two days later with symptomatic hypocalcaemia (tingling in bilateral upper extremities), and is found to have a calcium of 7.0 mg/dL (1.75mmol/l). She is restarted on her home regimen alongside intravenous calcium gluconate. Despite adherence with her outpatient medication regimen, it was discovered that while she had been receiving 1,500 mg of elemental calcium carbonate during the first admission, she had inadvertently been sent home with 1,500 mg of non-elemental calcium carbonate, which is 40% less than what was required. She was ultimately discharged on the correct regimen, with resolution of hypocalcaemia.
Discussion
Per discussion with the apothecary, our institutional protocol was reviewed, which noted that only the inpatient (and not outpatient) calcium carbonate dosages are listed as the elemental calcium composition. Elemental calcium is 40% of the total calcium carbonate dosage; as a result, our patient was inadvertently sent home on 1,500 mg of calcium carbonate, corresponding to 600 mg of elemental calcium four times per day, which is below the requirement to prevent hypocalcaemia.
Conclusion
It is important to ensure that the calcium supplementation a patient receives is calculated as the elemental calcium. This case depicts iatrogenic hypocalcaemia due to differences in the labelling of prescriptions in the inpatient versus outpatient setting, leading to inadvertent hypocalcaemia and harm.

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P69

Analysis of DXA use for the 50+ age group in denmark 2010-2022: successful targeting to persons at high risk of fracture?

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Background
DXA is a resource with waiting lists and limited capacity and there are concerns that significant capacity may be used in repeated assessment of people at low immediate risk of osteoporotic fractures. Danish guidelines recommend DXA in individuals above 50 with at least one clinical risk factor, including for example family history. The strongest predictors of fracture risk are age, sex, fracture history and glucocorticoid (GC) use. As the first step in establishing our national BMD research resource, we aimed to describe DXA usage over the past decade.
Methods
We obtained patient level data on DXA utilisation, fractures, and GC use from national Danish registers in persons aged 50+ as of 2010 and used a 5y look-back to identify prior DXA exams to classify DXAs as 'primary' or follow-up. Prior major osteoporotic fractures (MOF) in the preceding five years were retrieved from in- and outpatient contacts.
Results
Out of 896,538 DXA visits (Table 1), 48% were primary exams. Women accounted for 76% of primary exams and 84% of follow-up exams. The majority of exams were in people under 75 years of age. Among primary DXA visits, 32% were strongly justified by MOF or GC use. However, almost half of DXA visits were in non-GC users under 75 years of age without MOF. A declining trend in N of very short interval DXA (low value 90 days, 180 days) was observed (data not shown).

Calendar years 2010-2022	**Primary DXA**	**Follow-up DXA**
N of visits	506,330	390,208
Age	70.9 +- 8.9	72.4 +- 8.0
Age >75	164,576 (32.5%)	144,829 (37.1%)
Prior Major Ost Fx (5y)	74,588 (14.7%)	56,073 (14.4%)
Prior GC exposure (1y)	96,063 (19.0%)	65,949 (16.9%)

Conclusion
Initiatives to improve case-finding and reduce the need for follow-up DXA are needed to improve targeting of DXA to those at the greatest need.

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An unusual late presentation of syndromic hypocalcaemia

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A 32-year-old male of Lithuanian background presented to ED after a tonic-clonic seizure at work. There were no obvious precipitating factors, though he had started night shifts 6 months prior. Examination was significant for severe dental hypoplasia and abnormal facies. Biochemistry showed primary hypoparathyroidism: adjusted calcium mmol/L 1.47 (low), phosphate 1.30 mmol/L (high), magnesium 0.84 mmol/l, fT4 16.2 pmol/l, TSH 5.66 mU/L (high), PTH 1.4 pmol/l (low), vitamin D 22 nmol/L(low) Intracranial imaging showed grade I Chiari malformation (not felt to have contributed to seizures) Further history revealed recurrent childhood infections requiring hospitalisation, but no previous diagnosis of hypocalcaemia. He reported intermittent leg cramping in the weeks before presentation, but no paraesthesia. He was treated with IV calcium gluconate followed by oral calcium carbonate, high-dose cholecalciferol and alfacalcidol Bloods were sent for chromosomal analysis which revealed breakpoints within 22q11.2, with heterozygous deletion of approximately 2.2Mb of the DiGeorge/-Velo-Cardio-Facial Syndrome Critical Region.
Learning points
1. Patients with hypocalcaemia and dysmorphic features should have a chromosomal microarray analysis requested rather than the R153 hypoparathyroid gene panel, which only screens for single gene mutations; otherwise this diagnosis would have been missed.

2. This is a rare late presentation of DiGeorge' syndrome, most affected individuals will either develop hypocalcaemia during the neonatal period or be diagnosed during childhood due to developmental delay; late presentation of hypocalcaemia is unusual due to presumed compensatory hyperplasia of existing parathyroid tissue. Hypocalcaemia can be precipitated in adults during periods of stress.
3. The estimated prevalence of DiGeorge is 1/3000 – 1/6000 live births, but the number may be higher due to the condition's variability, and lack of neonatal screening.
4. The diagnosis should be made due to the necessity of screening for other syndromic sequalae which will be discussed.

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Calcium conundrum: the unexpected case of a young patient's parathyroid puzzle

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This case serves as a critical reminder of the complexities in diagnosing parathyroid disorders and the necessity of personalized management strategies. We present a 36-year-old female with a history of long-standing mental health issues, Type 2 diabetes, and hypertension was referred to our endocrine clinic due to significantly elevated corrected calcium levels of 2.83 mmol/L (normal range 2.2-2.6). The patient was asymptomatic. Her PTH levels were within the normal range but at the upper limit 6.4 pmol/l (normal range 0-6.9). Given her age, hyperparathyroidism is a possibility. Notably, her mother has undergone parathyroid surgery, and both her mother and sister are undergoing genetic testing for MEN syndrome (types 1 or 2), which has returned negative results. A 24-hour urinary calcium test revealed low levels of 1.8 mmol/24h (normal range 2.5-7.5), which is atypical for hyperparathyroidism. Therefore, we are cautious about proceeding with parathyroid surgery until we confirm she does not have familial hypocalciuric hypercalcemia (FHH), a benign condition that typically requires no treatment. Genetic testing for FHH also returned negative. The patient was previously on Dapagliflozin, which we speculated might affect urinary calcium excretion, although this has not been documented before. We advised her to discontinue Dapagliflozin for four weeks and retest her 24-hour urinary calcium. After stopping the medication, her urinary calcium increased to 8.5 mmol/24h. Localization scans indicated a probable right lower parathyroid adenoma, and she has now been scheduled for surgery. In summary, this case underscores the importance of thorough evaluation and genetic testing, particularly given her family's history of parathyroid disease. The subsequent resolution of her urinary calcium levels after medication adjustment further illuminates the interplay between pharmacotherapy and calcium metabolism.

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P72

The introduction of a parathyroid specialist nurse has improved the standard of care and compliance with trust guidelines for patients with primary hyperparathyroidism having a parathyroidectomy

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Primary Hyperparathyroidism (PHPT) is characterised by elevated serum calcium concentrations with inappropriately normal or elevated parathyroid hormone (PTH) concentrations. Parathyroidectomy is the only definitive treatment for PHPT. Hypoparathyroidism is a potential complication of this surgery, may be either transient or permanent, and is treated with calcium supplementation and activated vitamin D titrated to maintain serum calcium levels within safe parameters. Under-treatment results in hypocalcaemia which can cause problems including paraesthesia, arrhythmias, and tetany; whereas over-treatment may result in hypercalcaemia which can result in problems including lethargy, pancreatitis, and renal failure. Our Trust guidelines recommend that patients undergoing parathyroidectomy identified as high-risk for post-operative hypoparathyroidism are discharged with empirical calcium and 1-alfacalcidol supplementation to facilitate an early and safe discharge. Calcium and PTH are checked at 14 days post-operatively and adjusted according to an algorithm. Depending on these blood results treatment may be continued at full dose until the next clinic appointment, reduced with further blood tests planned, or stopped completely. In 2022 the average length of time from surgery to outpatient calcium check was 45 days (range 7-386 days; $n = 79$). In 2023 a Parathyroid Specialist Nurse was appointed and one of their tasks was to co-ordinate the 14 day post-operative blood test check. In 2023, after the introduction of the Specialist Nurse, the average length of time from surgery to outpatient calcium check had improved to 19 days (range 8-75 days; $n = 101$), with patients on average having their calcium check 26 days sooner, thus reducing the length of time they are potentially under- or over-treated with 1-alfacalcidol and calcium supplementation. The introduction of a Parathyroid Specialist Nurse has therefore improved the standard of post-operative care for patients undergoing a parathyroidectomy and improved compliance with our Trust guidelines, despite case numbers increasing from 79 to 101 (an increase of 22%).

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P73

Post-parathyroidectomy calciphylaxis in a patient with parathyroid adenoma: a rare complication

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Introduction
Calciphylaxis is a rare, life-threatening condition associated with hypercalcaemia. It is characterised by calcification of small and middle-sized arterioles within subcutaneous tissue, leading to compromised blood flow, tissue ischaemia and subsequent necrosis. While calciphylaxis typically occurs in chronic kidney disease (CKD), a small proportion of cases can present without CKD, referred to as non-uraemic calciphylaxis (NUC). Cases of NUC associated with primary hyperparathyroidism are rarely documented. Additionally, evidence-based management options for NUC in the context of hyperparathyroidism remain limited due to the rarity of the condition.
Case report
We present a case of an individual admitted following out-of-hospital cardiac arrest. She was previously healthy prior to this. Following successful resuscitation, the investigations revealed significantly high calcium levels at 4.46 mmol/L along with raised PTH at 261.2 pmol/l in keeping with primary hyperparathyroidism. After stabilization, she underwent an urgent parathyroidectomy with histopathology revealing a benign parathyroid adenoma. Notably, she had no history of hypercalcaemia symptoms before this event. Post-operatively, her calcium levels and parathyroid levels significantly dropped to 2.09mmol/L and 0.3 pmol/l respectively. Following her parathyroidectomy, she had a prolonged post-surgery recovery in the intensive care unit (ITU). She developed severely painful lesions in her groin and axilla regions. This were promptly reviewed by a dermatologist and biopsied. Histopathology confirmed the diagnosis of calciphylaxis. She was closely monitored, received regular wound debridement and early mobilisation with physiotherapy. Her calcium levels remained stable throughout her recovery period.
Conclusion
Calciphylaxis is a life-threatening condition, primarily affects patients who have chronic renal failure. A small proportion of patients of cases have been documented in the absence of renal disease known as non-uremic calciphylaxis. Patients who have undergone parathyroidectomy for primary hyperparathyroidism should be recognised as a potential risk factor for NUC. Early recognition and prompt treatment are critical for improving mortality outcomes in calciphylaxis.

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P74

Genetic cause for hypoparathyroidism in a 92-year-old

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We present an unusual case of longstanding hypoparathyroidism, for which a diagnosis was eventually reached at the age of 92 yrs. The patient presented in 2014 aged 83 years with symptomatic hypocalcaemia – corrected calcium was 1.1 mmol/L and PTH was 1.8 pmol/l. He was referred to our department in 2017 when it was noted he had a background of chronic kidney disease, hypertension, Paget's disease of the skull and a mild normocytic anaemia. The mild anaemia had been ongoing since 2010 when a level of 128 g/L was investigated and showed raised ferritin 423 ug/L (normal range 15-300), iron 34 umol/L (normal range 9 - 28) and transferrin saturations 65% (normal range 20-55). However, this was not noted at the time of his referral. The patient was reviewed annually in

clinic, calcium and vitamin D supplementation were ongoing, and his corrected calcium level remained stable at 1.94- 2.28 mmol/L during the period of 2017-2024. In 2024 at the age of 92, it was noted that he seemed clinically hypogonadal with little in the way of facial hair, unwrinkled complexion and a full head of scalp hair. This prompted a testosterone check which revealed a low level of 4.0 nmol/l (normal range 6.7 – 25.7) with an FSH of 28.9 IU/L and LH of 20.3 IU/l. His alkaline phosphatase was raised at 218u/L (normal range 30-130) and this had been the case from 2010, due to Paget's disease. His ALT was normal. His iron studies were requested and they revealed a similar picture to before with raised ferritin, iron and transferrin saturations. Genetics were sent for hereditary haemochromatosis which were homozygous for the pathological variant C282Y. Idiopathic hypoparathyroidism is a dissatisfying diagnosis and a cause may only be apparent if appropriate investigations are made.

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P75

Assessment of ^{99m}Tc-MIBI outcomes in patients on cinacalcet for primary hyperparathyroidism

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Introduction
Localization of parathyroid adenomas in primary hyperparathyroidism (PHPT) is achieved commonly using ^{99m}Tc-methoxyisobutylisonitrile with SPECT/CT (MIBI) and neck ultrasound (USS). Drugs interfering with calcium uptake such as calcium channel blockers or cinacalcet may interfere with the sensitivity of MIBI. The aim of our study was to assess the outcomes of MIBI in patients with severe PHPT who are treated with cinacalcet.
Methods
Data on all patients treated with cinacalcet for PHPT for any indication was collected. Patients who had MIBI scan after cinacalcet initiation were included. Data on PTH and calcium and concurrent ultrasound (USS) were collected
Results
n = 35 had MIBI after cinacalcet initiation (total cinacalcet patients = 121) Mean duration between cinacalcet initiation and MIBI was 194 days. 63% (n = 22) of MIBI scans were positive despite being on cinacalcet. MIBI was positive in 13/22 patients despite the calcium normalizing. Comparing the MIBI-positive vs. MIBI-negative, baseline PTH was higher (25.1 ± 18.8 vs. 16.0 ± 10.9 pmol/l); baseline adjusted calcium was comparable (3.02 ± 0.17 vs. 3.05 ± 0.25 mmol/l), both not statistically significant. In MIBI-negative patients, USS was also negative, suggesting this may be true negative. In patients with calcium ≥ 3mmol/l, MIBI was positive in 65% (13/20); in patients with calcium ≥ 2.85mmol/L with symptoms, MIBI was positive in 63%.
Conclusion
Cinacalcet is indicated in patients with severe hypercalcemia and contributes to symptom relief and admission avoidance. Pausing treatment to avoid interference to MIBI may be clinically challenging. With 65% of patients generally still getting a conclusive positive result, a pragmatic approach would be to perform MIBI on cinacalcet. Concurrent imaging with USS or alternate imaging modality scans could be performed as initial options to validate a negative MIBI scan; repeating MIBI after pausing cinacalcet treatment could be considered if deemed safe, practicable and necessary.

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P76

Utility of cinacalcet in primary hyperparathyroidism: thinking beyond the NICE guidelines

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Introduction
Cinacalcet is an effective treatment for primary hyperparathyroidism (PHPT). NICE recommends cinacalcet if calcium ≥ 3.0mmol/l or ≥ 2.85 with symptoms, especially when surgery is not an immediate option. The aim of this study was to assess the utility, efficacy and impact of cinacalcet on the overall management of PHPT.
Methods
Data on all patients who were initiated on cinacalcet was collected. Data on indication for cinacalcet, baseline calcium, lowest calcium reached, hospital admissions for hypercalcaemia before and after initiation were analysed.
Results
n = 121 Mean age: 72 years (25-97), 77% females. Mean calcium at initiation: 2.97mmol/l (2.66-3.58); PTH 18.4 pmol/l (2.5-107) Mean duration of follow up: 26 months (2-111). Mean average dose of cinacalcet: 42 mg/day (0-270) [9 patients discontinued due to intolerance] Indications for treatment were:
- Ca ≥ 3.0mmol/l = 53 (44%)
- Ca ≥ 2.85 with symptoms = 22 (18% based on NICE criteria).
- Ca ≥ 2.85 with end organ damage = 14 and failed surgery = 2 (13% in total);
- Other indications: Ca ≥ 2.85, asymptomatic and without end organ damage = 16; Ca < 2.85 and symptomatic = 5; Ca < 2.85 and asymptomatic = 8; others = 1

Mean number of hospital admission for hypercalcaemia reduced from 0.83 before cinacalcet to 0.51/patient. 33 patients reached lowest calcium between 2.2-2.4mmol/l with 3 developing biochemical hypocalcaemia during treatment. 31 patients still had Ca > 2.6 at final review, with 27 had Ca < 2.85 therefore less likely to be symptomatic.
Conclusion
Cinacalcet is an effective treatment for PHPT with substantial reduction in hospital admissions for severe hypercalcaemia. 75% of patients were treated based on biochemical NICE criteria or surgical criteria. Though NICE does not propose a target calcium on treatment to achieve with cinacalcet, calcium of 2.4-2.6 may be adequate for symptomatic relief, therefore 25% of the patients could be on a lesser dose thereby helping with cost reduction.

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P77

Delayed diagnosis of normocalcaemic hyperparathyroidism resulting in multiple fractures, resistant osteoporosis and a life in pain: a case report

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Introduction
In patients with severe, unexplained osteoporosis accompanied by normal calcium and elevated parathyroid hormone (PTH), normocalcemic primary hyperparathyroidism (NHPT) should be considered after excluding secondary hyperparathyroidism (SHPT)[1]. This case underscores the diagnostic challenges of NHPT, particularly given frequent occurrence of small and multiple adenomas[1,2] and consequences of delayed parathyroidectomy, leading to multiple fractures, misdiagnosis of fibromyalgia, and complications from bisphosphonate treatment.
Patient Case
Results A 69-year-old woman presented with persistent bone pain and 20 years of worsening osteoporosis, complicated by multiple fractures. Her treatments included Hormonal Replacement Therapy at age 49, discontinued due to weight gain, along with calcichew-D3 and oral bisphosphonates, causing gastrointestinal discomfort due to hiatus hernia, hence switched to IV zoledronate. Between 2004 and 2019, she experienced a bimalleolar, tibia and fibula, pubic ramus and anterior acetabulum fracture. She has stable Chronic Kidney Disease Stage 3. Her chronic pain was diagnosed as fibromyalgia, a condition with higher prevalence in NHPT patients[3]. She received SSRIs, increasing the risk of bone loss and fractures[4]. She also has temporomandibular joint dysfunction; a condition associated with elevated PTH[5]. Despite having severe osteoporosis, she underwent contraindicated chiropractic spinal manipulation therapy (SMT)[6]. In 2024, NHPT was suspected due to persistently elevated PTH levels despite corrected vitamin D (Table 1). Urinary studies showed calcium-creatinine ratio = 0.028 and normal 24-hour urinary calcium of 5.9 mmol/day, excluding familial hypocalciuric hypercalcemia. This makes NHPT the most likely diagnosis. Imaging suggested potential thyroid asymmetry, but no clear parathyroidadenoma was confirmed - hence the patient is booked for 4D-CT.

Table 1.

Oct 21	Dec 22	Feb 24	Sep 24
2,55	2,58	2,5	2,45
8,8	9,1	10,1	13,4

References
1. Leslie & Levine, 2024.
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3. Costa *et al*, 2016.
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P78

A case of hypercalcaemia: primary hyperparathyroidism and familial hypocalciuric hypercalcaemia

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History
The coexistence of primary hyperparathyroidism and familial hypocalciuric hypercalcemia is exceedingly rare. We present the case of a young woman in her thirties who presented with hypercalcemia detected on routine blood tests. She had no significant medical or family history of hypercalcemia.
Investigations
Her serum calcium was consistently around 3.2 mmol/l, with elevated parathyroid hormone levels at 110 ng/l. Phosphate was low at 0.52 mmol/L and vitamin D levels were normal.
Management
She was initially treated with intravenous fluids as an inpatient and started on Cinacalcet, with plans for outpatient follow-up. She continued Cinacalcet and underwent localisation studies with a Sestamibi scan and neck ultrasound. Scans revealed no parathyroid adenomas. The urine calcium creatinine clearance ratio excluded familial hypocalciuric hypercalcemia (FHH). The serum calcium remained high at 2.94 mmol/l. She underwent bilateral neck exploration/parathyroidectomy - it showed two parathyroid lipoadenomas, which were resected. Post-operatively, her calcium remained high, and Cinacalcet was restarted. Genetic testing results were negative for MEN-1, but the testing confirmed a diagnosis of FHH. The choline PET-CT and CT 4D parathyroid scan failed to show evidence of additional parathyroid adenomas. Long-term options included continuing Cinacalcet or considering repeat surgery. The patient opted for repeat surgery to pursue a definitive cure for her hypercalcemia and avoid the long-term use of Cinacalcet as she was planning for future pregnancies.
Conclusion
This case highlights the complexities in diagnosing and managing concurrent primary hyperparathyroidism and familial hypocalciuric hypercalcemia. The urine test results were not suggestive of FHH and therefore were misleading in this case. This case also emphasises the need for a multidisciplinary team approach in managing complex cases of this nature.

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P79

Cinacalcet use in primary hyperparathyroidism – a retrospective look at patient outcomes in a london hospital

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Introduction
Cinacalcet, a calcimimetic first approved for use in 2004, has become a mainstay of treatment in those awaiting or unable to undergo surgery for primary hyperparathyroidism. In this retrospective study, we aimed to map clinical outcomes in patients who had been prescribed cinacalcet for a suspected or confirmed diagnosis of primary hyperparathyroidism, between 1st October 2022 and 30th September 2024, and to compare our practice with NICE guideline *NG132*, published in 2019.
Methodology
All instances where cinacalcet was dispensed from a pharmacy within the trust were logged – biochemical, demographic and clinical data were then gathered. Any patients with chronic or end-stage renal disease were excluded.
Results
Eighty-four patients were identified - 55 female (65%) and 29 male - with ages ranging from 25-90 (mean age 67). 37% ($n = 31$) were referred for parathyroidectomy (mean age 50); 16% ($n = 14$) went on to have surgery (mean age 56). Two patients had recurrence of hypercalcaemia post-operatively, and were subsequently restarted on cinacalcet; the remainder were cured. Seventy-one of the 84 patients were prescribed cinacalcet after *NG132* was published – of these, 49% ($n = 35$) were prescribed cinacalcet in adherence with the guidelines; in those where cinacalcet was prescribed outwith the guidelines, all but one was prescribed cinacalcet while awaiting surgery.
Conclusions
Cinacalcet was prescribed in adherence with NICE guideline *NG132* in just under half of cases; the overwhelming majority of prescriptions outwith the guidelines were for use as bridging therapy while awaiting parathyroid surgery – this is consistent with evidence elsewhere within the literature, and should be a key consideration to take into account for future guidelines, given the well-documented use of cinacalcet peri-operatively. Surgical outcomes were very favourable, with 85% of patients cured following surgery.

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P80

Familial hypocalciuric hypercalcaemia and familial combined dyslipidemia in a case of recurrent acute pancreatitis: a clinical report

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Familial Hypocalciuric Hypercalcaemia (FHH) and Familial Combined Hyperlipidaemia (FCH) are inherited metabolic disorders characterized by dysregulation in calcium and lipid levels, respectively. FHH is caused by a mutation in the calcium-sensing receptor gene (CASR) resulting in reduced calcium excretion and resultant mild chronic hypercalcaemia. FCH is a relatively more common polygenic disorder with lipid derangements like increased triglycerides and cholesterol and reduced protective high-density lipoproteins (HDL). Hypercalcaemia and hypertriglyceridaemia are recognized individual triggers for acute pancreatitis but their co-existence in patients with both FHH and FCH are rare and poorly studied. A 40-year-old man presented to his GP with 3 years of episodic pain abdomen, nausea and vomiting- consistent with sub-acute pancreatitis. His work up showed a finding of persistent moderate hypercalcaemia (Adjusted Calcium 2.8-2.9). After 2 years he was noted to have a urine calcium-to-creatinine of 0.006. He was diagnosed with FHH after a CASR gene mutation was confirmed. Unusual for FHH, he required cinacalcet to correct labile calcium levels. Recently, he presented to the ED with severe abdominal pain, nausea, and vomiting. Lab tests showed triglycerides of 37 mmol/l, amylase of 1000 mmol/l, and adjusted calcium of 2.65 mmol/l. Management of his acute pancreatitis included intravenous fluids, insulin therapy to lower triglycerides acutely and monitoring in intensive care unit. Once stabilised, his long-term management focused on dietary modifications and lipid-lowering measures (including fibrates and omega-3 fatty acids) alongside cinacalcet to mitigate the synergistic effect of the two metabolic disorders. This case highlights the importance of early recognition and management of FHH and FCH through screening and genetic testing. Prompt monitoring and control will prevent complications such as pancreatitis. Further research on the interplay between calcium and lipid metabolism will have strong value in preventative medicine and will aid in personalizing treatment strategies in affected individuals.

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P81

Cinacalcet in familial hypocalciuric hypercalcaemia: friend or foe?

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A 29-year-old-female presented to the emergency department with a 4 week history of polyuria, polydipsia and night sweats. Her adjusted calcium (Aca) was elevated at 3.12 mmol/L (2.2-2.6). Clinical examination was unremarkable. Her past medical history included migraines. There was no relevant family history. Repeat biochemistry showed an ACa 3.14 mmol/l, phosphate of 0.55 mmol/L (0.8-1.5), parathyroid hormone (PTH) of 8.4 pmol/l (3.1-6.8), eGFR > 90 and Vitamin D of 45nmol/l (51-163). Her ACa remained at 3.03 mmol/L despite intravenous fluids. Given the significantly raised ACa and osmotic symptoms, she was started on calcimimetic Cinacalcet 30 mg twice daily for suspected primary hyperparathyroidism (PHPT), with improvement in her symptoms and biochemistry (including normalisation of PTH). Parathyroid imaging and DEXA were unremarkable. Her 24 hour urinary calcium creatinine ratio was low at 0.0092, and remained low at 0.0021 when repeated off Cinacalcet. Genetic screening revealed heterogenicity of the calcium sensing receptor (CaSR) missense variant, confirming Familial Hypocalciuric Hypercalcaemia (FHH) Type 1. She was restarted on Cinacalcet 30 mg twice daily and her latest ACa was 2.61 mmol/l. She is tolerating Cinacalcet well though reports occasional muscle cramps and paraesthesia. FHH causes lifelong hypercalcaemia similar to that of PHPT. The former is often asymptomatic or mildly symptomatic without increased risk of complications such as renal calculi and osteoporosis favouring conservative management over pharmacological or surgical approaches. Recent case reports suggest calcimimetics may have a role in FHH where ACa is persistently raised $>$ 0.25mmol/L above the upper limit of normal or if symptomatic, with subjective and biochemical improvement defining treatment success. This case demonstrates successful treatment with Cincacalet, with few

adverse effects, suggesting allosteric modulation of CaSR with Cinacalcet may have a role in FHH. Long-term follow up and randomised controlled trials are needed to explore its potential.

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P82

Burden of managing hypoparathyroidism medication regimens: a patient survey

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Introduction
This project assessed the burden of managing hypoparathyroidism with a medication regimen of conventional therapy (oral calcium and/or active vitamin D) in the UK.
Methodology
An online cross-sectional patient survey was conducted in June 2024. Eligible respondents were adults (≥18 years) diagnosed with hypoparathyroidism persisting for ≥12 months and taking conventional therapy. Data collected included patient characteristics, medication regimens as well as the impact of managing this medication regimen and subsequent treatment satisfaction. Respondents were recruited via Parathyroid UK's mailing list and data were aggregated and summarised using descriptive statistics.
Results
Of the 402 respondents, the majority (86.8%) were female, aged 36-55 years. Most were diagnosed post-surgery (72.4%) and took both oral calcium and active vitamin D (63.4%). Fewer than half of respondents reported satisfaction with their treatment regimen (44.1%). Treatment dissatisfaction was driven by poor communication with healthcare professionals (82.6%), concerns about long-term side effects (69.3%), and the burden of managing their medication regimen (55.1%).
Conclusion
These results show that adults with hypoparathyroidism have evident treatment dissatisfaction, partly driven by the burden of managing their medication regimen. These results suggest that programmes to improve physician communication on hypoparathyroidism should be considered and highlight the need for an effective and safe treatment with reduced risk of long-term complications.

Table 1. Medication regimen and treatment satisfaction

Medication Regimen	**N (%)**
Oral active vitamin D only	131 (32.6)
Oral calcium only	16 (4.0)
Both	255 (63.4)
Treatment Satisfaction	
Dissatisfied or very dissatisfied	141 (35.1)
Neither	84 (20.9)
Satisfied or very satisfied	177 (44.1)

Table 2: Reasons for treatment dissatisfaction[a]

	N (%)
Poor communication/lack of support from HCPs	186 (82.6)
Risk of long-term complications (eg heart and kidney) and side effects	156 (69.3)
Burden of managing medication regimen	124 (55.1)
Other	102 (45.4)

[a]Completed by respondents "dissatisfied/very dissatisfied" or "neither" (n = 225)

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P83

A case of severe hypercalcaemia - is it parathyroid carcinoma

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We present the case of an elderly man who was referred by his GP for hypercalcaemia. The patient had a preexisting large right-sided thyroid swelling but no other significant medical history. Blood tests revealed high calcium levels and significantly elevated levels of parathyroid hormone (PTH), which is unusual in a typical case of primary hyperparathyroidism secondary to parathyroid adenoma. The biochemical findings raised suspicion towards a diagnosis of parathyroid carcinoma. He was initially treated with intravenous Zoledronic acid and fluids. However, his calcium levels remained persistently high. Next cinacalcet therapy was initiated, the dosage of cinacalcet was gradually increased up to the maximum. Despite maximum pharmacological treatment, calcium, and PTH levels remained persistently elevated. (calcium 3.28 and PTH 90.9). These biochemical results favoured a carcinoma rather than an adenoma. However confirming the diagnosis was a challenge, both nuclear and CT scans, typically instrumental in identifying such conditions, showed an 8.9 cm cystic mass in the thyroid. However, an FNAC which was done failed to provide conclusive evidence. The case was discussed with ENT and the decision was made for emergency surgery. The surgery included a right hemithyroidectomy, parathyroidectomy, and excision of the cyst. Surgery was the definitive treatment for this gentleman, addressing both his compressive symptoms and reducing his calcium and PTH levels. Cystic parathyroid adenomas exhibit varying clinical presentations, from mild symptomatic hyperparathyroidism, where patients experience fatigue or weakness to more serious presentations such as hypercalcaemic crisis or compression of surrounding structures. Parathyroid cysts can also be incidentally discovered. This diversity in clinical presentation underscores the importance of cystic parathyroid adenoma as a potential differential diagnosis in patients presenting with hyperparathyroidism or neck masses. It is also important to differentiate parathyroid adenoma from cystic lesions since they can lead to severe hypercalcaemic crises and their risk of malignant transformation.

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P84

Profound hypercalcaemia secondary to immobilisation in a patient with complex cyanotic congenital heart disease

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Background
Profound hypercalcaemia secondary to immobilisation is an exceptionally rare condition, characterized by the efflux of calcium from bones due to increased osteoclastic activity. It necessitates careful evaluation to exclude more common causes such as primary hyperparathyroidism and malignancy.
Case Presentation
We present the case of a 21-year-old male with a history of complex cyanotic congenital heart disease, who was referred to the Endocrinology outpatient clinic from Cardiology due to an incidental finding of severe hypercalcaemia (corrected calcium level of 4.2 mmol/l). The patient had undergone a Fontan procedure, resulting in protein-losing enteropathy, a common complication associated with congenital heart disease. His phosphate levels were normal (0.88 mmol/l), and parathyroid hormone (PTH) levels were within the normal range (7.54 pmol/l). Bone-specific alkaline phosphatase levels were also normal, indicating impaired bone remodelling favouring osteoclastic activity. The patient, mostly wheelchair-bound, appeared cyanosed and cachectic upon examination.
Management and Outcome
Due to the complexity of his underlying conditions, the patient was promptly transferred to the congenital heart disease department for careful fluid resuscitation. He received approximately 2 litres of normal saline over 24 hours, followed by a pamidronate infusion. A CT scan of the chest, abdomen, and pelvis revealed progressive dysplastic liver nodules secondary to the Fontan procedure, with no evidence of malignancy. After 72 hours of fluid resuscitation, his corrected calcium levels decreased to 3.3 mmol/l. He was subsequently referred to the rehabilitation team for early mobilization to prevent recurrent hypercalcaemia.
Conclusion
This case highlights the rarity of immobilisation-induced hypercalcaemia outside of traumatic spinal cord injuries. It underscores the diagnostic challenges and the necessity for a multidisciplinary approach involving endocrinologists, rehabilitation specialists, and congenital heart disease experts. Bisphosphonates and Denosumab remain the cornerstone of management, inhibiting osteoclastic bone resorption, the primary etiological factor in immobilisation hypercalcaemia.

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P85

Hyperparathyroidism: unusual site, uncommon surgery

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Introduction
Ectopic parathyroid glands can occur early during embryological development[1]. Their localisation and surgical management may prove challenging if required to cure hyperparathyroidism.
Case report
A 53-year-old lady presented with non-specific aches and pains, she was biochemically diagnosed with primary hyperparathyroidism and bone densitometry confirmed osteoporosis at femoral neck. Surgery was planned in view of young age, high fracture risk and persistent symptoms. An ultrasound scan did not identify an adenoma in the neck, but SPECT-CT/parathyroid scintigraphy demonstrated faint uptake in the anterior mediastinum. While further management plan was being discussed, she was admitted to a mental health ward with psychotic depression. Her serum calcium rose to >3.0mmol/L and she was commenced on cinacalcet. After discharge, when she was clinically and biochemically stable, she had a 4D-CT scan which confirmed an 8mm nodule in the anterior mediastinum corresponding to the area of abnormal uptake on scintigraphy, consistent with an ectopic parathyroid adenoma. However, with a potential for open-chest surgery, surgeons sought further confirmation. A C^{11}-methionine PET scan confirmed that the gland identified was highly likely to be an ectopic parathyroid adenoma. The adenoma was successfully removed with robotic surgery, obviating the need for open surgery and she was confirmed to have been cured by histological and biochemical criteria.
Conclusion and discussion
Ectopic parathyroid glands pose a diagnostic and therapeutic challenge. In this case ultrasound, scintigraphy, 4D-CT, and ultimately C^{11}-methionine PET scan were needed for definite localisation. Robotic surgical techniques saved this lady from having a sternotomy. There was added interest of the psychiatric illness, which was possibly exacerbated by hypercalcaemia, but certainly made her hypercalcaemia worse.

[1]Chan TJ, Libutti SK, McCart A, Chen C, Khan A, Skarulis MK *et al*. Persistent primary hyperparathyroidism caused by adenomas identified in pharyngeal or adjacent structures. World J Surg. 2003. 27(6):675-9

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P86

Autoimmune primary hypoparathyroidism in a COVID-19 vaccine recipient – is there a link?

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An 83-year-old man was admitted from rheumatology clinic with severe symptomatic hypocalcaemia and suppressed parathyroid hormone (PTH) having been referred with a 5-month history of worsening weakness, cramping and paraesthesia. Given the recent onset of symptoms and a record of a normal adjusted calcium in 2014 the diagnosis of new onset hypoparathyroidism was made and he was treated as per severe hypocalcaemia protocol. Admission blood tests showed low adjusted calcium (1.2mmol/l) and low PTH levels (<0.5 pmol/l), with normal phosphate, alkaline phosphatase, albumin and magnesium, and sufficient 25-hydroxyvitamin D levels. Underlying causes of hypoparathyroidism were considered. He had no history of surgery, irradiation or trauma to the neck. An HIV screen, iron studies, serum copper, and 9am serum cortisol were normal. Antiparathyroid antibodies were negative. A CT neck, thorax, abdomen and pelvis did not reveal any structural abnormalities in his neck or evidence of malignancy. Of note, he had received the first and second dose of the Oxford-AstraZeneca SARS-CoV-2 (ChAdOx1 nCoV-19) vaccines, three months and one month respectively, prior to the onset of his symptoms. Genetic syndromes were not considered given the late onset and absence of family history of hypoparathyroidism. His diagnosis is likely to be antibody-negative hypoparathyroidism and there has been no resolution on long-term follow up. It is rare to encounter new-onset hypoparathyroidism in the elderly and most cases occur after neck surgery or radiation. Autoimmune hypoparathyroidism, although rare, should still be considered in this age group after thorough investigation for other underlying causes. At present, there is only one other case report suggesting a possible link between the COVID-19 vaccine and development of hypoparathyroidism, however, whether this association is coincidental or causal remains to be elucidated. This is the first case report describing new-onset and persistent autoimmune hypoparathyroidism in an elderly patient after mRNA COVID-19 vaccination.

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Endocrine Cancer and Late Effects

P87

Graves' disease following bone marrow transplantation: a challenging condition to manage

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Graves' disease (GD) following bone marrow transplantation (BMT) is rare. The pathophysiology is uncertain. We present two challenging cases of GD following BMT. Case 1: 45-year-old female, with previous history aged 39 of T-cell lymphoma requiring treatment with CHOP-14 and autologous stem cell transplantation, presented with thyrotoxicosis secondary to GD (TSH <0.01 mU/l; FT4 57.9 pmol/l; FT3 >46.08 pmol/l, TRAb >30 IU/l). She experienced symptoms typical of thyrotoxicosis. There was a small goitre and no thyroid eye disease (TED). Despite compliance with high dose carbimazole for >8 months, thyrotoxicosis persisted (TSH<0.01 mU/l, FT4 32.9-52.4 pmol/l, FT3 >46.08 pmol/l). There was associated liver derangement. She received potassium iodide pre-operatively and underwent thyroidectomy, achieving euthyroidism on levothyroxine. Histology was compatible with GD with minimal inflammation. Case 2: 43-year-old female patient with childhood onset aplastic anaemia, received cyclophosphamide chemotherapy conditioning, total body irradiation and stem cell allograft, complicated by graft versus host disease (GVHD). She was receiving long-term levothyroxine for subclinical hypothyroidism but, presented with new onset thyrotoxicosis despite stopping levothyroxine (TSH < 0.01 mU/l, FT4 25.7 pmol/l, FT3 >30.72 pmol/l, TRAb 11.8 IU/l). She started carbimazole, but has persistent thyrotoxicosis, liver derangement, TED CAS 3, diffuse thyroid enlargement and growth of TR3 nodules on thyroid ultrasound. She is awaiting thyroidectomy. Literature reporting GD following BMT is limited to few cases ($n = 14$) implicating possibility of two mechanisms: GVHD and autoreactivity from transfer of donor lymphocytes. GD onset was reported 5 months to 14 years following BMT. Treatments for GD, where reported, included antithyroid medication ($n = 9$); surgery first-line/following relapse ($n = 3$), radioiodine ($n = 1$). TSH receptor antibody levels were commonly reported as positive/high (TRAb 3.79-34.4 IU/l). Further research into the pathophysiology, monitoring and management is needed to optimise management of such challenging cases.

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P88

A case of primary adrenal lymphoma presenting as primary adrenal insufficiency and hypercalcaemia and literature review

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Background
Primary adrenal lymphoma (PAL) is an extremely rare condition, typically involving bilateral adrenal glands. It has a male predominance and generally presents in elderly. Adrenal insufficiency, abdominal pain, and systemic symptoms such as weight loss and fatigue are common presentations.
Case presentation
We present a case of a 69-year-old male admitted with feature of adrenal failure including tanned skin, 20 kg weight loss over 5 months.
Investigation
Initial investigation showed normocytic anaemia (Hb 91 g/l), hyponatremia (Na 132 mmol/l), and hypercalcemia (adjusted Ca 3.32 mmol/l). The unusual presentation of hypercalcaemia and significant weight loss led to further investigation. A short Synacthen test confirmed adrenal insufficiency with a serum cortisol peak of 60 nmol/l, elevated ACTH >1250 ng/l. CT Abdomen and Pelvis revealed bilateral adrenal hyperplasia and 75mm left adrenal mass. Adrenal androgens and plasma metanephrines were normal. PET CT Scan confirmed bilaterally avid adrenal glands. Endoscopic ultrasound-guided biopsy left adrenal gland was conducted and revealed high-grade diffuse large B-cell lymphoma with a non-germinal centre double expresser (BCL2+/c-Myc+) immunophenotype.

Management
Replacement hydrocortisone therapy was commenced. Calcium level normalized after 3 days of intravenous saline. Patient received eight cycles of chemotherapy (POLA-R-CHP). A repeat PET CT after the third cycle showed complete metabolic resolution of adrenal uptake. However, he continued to required steroid replacement (9am cortisol was low at 51nmol/l). The recovery of his adrenal function post-lymphoma treatment remains uncertain.
Conclusions
Primary adrenal lymphoma should be one of the differential diagnoses of adrenal insufficiency, particularly in the elderly in the setting of negative 21-hydroxylase antibody and/or those presented with hypercalcemia. While caution not to biopsy a potential primary adrenocortical carcinoma, bilateral adrenal masses of unknown origin or in individuals with suspected extra-adrenal malignancy should be biopsied quickly when pheochromocytoma is excluded biochemically.

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P89

Residual pancreatic function after total pancreatectomy: two cases and implications for diabetes care

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Introduction
Type 3c diabetes (pancreatogenic diabetes) affects 20% of individuals following partial pancreatectomy and 86% of individuals following total pancreatectomy. No guidelines advise on routine C-peptide measurement post pancreatectomy to help diabetes management. We present two cases of post-total pancreatectomy where C-peptide measurement significantly altered management.
Case Report
Case A was an 80-year-old woman treated for intraductal papillary mucinous neoplasm (IPMN) with total-pancreatectomy. Post-operatively, the patient developed hyperglycaemia and was started on a basal-bolus insulin regimen. Two months post-operatively, she was seen in the diabetes clinic where CGM showed low glucose variability (CV 24.1%) and a good time in range (42%). Random C-peptide was elevated at 276 pmol/l, suggesting residual pancreatic function. Diabetes management was simplified to basal insulin with gliclazide. *Case B* was a 65-year-old man who underwent Folfirinox chemotherapy followed by a total pancreatectomy for adenocarcinoma of the pancreas. Post-operatively, the patient had hyperglycaemia and was started on a basal-bolus regimen. Two months later, he was seen in a diabetes clinic where CGM similarly showed low glucose variability (CV 20.7%) and excellent time in range (81%). Random C-peptide was significantly elevated at 1,050 pmol/l, and he has successfully weaned off all diabetes medications (TIR 83% off medication). CT abdomen pelvis showed a fluid-filled structure (6.7 x 7.7 cm) at the site of the pancreatic tail bed which may represent post-surgical collection with debris or tumour recurrence.
Discussion
These cases highlight the potential significance of post-operative C-peptide testing in patients undergoing pancreatectomy. Both patients exhibited substantial endogenous insulin production, leading to simplified or discontinued insulin therapy. Routine C-peptide measurement may help to guide clinical management of type 3c diabetes post-pancreatectomy and prevent unnecessary insulin prescriptions

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P90

Clinical conundrum of a neuroendocrine tumour in a perimenopausal woman

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Carcinoid heart disease and ureteric obstruction secondary to retroperitoneal fibrosis are rare but serious complications of neuroendocrine tumours (NETs). We report the case of a 52-year-old woman with a four-year history of diarrhoea of unknown cause, malignant hypertension, dizziness, and intermittent flushing, which were initially misattributed to menopausal symptoms. She presented to hospital with lethargy, worsening abdominal pain and an acute kidney injury from ureteric obstruction. On examination a pansystolic murmur was auscultated, and transthoracic echocardiography revealed right heart dilation, severe torrential tricuspid regurgitation, moderate-to-severe pulmonary regurgitation, moderate mitral regurgitation, probable pulmonary hypertension and bilateral atrial dilation. The left ventricular systolic function was moderately impaired (45-50%). A ventilation-perfusion scan ruled out any pulmonary embolism to explain the severe tricuspid regurgitation. Contrast-enhanced CT identified a primary carcinoid tumour in the ileocecal region with multiple hepatic metastases, a distal paraesophageal lesion, and retroperitoneal fibrosis resulting in medially deviated ureters and moderate bilateral hydronephrosis. Elevated biochemical markers, including Chromogranin A, B, and 24-hour urinary 5-HIAA, supported the diagnosis. Octreotide scintigraphy showed uptake in the ileal mass but no significant uptake in the liver, lymph nodes, or heart. These findings confirmed Stage IV small bowel NET with multi-organ involvement. Despite initial bilateral double J stenting, nephrostomies were later required due to stent failure. Symptomatic management included Lanreotide therapy, with Octreotide infusions administered prior and during procedures to prevent carcinoid crisis. Ongoing follow-up with Cardiology will determine the need for valvular replacement and if Lanreotide has improved valvular functions. This case underscores the necessity of a multidisciplinary team approach in managing complex NET presentations.

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P91

Applying shallow whole genome sequencing to decipher genomic signatures in thyroid cancer – insight from a case study

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Shallow Whole Genome Sequencing (sWGS) can detect Copy Number Alterations (CNAs) across the entire genome. It is more affordable than other DNA sequencing techniques and requires low DNA input. sWGS of circulating cell free DNA (cfDNA) has shown promising results in the surveillance of various carcinomas. However, little is known regarding its utility in thyroid carcinoma (TC). In this study, we investigated sWGS as a surveillance tool in a patient with follicular TC (FTC).
Aims and Objectives
Explore concordance of CNAs identified between tumour DNA and plasma cfDNA. Compare Tumour Fraction (TF) between longitudinally collected cfDNA samples. Interpret changes in TF against thyroglobulin levels and clinical imaging.
Case History
A 71-year-old patient was under FTC surveillance after undergoing total thyroidectomy and radioiodine. Tumour DNA was extracted from Formalin-Fixed Paraffin-Embedded (FFPE) tumour blocks using GeneRead™ DNA FFPE kit. cfDNA was extracted from 2 plasma samples collected over 6 months using the QIAMP® circulating nucleic acid kit. sWGS was performed using the Ion RepoSeqPGS™ platform. Thyroglobulin and clinical imaging were assessed at intervals dictated by oncology follow-up.
Results
sWGS showed matching CNA pattern of tumour DNA and cfDNA in the first plasma sample at 42% TF. Thyroglobulin was detectable at 109.7μg/l. Imaging showed probable intraparotid lymph node metastases. Detectable plasma CNAs and thyroglobulin fits with this clinic picture. Second plasma sample is awaiting analysis. Between plasma samples, CT imaging showed new bone metastases with rising thyroglobulin and the patient unfortunately died shortly after second sample collection.
Discussion
Matching CNAs between primary tumour DNA and cfDNA are detectable in in this case using sWGS and it would be interesting to see if TF increases in line with tumour progression in the second sample. sWGS is a low-cost DNA sequencing technique and further research is warranted to support its role in surveillance of TC.

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P92

Characterisation of androgen steroidogenesis in mucinous ovarian cancer

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Background
In UK females, ovarian cancer (OC) is the 6th most common cancer and the most lethal gynaecological malignancy. Epithelial ovarian carcinoma (EOC) makes up 90% of OC. EOC is a heterogenous disease and is further categorised into subtypes. Mucinous Ovarian Carcinoma (MOC) is a rare EOC subtype, accounting for 3-5%. MOCs are often characterised as indolent, however, they are resistant to first-line platinum-based chemotherapies employed to treat EOC. Previous work from our laboratory suggests steroidal metabolism in MOC patients may be distinct from other EOC subtypes and healthy controls. Thus, understanding these pathways may lead to improved MOC diagnosis and treatment.
Methods
Expression of steroidogenesis enzymes and receptors in MOC cells were assessed by analysis of two publicly available datasets and validated through RT-qPCR. EOC cells androgen metabolism was investigated using liquid chromatography-tandem mass spectrometry. The effect of various steroids on MOC cell proliferation was determined through BrdU incorporation assays.
Results
SRD5A1/3 and HSD17B2/4 RNA expression is comparable between MOC and HGSOC. AKR1C3 is more highly expressed in MOC (2-10 TPM) compared to HGSOC (1-6 TPM). SRD5A2 was not expressed in MOC but was present at low levels in HGSOC (<1 TMP). The androgen receptor (AR) was lowly expressed, except in OVCAR3 (HGSOC, 3-4 TMP). RT-qPCR mimicked these findings; however, low levels of AR were expressed in all MOC lines, particularly in RMUG-S (>5 times AR expression of other MOC). Following testosterone treatment, synthesis of the less biologically active adione was >6 times higher in MOC than HGSOC despite comparable HSD17B2/4 expression. Seventy-two-hour androgen treatment resulted in up to a 50% reduction in RMUG-S proliferation; other MOC cell lines were not significantly affected.
Conclusion
Androgen metabolism is distinct between MOC and HGSOC. Furthermore, androgens may have an anti-proliferative effect on MOC, unlike in HGSOC.

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Immune checkpoint inhibitors and endocrinopathies

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Background
The use of immune checkpoint inhibitors (iCPIs) has significantly increased in the treatment of various malignancies, leading to a rise in immune-related adverse events (irAEs), including endocrine toxicities.
Objective
We aim to identify the prevalence and management of endocrinopathies in cancer patients treated with iCPIs in our centre.
Methods
A retrospective audit of cancer patients who received iCPIs was conducted. 40 cases of each iCPIs group from clinical database (Clinical records, electronic discharge templates and laboratory report) were reviewed. The need for secondary interventions, such as endocrinology consultations, was also analysed.
Results
A total of 160 cases (40% female, treated for 16 different types of cancer) were identified. Number of patients received iCPIs therapy were Pembrolizumab ($n = 40$), combination Nivolumab and Ipilimumab (40). Atezolizumab ($n = 38$), Durvalumab ($n = 15$), Avelumab ($n = 20$), and Duvalumab ($n = 15$). Incidence of endocrinopathies were autoimmune hypothyroidism (16.8%), adrenal insufficiency (2.5%), hyperthyroidism (1.25%), hypophysitis (1.25%) and diabetes (1.25%). All patients received monitoring blood tests for thyroid function and cortisol level checked after initiation of iCPIS. The median and mean duration of initiation of iCPIs to the diagnosis endocrinopathy were 144 and 201 days respectively (range 8 - 558). Endocrinopathies dose not linked with a specific type or stage of underlying cancer diagnosis. One patient receiving Pembrolizumab was hospitalized for an adrenal crisis. In patients on Atezolizumab and one case of diabetes ketoacidosis despite frequent monitoring. 7.5% of patients treated with iCPIs required endocrinology follow up.
Conclusion
The audit identified a notable prevalence of iCPIs related endocrinopathies. These toxicities often present with non-specific symptoms, making early detection challenging and may result in emergency hospital admission. Establishing a high index of suspicion and awareness of this link is crucial for wider medical teams. With increasing use of iCPIs, there should be a proper endocrine service provision need to be considered.

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P94

A potential new role for the proto-oncogene PBF in endocrine cancer as a regulator of endothelial cells and angiogenesis

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The proto-oncogene pituitary tumor-transforming gene (PTTG)-binding factor (PBF/PTTG1IP) has been implicated in multiple malignancies, including thyroid cancer, where PBF overexpression is associated with tumour progression and poorer prognosis. PBF promotes several tumourigenic processes such as cell migration and invasion and, although its primary function remains unclear, a physiological role for PBF in cell motility has recently been identified. PBF is ubiquitously expressed and whole genome transcriptomics studies in normal tissue suggest that the highest PBF expression is within blood vessels. Additionally, single cell transcriptomics data from numerous tissues including ovary, lung, liver and testes show that PBF expression is highest in endothelial cells within these tissues. However, the role of PBF in endothelial cells is completely uncharacterised. Given the critical role of angiogenesis in tumour growth and metastasis we hypothesised that PBF is a novel regulator of angiogenesis via induction of endothelial cell motility. Our preliminary studies have utilised siRNA-mediated PBF knockdown in human umbilical cord vein endothelial cells (HUVECs). Interestingly, we observed that reduced PBF expression increased endothelial cell tube formation in 2D Matrigel tube formation assays, suggesting that PBF may negatively regulate angiogenesis. This assay mimics multiple steps of angiogenesis including cell differentiation, reorganisation, and adhesion. However, intriguingly no difference was found in the rate of wound recovery when PBF levels were reduced in scratch wound assays indicating that PBF's effects may be specific to responding to angiogenic stimuli response rather than general endothelial cell motility. These findings suggest that PBF could function as an angiogenic regulator in endothelial cells offering new insights into its role in vascular biology. This study represents the first steps towards uncovering the function of PBF in endothelial cells and may reveal a role for PBF in endothelial-driven processes linked to endocrine malignancy.

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The use of empagliflozin for paraneoplastic siadh: observations from a real-world cohort treated at a tertiary oncology centre

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Paraneoplastic syndrome of inappropriate antidiuretic hormone (pSIADH) is common and increases cancer-related morbidity. In addition to anti-cancer therapy, the usual management of pSIADH includes fluid restriction and pharmacotherapy with demeclocycline or vasopressin receptor antagonists. These measures show variable effectiveness, require intense monitoring, and can cause serious toxicity. Previous studies have demonstrated the efficacy of the sodium-glucose cotransporter-2 inhibitor empagliflozin in managing patients with SIADH. We report our experience of empagliflozin use specifically in patients with pSIADH due to metastatic cancer at The Christie Hospital, a tertiary oncology centre in North-West England. Fifteen patients with pSIADH attending our acute oncology unit were commenced on empaglifozin between September 2023 and August 2024. Baseline characteristics, indication, and response to

treatment are described in Table 1. One patient reported nocturia as a side-effect, however there were no episodes of ketoacidosis or urinary tract infections recorded in our cohort. Despite the small cohort, our findings indicate a potential role for empagliflozin in managing pSIADH. Further research is needed to corroborate our observations.

Variable	Number/Finding	Comments
Sex		
Male	8	
Female	7	
Primary Malignancy		
Small-cell lung	10	
Non-small-cell lung	1	
Prostate	2	
Vulval	1	
Lymphoma	1	
Baseline Sodium (mmol/l)		
Median (min-max range)	119 (116-126)	
Indication for treatment		
Suboptimal/poor response to other measures		
Tolvaptan	1	
Demeclocycline	3	
Fluid Restriction alone	3	
Hyperglycaemia + SIADH	3	
Side-effects	1	
Cautions/contra-indications with other agents	4	
Dose		
10 mg	7	
25 mg	8	
Sustained improvement in sodium to > 125 mmol/L		
1 week	13/15	
1 month	8/11	13/15 died due to progressive cancer.
3 months	7/9	1 stopped empagliflozin (after
6 months	4/5	6-months) due to resolution
9 mont7/hs	2/2	of pSIADH
12 months	1/1	
Median Sodium in mmol/L (min-max range)		
1 week	127 (116-138)	
1 month	131 (118-139)	
3 months	130 (114-141)	
6 months	133 (122-142)	

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Metabolism, Obesity and Diabetes

P96

Association of serum klotho levels with chronic kidney disease and mortality in patients with type 2 diabetes: evidence from Chinese cohort and NHANES databases

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Background
The klotho is crucial in diabetes and its related complications. This study seeks to explore the link between klotho levels and the risk of chronic kidney disease (CKD) as well as all-cause and cardiovascular mortality among individuals with type 2 diabetes mellitus (T2DM).
Methods
The investigation involved 126 Chinese T2DM patients and 4,451 individuals from the NHANES database. To evaluate the relationship between klotho levels and CKD risk, multivariate logistic regression was utilized. Additionally, restricted cubic spline (RCS) regression analysis was conducted to examine the nonlinear relationship between klotho levels and CKD incidence. RCS Cox regression was employed to analyze the correlation between klotho and both all-cause and cardiovascular mortality.
Results
In the Chinese cohort, klotho levels were notably elevated in T2DM patients without CKD compared to those with CKD. The NHANES data revealed a significant inverse relationship between klotho levels and diabetic kidney disease (DKD) risk, especially in patients with elevated klotho levels, where the likelihood of DKD was markedly diminished. Nonlinear analysis further illustrated a substantial nonlinear connection between klotho levels and DKD risk; serum klotho levels below 880.78 pg/ml were linked to increased CKD risk in T2DM patients, showing significant gender disparities. When compared to the T2DM group, the DKD group had markedly higher all-cause and cardiovascular mortality rates. Cox regression findings indicated that elevated klotho levels could mitigate all-cause mortality in T2DM patients. The relationship between klotho levels and all-cause mortality was also nonlinear, with the minimal risk found at klotho levels between 776.95 pg/mL and 812.69 pg/mL, varying by gender.
Conclusion
There exists a notable association between klotho levels and CKD risk, along with mortality in T2DM patients, with varying effects based on gender. These results highlight the potential importance of klotho as both a biomarker and a therapeutic target.

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The metabolic syndrome traits differentially and cumulatively influence micro- and macrovascular disease risk in patients with type 1 diabetes

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Introduction
The impact of the metabolic syndrome (MetS) traits on micro- and macrovascular complications of type 1 diabetes (T1D) is poorly understood. Therefore, we aimed to use large cohort data to determine which MetS component was most associated with micro- and macrovascular disease in T1D patients, whilst assessing whether additional components incrementally increased risk.
Methods
We conducted a retrospective cohort study using anonymised data from TriNetX, a global federated database. The exposure arm was T1D patients (defined via International Classification of Diseases, 10th Revision coding), and ≥ 1 MetS components (obesity/central adiposity, hypertension, or dyslipidaemia), compared with a reference arm of T1D patients without any MetS components. We propensity score matched (1:1) for confounders with 5 years follow-up. Primary outcomes included microvascular (peripheral neuropathy, retinopathy, and nephropathy) and macrovascular (cardiovascular and cerebrovascular events) disease. Secondary analyses assessed the impact of additional MetS components on these outcomes.
Results
T1D plus hypertension was associated with the highest risk of micro- (n 17,800, (HR 1.60 [95% CI 1.42, 1.81])) outcomes, whereas T1D plus dyslipidaemia was associated with the highest risk of and macrovascular ($n = 14,829$ (HR 1.69 [95% CI 1.46, 1.95])) disease when assessing the MetS components differentially. T1D and all MetS components was associated with the highest overall risk of micro- ($n = 12,269$ (HR 1.78 [95% CI 1.55, 2.03])) and macrovascular ($n = 9,642$ (HR 3.51 [95% CI 3.08, 4.00])) disease.
Conclusion
We demonstrate a differential and cumulative association between the MetS and risk of microvascular and macrovascular disease in T1D patients. Hypertension complicating T1D was associated with the highest individual risk of micro- and macrovascular disease, although the greatest risk was seen in those with all MetS components. Early identification of MetS in T1D should be prioritised and include screening of high-risk patients and consideration of dual medical therapy.

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daLUXendins reveal dual GLP1R/GIPR agonist targets in the pancreas and brain

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Background
Tirzepatide is a biased dual GLP1R/GIPR agonist with excellent efficacy for weight loss and glucose control in people living with obesity or type 2 diabetes. However, cellular targets and understanding of its biased agonism is yet to be fully elucidated, but could inform development of further dual and triple incretin therapies.
Method
We synthesised and tested two novel fluorescent GLP1R/GIPR probes, daLUXendin544 and daLUXendin660, allowing visualisation and interrogation of dual agonist cell targets. The probes are structurally similar to tirzepatide except for substitution of a C-terminal serine with cysteine to facilitate Cy3 or Cy5 fluorophore conjugation.
Results
daLUXendin544/660 demonstrate high potency (cAMP) and strong binding affinity at both the mouse and human GLP1R and GIPR. Advantageously, daLUXendin544/660 show 2:1 functional selectivity for mouse GLP1R over mouse GIPR. Through co-localisation studies in cell lines, daLUXendin544/660 show specificity for human and mouse GLP1R and GIPR with no labelling in non-transfected cells. In GLP1RKO islets, probe fluorescence was reduced versus WT islets with further reduction in daLUXendin544 fluorescence following pre-incubation with GIP. In fixed mouse islets, as well as human iPSC-derived islet-like structures, daLUXendin544/660 bind to all cell types with labelling strongest in insulin-positive cells versus glucagon- or somatostatin-positive cells. Further, daLUXendin660 is able to label *in vivo*, with strong labelling in islets isolated from GLP1R-Cre:tdRFP and GIPR-Cre:GFP mice 60 minutes after injection with daLUXendin660. Following IV injection, daLUXendin660 also labels the median eminence, area postrema and other circumventricular organs with an incomplete blood-brain barrier but does not penetrate any further into the brain. Finally, we use single molecule localisation microscopy to show that daLUXendin660 engages more receptor nanodomains than single GLP1R/GIPR probes.
Conclusion
We present daLUXendin544 and daLUXendin660, highly specific fluorescent GLP1R/GIPR probes that reveal dual agonist targets in the pancreas and brain.

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P99

Ghrelin and peptide YY can predict gestational diabetes and fetal Macrosomia in women at high risk

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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 foetal health outcomes. The diagnosis of GDM using the current gold standard of the 75g Oral Glucose Tolerance Test (OGTT) is fraught with many challenges. Studies have shown the potential of maternal gut peptides in diagnosing gestational diabetes.
Aim
The study aims to determine the potential utility of maternal gut peptides as diagnostic markers or screening tools for gestational diabetes mellitus (GDM).
Method
This diagnostic accuracy cross-sectional study compares the maternal gut peptides with the standard (75g OGTT) for screening women for GDM. The study recruited 215 pregnant women at high risk of GDM at 24-28 weeks gestation. The participants had GLP1, GIP, Ghrelin and peptide YY measured using the Sandwich-ELISA technique. Fetal and maternal outcomes were recorded at delivery. A receiver operating characteristic (ROC) curve was constructed to determine the ability to discriminate between GDM and non-GDM cases.
Results
The mean age of the 215 study participants was 30.59 years. Multiparous women (parity of 1 to 4) comprised 59.1%, and grand multipara were 34.0%. Mean Ghrelin and Peptide YY values at baseline were 461.36 ± 319.38, 41.93 ± 33.15 and 459.91 ± 189.23, 105.57 ± 159.18, pmol/l, respectively. At 0 minutes (basal), only ghrelin showed a statistically significant area under the curve of 0.925, p-value <0.001, with a sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and diagnostic accuracy of 81.8%, 26.3%, 3.11, 0.25, and 0.850, respectively. At 120 mins, ghrelin and peptide YY showed an AUC of 0.882 and 0.830, a sensitivity of 85.7% and 81.0%, and a sensitivity of 19.1% and 25.0% with p values <0.001, respectively.
Conclusion and Major Recommendation
Ghrelin and peptide YY showed good potential as potential diagnostic markers for GDM.

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P100

Correlation between hypogonadism and activity level in rheumatoid arthritis in patients at a south american hospital

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Introduction
Rheumatoid arthritis (RA) is a chronic immunoinflammatory disease that significantly impacts men in South America. Hypogonadism may be more prevalent in patients with RA, and testosterone deficiency could worsen disease severity. Understanding the relationship between testosterone levels and RA activity is crucial for improving patient management.
Objective
This study aims to evaluate the incidence of hypogonadism in men with rheumatoid arthritis and analyze its correlation with disease activity and concomitant illnesses.
Materials and Methods
A continuous study was conducted at a South American hospital, involving 50 men with RA receiving inpatient treatment. Total testosterone levels were measured, categorizing patients into subgroups with normal (>12 nmol/l) and reduced levels. Intergroup comparisons were made on clinical indicators used to assess RA stage and activity, alongside demographic characteristics. A correlation analysis was performed between total testosterone levels and clinical and laboratory parameters.
Results
The frequency of testosterone deficiency in the study group was 40%. Significant correlations were observed between total testosterone levels and body mass index (BMI) ($r=-0.32$), blood uric acid ($r=-0.23$), and C-reactive protein ($r=-0.15$). Patients with hypogonadism had a higher BMI (32.1 ± 6.8 vs. 25.2 ± 3.0 kg/m^2; $P < 0.001$) and poorer disease control (DAS28 >5.1 in 36% vs. 4%; $P = 0.003$).
Discussion
The findings suggest that testosterone levels and hypogonadism are associated with RA stage and activity. Testosterone deficiency correlates with increased body weight and obesity, indicating the need for a multidisciplinary approach in RA management.
Conclusion
Assessing testosterone levels in men with RA is vital for understanding disease progression, as deficiency is linked to a more active disease course and higher obesity risk. A comprehensive approach considering these variables is essential for improved patient care.

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P101

Report of the first case of DICER1 syndrome in a patient from a south american hospital

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Introduction
DICER1 syndrome is a rare inherited disorder characterized by the progressive development of benign and malignant lesions, primarily during childhood and early adulthood. This syndrome arises from dysfunction of the DICER endoribonuclease, which is crucial for processing microRNA, leading to the regulation of oncogenes and tumor suppressor genes. The clinical manifestations of dyseropathies associated with DICER1 syndrome are diverse and may include endocrine conditions (such as multinodular goiter, well-differentiated thyroid cancer, ovarian stromal tumors, and pituitary blastomas) as well as non-endocrine tumors (including pleuropulmonary blastoma, cystic nephroma, pineoblastoma, and rhabdomyosarcoma).
Case presentation
We present a case of a male patient in his thirties from South America who exhibited clinical symptoms of multinodular goiter and cystic nephroma. Genetic testing was performed, confirming a mutation in the DICER1 gene in exon 17, which replaces arginine with serine, thus confirming the diagnosis.
Discussion
The occurrence of somatic mutations in the DICER1 gene plays a critical role in the pathogenesis of dyseropathies and influences the trajectory of oncogenesis. DICER1 syndrome is often underdiagnosed, leading to delayed identification of disease components, late diagnosis of neoplasias, and insufficient family counseling. Early diagnosis and the establishment of screening programs are essential for the management of these patients, as they can significantly reduce the risks of developing more malignant and aggressive forms of the disease.
Conclusion
This case underscores the need for heightened awareness of DICER1 syndrome among healthcare providers to facilitate early diagnosis and intervention, ultimately improving patient outcomes and enabling timely family counseling.

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P102

Lipoprotein(a) (LPa) measurement in adults with type 1 diabetes (T1DM): is this a useful clinical tool to refine cardiovascular risk stratification?

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Background
LPa is an established independent risk factor for atherosclerotic cardiovascular disease (ASCVD). There is currently no consensus regarding the need for routine LPa measurement in T1DM patients in UK clinical practice, despite evidence suggesting that high LPa is a significant risk factor in T1DM that may relate to poor metabolic control and vascular complications.
Methods
T1DM patients attending a hospital clinic underwent LPa testing during their annual review blood tests. The group was divided into tertiles according to LPa levels (low, 0-30, intermediate, 30-120 and high, >120nmol/l) and associations between LPa and clinical and metabolic characteristics were then explored. Those with high LPa levels were individually assessed to ascertain how LPa measurement had impacted on clinical management.
Results (mean ± SD)
For all patients ($n = 96$) (49M, 47F), age was 52 ± 16yrs, diabetes duration, 29 ± 17yrs, HbA1c 62 ± 14mmol/mol, non-HDL-C 2.7 ± 0.92mmol/L and LPa 24(10-59) nmol/l (median (IQR)). Frequency (%) of complications was 13(ASCVD), 41(hypertension), 59(retinopathy), 18(nephropathy). 63% received statins and 7% were smokers. LPa levels correlated with non-HDL-C ($r = .21$, $P < 0.05$) but not with HbA1c nor micro/macro-vascular disease status. Those with high LPa levels (11%) were more likely to have a family history of ASCVD ($X^2 17.2$, $P < 0.01$). Amongst the high LPa group, clinical management of cardiovascular risk factors was impacted by the LPa result in 82% of patients. In 7% of cases, LPa > 200nmol/l.
Conclusion
LPa levels were not related to either glycaemia or vascular complications in our T1DM cohort, although those with higher LPa levels were more likely to have a family history of ASCVD. High LPa levels were present in a significant proportion of patients leading to intensification of cardiovascular risk factor management in the majority of those cases. LPa measurement in T1DM serves as a useful clinical tool to refine cardiovascular risk stratification.

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P103

Macrophage androgen metabolism influence muscle cell metabolism

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Background
Macrophages the key players in coordinating muscle regeneration in response to injury and damage, where androgens such as testosterone (T) and dihydrotestosterone (DHT) contribute to anabolic muscle metabolism. We have shown that androgen metabolism in macrophages is dynamically regulated by inflammation. We propose that this process may be dysregulated in inflammatory disease.
Methods
Primary human macrophages from healthy donors, were polarised (TNFα/IFNγ) or left unpolarised before treatment with DHT precursors (T & A4;100 nmol/l). Treated macrophages or conditioned media were then incubated or co-cultured with primary muscle myotube and myoblast cultures generated from healthy human quadriceps. Macrophage DHT synthesis was measured by LCMS. Muscle myotube thickness (microscopy), markers of muscle metabolism (qRT-PCR), cell migration (scratch assay), proliferation assay (BrdU), and protein synthesis (synthesis assay) were then assessed.
Results
Inflammatory-activated macrophages showed a unique regulation of steroid metabolism increasing DHT activation from T and A4. Conditioned media or co-culture of activated macrophages resulted in attenuated myotube fiber size without influencing the metabolic gene expression profile. Conditioned media with T increased proliferation after 48 hours ($P = 0.0768$) and 72 hours ($P = 0.0738$) treatment in myoblasts without changing cell viability. The conditioned media with T decreased catabolic Foxo1 and anti-anabolic Myostatin (Mstn) and increased differentiation marker Myodesmin gene expression after 24-hour treatment. In contrast, the addition of T to these inflammatory macrophages increased fiber thickness ($P < 0.001$, ***). DHT treatment did not increase the protein synthesis rate compared to control. Examination in myoblasts revealed that inflammatory macrophage-conditioned media increased cell migration and proliferation independently of T precursor treatment.
Conclusions
This study reveals that inflammatory-activated macrophages dynamically regulate androgen metabolism, and influence myotube thickness and metabolism. Whether this process is dysregulated in chronic inflammatory diseases resulting in a maladaptive response to muscle injury and regeneration has yet to be determined.

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P104

Acetate alleviates glucose dysregulation and atherogenic dyslipidemia in experimentally-induced PCOS

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Background
Polycystic ovarian syndrome (PCOS) is a female reproductive disorder which has its origin from both endocrine and metabolic disruptions, affecting about 6-20% of women in the reproductive age, globally. Atherogenic dyslipidemia refers to alterations in circulating lipid levels, which is a contributing factor to cardiovascular and renal complications in PCOS. Acetate, a short-chain fatty acid has been reported to attenuate endocrine-metabolic complications as well as improve glucose homeostasis, hence, this study was designed to explore the effect of acetate on glucose dysregulation and dyslipidemia in experimentally-induced PCOS.
Materials and method
Female Wistar rats at eight-weeks-old were procured and assigned into four groups ($n = 6$); Control (CTL), Letrozole (LET), Acetate (ACT), LET + ACT.

Letrozole (aromatase inhibitor; 1 mg/kg) administration for 3 weeks induced PCOS, and treatment with acetate was by supplementation during LET administration.
Results
Rats with PCOS presented hyperandrogenism/hypoestrogenism as observed by elevated levels of testosterone, LH/FSH ratio, with a decrease in 17-β estradiol and SHBG levels when compared with the negative control group. In addition, PCOS rats expressed significant increase in body and ovarian weight, fasting insulin, HOMA-β levels. Similarly, TC, LDL, TC/HDL ratio, IL-6, LDH were elevated in PCOS rats, with a decrease in HDL, nitric oxide and kisspeptin in rats with PCOS when compared with control group.
Conclusion
The present study revealed that acetate alleviates atherogenic dyslipidemia and metabolic disturbance in PCOS animal model by modulating kisspeptin level.
Keywords: Acetate; Atherogenic dyslipidemia; Hormonal imbalance; Kisspeptin; PCOS

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P105

Hypoglycaemic episodes in type 2 diabetes mimicking as remission of diabetes: a case of paraneoplastic hypoglycaemia

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Non-islet cell tumour hypoglycaemia (NICTH) is a rare paraneoplastic condition associated with epithelial or mesenchymal tumours. We report a case of NICTH in a man with poorly controlled diabetes who was initially thought to have diabetes remission. A 50-year-old man with a 4-year history of diabetes (HbA1c 12% at diagnosis) reported improvement in diabetes control within a year (HbA1c 5%) with oral glucose-lowering agents (OGLA). His OGLA were subsequently stopped, and he was labelled by primary care as achieving diabetes remission, maintaining a HbA1c of $<6\%$ without treatment or lifestyle modifications. He was referred to Endocrinology after developing new-onset episodic blurred vision and tremors on fasting, associated with 5-kg weight gain over 6-months. Symptoms resolved with meals. Capillary blood glucose was reported to be <3mmol/L during these episodes. Clinical examination noted a hard suprapubic mass. In view of unexplained hypoglycaemia, a 72-hour supervised fast was performed and precipitated hypoglycaemia at 7-hours (plasma glucose 2.6mmol/l) with serum ketone <0.6mmol/l, C-peptide 31 pmol/l (260-1729 pmol/l) and insulin <1.6mU/L (2.6-24.9mU/l). Plasma glucose increased from 2.6mmol/L to 4.7mmol/L with IV glucagon 1 mg at fast termination, suspicious for insulin-like growth factor-2 (IGF2) excess. Computed tomography of the abdomen confirmed a 15.5x11.5x13.4 cm lobulated soft-tissue mass in the lower abdomen. Serum IGF1 and IGF2 were 34µg/L (IGF1 79-205µg/l) and 1154ng/ml (IGF2 333-967ng/mL) respectively. IGF2:IGF1 ratio was 33 (normal value <3.0), confirming IGF2 excess. He was started on prednisolone and advised on frequent meals containing complex carbohydrates. He subsequently underwent complete open resection of his pelvic tumour. Histology revealed a solitary fibrous tumour with immunohistochemical staining of patchy STAT-6 expression. Hypoglycaemic episodes resolved post-operatively and repeat IGF2 measurement is pending. NICTH can mimic spontaneous remission of diabetes and progress to symptomatic hypoglycaemia. Clinicians should maintain a high index of suspicion for paraneoplastic phenomenon in patients with diabetes reporting unexplained hypoglycaemia.

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P106

Socio-demographic correlates of vitamin B12 insufficiency among patients with type 2 diabetes mellitus (T2DM) in kano, north-western nigeria

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Background
Vitamin B12 insufficiency is very common among patients with T2DM particularly those on metformin therapy. Low levels could lead to hyperhomocysteinemia, which has been associated with macrovascular complications. It also causes peripheral neuropathy. A substantial number of patients with T2DM in Kano are on metformin therapy. However, no study on low vitamin B_{12} levels has being conducted in Kano despite being one of the most populous black city in Africa.
Methods
The study was a hospital-based case-control, prospective, analytical, observational study, conducted in a tertiary facility in Kano, Northwestern Nigeria. The study participants were patients attending the adult diabetes clinic at Muhammad Abdullahi Wase Teaching Hospital, Kano. Three hundred participants were recruited, 100 metformin-exposed T2DM, 100 T2DM metformin-naïve and 100 non-diabetic participants. Data was collected using a questionnaire after getting approval from the ethics committee of the health authorities in Kano State. Vitamin B12 was assayed using Beckman access immunoassay system. Vitamin B12 insufficiency was defined as levels less than or equal to 300pg/ml. Statistical analysis of the data was done with the software package SPSS (Statistical Package for Social Sciences) for windows version 16.0.
Results
The overall prevalence of vitamin B12 insufficiency was 29%. Prevalence among metformin-exposed T2DM patients was 46%, among metformin naïve T2DM patients was 26% and among normal participants, it was 15% ($P < 0.05$). Female gender and low monthly income (less than 40USD) were significantly associated with vitamin B12 insufficiency among metformin-exposed T2DM participants ($P < 0.05$). Among the metformin-naïve participants and apparently normal individuals, there was no such relationship.
Conclusion
Metformin exposure leads to high prevalence of vitamin B12 insufficiency among T2DM patients. Being a female with low socioeconomic status further increases the risk of low vitamin B12 levels. Kano has a substantial number poor people.
Key words
Vitamin B12 insufficiency, Type 2 Diabetes mellitus, Metformin, Kano

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P107

Voluntary exercise normalises the preferential metabolic energy source in a mouse model of down syndrome

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Introduction
Down syndrome (DS) is associated with chronotropic incompetence and gait disturbances which reduces exercise capacity in this population. Moreover, mitochondrial dysfunction has been described in several cell types in DS, and has been linked to metabolic inflexibility and poorer exercise endurance in the general population. However, the effect of aging on exercise capacity in DS and on metabolic substrate utilisation remains to be fully explored.
Methods
Male and female Dp1Tyb (DS) and wild-type (WT) mice were used in this study at 9 weeks, 18 weeks and 14 months of age for calorimetric studies (TSE Phenomaster). Exercise to exhaustion was evaluated on a treadmill at 28 weeks of age. Gastrocnemius tissue was used to evaluate the oxygen consumption rate (OCR) in an Oxygraph-2k system, and for metabolomics and transcriptomics studies.
Results
Despite similar ambulatory activity, male and female DS mice had a steeper decline in voluntary exercise on the running wheel with age compared to WT. Worse endurance was confirmed by treadmill exercise to exhaustion showing reduced VO_2, and VO_2^{Max}, and higher plasma lactate. Calorimetric studies revealed a preference for carbohydrates as a metabolic substrate in young (9 and 18 weeks) male DS animals and both sexes of aged DS animals, which was normalised by voluntary exercise on the running wheel. OCR revealed mitochondrial dysfunction in the gastrocnemius muscle, confirmed by transcriptomic analyses.
Conclusions
DS was associated with a faster physical capacity decline, potentially linked to mitochondrial dysfunction of the gastrocnemius muscle leading to metabolic

inflexibility. Regular voluntary exercise normalised the preferential metabolic source of energy. This data can help tailor exercise routine recommendations in the DS population aiming at improving or preventing metabolic diseases such as obesity and diabetes.

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P108

Guidance for the planning and prescribing of GLP-1 agonists in a multi-disciplinary team, tier 3, specialist weight management service

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Objective
Examine clinical outcomes of GLP-1 agonist use for weight loss in pre-diabetic patients in a Tier 3, Specialist Weight Management Service (SWMS). To guide future resource planning within these services by determining which patients benefit most from GLP-1 agonists.
Design
Retrospective Clinical Analysis
Setting
South Tees NHS Foundation Trust
Participants
117 participants aged ≥18 years prescribed Liraglutide to aid weight loss in the South Tees, Tier 3, Specialist Weight Management Service between 2020 and 2024. Patients prescribed Liraglutide for less than 6 months were discarded, leaving 70 patient records used for trend analysis. Patient records were used for trend analysis.
Main Outcome Measure
Assess GLP-1 agonist efficacy for weight loss in pre-diabetic patients in a Tier 3, SWMS. Data was stratified based on various factors to explore patient characteristics to help guide future, Tier 3, SWMS resource planning.
Results
The 70 patients lost an average of 7.8% of their starting body weight across 6 months, rising to 9.5% in those with a treatment duration ≥12 months. Of the 70 patients, 28.6% lost ≥10% of their total body weight when treated for ≥ 6 months, with 72.8% losing ≥ 5% with the same treatment duration. Data showed a clear correlation between patients with ≥4 co-morbidities and increased percentage weight loss when accounting for variables including initial HbA1c, IMD score and treatment duration. Age and sex also proved significant factors.
Conclusion
Prescribing of Liraglutide alongside a Tier 3, SWMS resulted in 44% more participants achieving ≥10% weight loss shown in the SCALE Obesity and Pre-diabetes study[1]. Additionally, older patients with ≥4 co-morbidities lost a greater amount of weight on average, than younger patients with <4 co-morbidities, suggesting how to best prioritise, and inform effective resource allocation for GLP-1 agonist prescribing in the setting of Tier 3 SWMS.
Reference
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P109

Genetic associations between SGLT2 inhibition, DPP4 inhibition or GLP1R agonism and prostate cancer risk: a two-sample mendelian randomisation study

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Background
Epidemiological studies have linked the use of the anti-diabetic medications, sodium-glucose co-transporter-2 inhibitors (SGLT2I), dipeptidyl peptidase-4 inhibitors (DPP4I) and glucagon-like peptide-1 receptor agonists (GLP1RA), with prostate cancer risk. However, these studies cannot infer causality.
Methods
This was a two-sample Mendelian randomization (MR) using genome-wide association study data designed to identify causal relationships between SGLT2I, DPP4I or GLP1RA and prostate cancer. Genetic associations with HbA1c and risk of prostate cancer were extracted from IEU Open-GWAS Project database with GWAS id ukb-d-30750_irnt (UK Biobank cohort) and ebi-a-GCST006085 (European Molecular Biology Laboratory's European Bioinformatics Institute cohort), respectively. The two GWAS datasets chosen were obtained from individuals of European ancestry to minimise potential bias from population stratification. The encoding genes targeted by SGLT2I, DPP4I and GLP1RA were SGC5A2, DPP4 and GLP1R, located in Chr16: 31494323-31502181, Chr2: 162848755-162930904 and Chr6: 39016557-39059079, respectively.
Results
A total of 31, 2 and 5 single nucleotide variants (SNVs) were used for SGC5A2, DPP4 and GLP1R. Our MR analysis results supported a causal relationship between genetic variation in SLC5A2 and DPP4 and reduced risk of prostate cancer at the Bonferroni-corrected threshold, with odds ratios (OR) [95% confidence intervals] of 0.47 [0.38-0.58] and 0.35 [0.24-0.53], but not for GLP1R (OR: 1.39 [0.93-2.07]). Sensitivity analyses by the leave-one-out method did not significantly alter the OR for SGLT2I.
Conclusions
The two-sample MR analysis found that SGLT2 and DPP4 inhibition, but not GLP1R agonism, was associated with lower risks of developing prostate cancer.

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P110

GLP1 receptor agonist with add-on SGLT2 inhibitor therapy is associated with lower risks of major adverse cardiovascular events: a population-based and machine learning causal inference analysis

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Background
Both GLP-1 receptor agonists (GLP1a) and sodium-glucose cotransporter-2 (SGLT2) inhibitors confer benefits against cardiovascular diseases in type 2 diabetes mellitus (T2DM). However, the effects of SGLT2I add-on therapy amongst patients already on GLP1a users remain unknown.
Objective
This real-world study compared the risks of cardiovascular diseases in GLP1a users with or without SGLT2I add-on therapy.
Methods
This was a retrospective population-based cohort study of patients with type-2 diabetes mellitus (T2DM) on GLP1a between 1st January 2015 and 31st December 2020 using a territory-wide registry from Hong Kong. The primary outcomes were new-onset myocardial infarction, atrial fibrillation, heart failure, and stroke/transient ischaemic attack (TIA). The secondary outcome was all-cause mortality. Propensity score matching (1:2 ratio) using the nearest neighbour search was performed. Multivariable Cox regression was used to identify significant associations. The machine learning causal inference analysis was used to estimate the treatment effects.
Results
This cohort included 2526 T2DM patients on GLP1a (median age: 52.5 years old [SD: 10.9]; 57.34 % males). The SGLT2I users and non-SGLT2I users consisted of 1968 patients and 558 patients, respectively. After matching, non-SGLT2I users were associated with high risks of myocardial infarction (Hazard ratio [HR]: 2.91; 95% Confidence Interval [CI]: 1.30-6.59) and heart failure (HR: 2.49; 95% CI: 1.22-5.08) compared to non-SGLT2I users after adjusting for demographics, comorbidities, medications, renal function, and glycaemic tests. However, non-SGLT2I users were not associated with the risks of atrial fibrillation (HR: 1.52; 95% CI: 0.65-3.53) and stroke/TIA (HR: 1.72; 95% CI: 0.70-4.24). The results remained consistent in the competing risk and the sensitivity analyses.
Conclusions
GLP1Ra with SGLT2I add-on therapy is associated with lower risks of MACE, myocardial infarction and heart failure. The results remained consistent in the machine learning causal inference analysis.

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P111

Impact of bariatric surgery on sleep apnea in patients at a south american hospital

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Introduction
Bariatric surgery has been associated with improvements in obesity-related conditions, including obstructive sleep apnea syndrome (OSAS). This study aimed to explore the relationship between OSAS severity and body mass index (BMI) reduction in obese patients undergoing bariatric surgery.
Objective
To evaluate the impact of bariatric surgery on OSAS severity by assessing changes in the apnea-hypopnea index (AHI) and BMI over a two-year follow-up.
Materials and Methods
A total of 100 obese patients (59 men and 41 women) with a BMI $\geq$35 kg/m^2 and a mean age of 64 $\pm$ 3 years were included. Patients underwent either sleeve gastrectomy (SG) or gastric bypass (GB). Anthropometric data (BMI and weight changes) were collected preoperatively and during follow-up (at least two years). Statistical analysis was performed using non-parametric methods.
Results
Polysomnographic or cardiorespiratory studies revealed a significant reduction in OSAS severity post-surgery. The average AHI decreased from 19.3 $\pm$ 7.5 to 9.6 $\pm$ 4.8 ($P < 0.001$). Additionally, metabolic parameters improved following surgery.
Discussion
Bariatric surgery resulted in a marked improvement in OSAS severity across all patients, with some experiencing complete normalization of the AHI. This reduction in OSAS was closely associated with a decrease in BMI, supporting the effectiveness of weight loss interventions in managing sleep-disordered breathing.
Conclusion
Bariatric surgery significantly reduces OSAS severity, with some patients achieving full normalization of the AHI. These findings emphasize the importance of bariatric surgery as a therapeutic option for obese patients with OSAS.
Keywords
bariatric surgery, obstructive sleep apnea, apnea-hypopnea index, obesity, body mass index.
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P112

Remission of type 2 diabetes in patients undergoing bariatric surgery at a south american hospital

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Introduction
Obesity significantly increases cardiovascular risk and is associated with various diseases, including type 2 diabetes mellitus (T2DM). Weight loss improves glycemic control, and bariatric surgery is the most effective treatment for obesity, often leading to weight loss and improved glycemic control, potentially achieving T2DM remission. This study aims to compare the effectiveness of sleeve gastrectomy (SG) and gastric bypass (GB) in achieving T2DM remission in obese patients.
Objective
To evaluate the efficacy of SG and GB in inducing T2DM remission in obese patients.
Materials and Methods
A total of 100 patients (59 men and 41 women) with a BMI $\geq$35 kg/m^2 and a mean age of 64 $\pm$ 3 years were included. Patients underwent SG ($n = 41$) or GB ($n = 59$). Anthropometric data (BMI, postoperative weight changes) and laboratory parameters (HbA1c, C-peptide, insulin, fasting venous glucose) were assessed initially and during the two-year follow-up. The insulin resistance index (HOMA-IR) was calculated, and patients were evaluated for T2DM remission based on established criteria.
Results
No significant differences were found in achieving complete T2DM remission between SG and GB groups, with remission rates of 14 patients (SG) and 12 patients (GB), with p-values of 0.082 and 0.114, respectively. Maintaining weight loss is crucial for achieving and sustaining T2DM remission, but a multifactorial approach beyond achieving a target BMI is necessary.
Conclusion
Both SG and GB are effective in achieving T2DM remission in obese patients, with no significant difference in outcomes between the two surgical methods. Effective weight reduction and a comprehensive approach are essential for successful long-term diabetes management.
Keywords
type 2 diabetes, bariatric surgery, sleeve gastrectomy, gastric bypass, obesity, remission.
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P113

Clinical features and laboratory variables in patients with primary and secondary hyperparathyroidism at a south american hospital

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Introduction
This study aims to evaluate the role of neck gammagraphy in comparison with clinical features and laboratory parameters in patients with various types of primary and secondary hyperparathyroidism (HPT).
Objective
To analyze the clinical presentation and laboratory findings of patients diagnosed with primary or secondary HPT.
Materials and Methods
A retrospective single-center study included data from 100 consecutively selected patients diagnosed with primary or secondary HPT. This cohort comprised 48 patients with hypercalcemic primary hyperparathyroidism (hPHPT), 13 with normocalcemic primary hyperparathyroidism (nPHPT), and 25 with secondary hyperparathyroidism (SHPT) due to acquired vitamin D deficiency. The study was conducted at the Hospital Universitario de los Andes in Mérida, Venezuela, during 2021, utilizing neck ultrasonography results and known laboratory markers, alongside SPECT/CT imaging using technetium-99m methoxyisobutylisonitrile (99mTc-MIBI).
Results and Discussion
Among the 100 patients with HPT, 72% reported symptoms. Bone pain ($P = 0.0031$) and cramps ($P = 0.004$) were more prevalent in hPHPT. Maximum parathyroid hormone (PTH), phosphorus, and alkaline phosphatase levels were highest in patients with end-stage renal disease (ESRD), while total and ionized calcium peaked in hPHPT patients. The lowest incidence of vitamin D deficiency was in nPHPT patients. The sensitivity of SPECT/CT in detecting altered parathyroid glands was 97% for hPHPT and 92% for nPHPT. Ectopic pancreatic findings in hPHPT occurred in 18% of patients, with rapid adenoma detection in 36%. A correlation was found between radioisotope accumulation intensity in altered parathyroid glands and their diameter ($P = 0.003$).
Conclusion
SPECT/CT serves as a key method for visualizing altered parathyroid glands in the preoperative evaluation of patients with PHPT and SHPT in ESRD. This method is diagnostically valuable for patients with vitamin D deficiency and elevated PTH and calcium levels to identify nodular forms of pancreatic hyperplasia.
Keywords
primary hyperparathyroidism, secondary hyperparathyroidism
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P114

Influence of maternal weight on the course of fetal macrosomia in patients at a south american hospital

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Introduction
This study characterizes the clinical profile of women delivering large babies and evaluates the influence of maternal body weight on pregnancy outcomes.
Objective
To analyze maternal factors affecting fetal macrosomia, focusing on maternal weight and associated complications.
Materials and Methods
A retrospective analysis of 100 medical records from women who delivered babies weighing $\geq$4,000 g at the Maternity Hospital of the Universidad de los Andes in Mérida, Venezuela, in 2022 was conducted. Participants were divided into two groups: Group 1 (63 women with BMI $<$25 kg/m^2) and Group 2 (37 women with BMI $\geq$25 kg/m^2). Comparative analyses included age, pre-pregnancy and pre-delivery anthropometry, pelvimetry, presence of concomitant diseases, fetal measurements, newborn weight, and delivery complications. Statistical analysis was performed using Microsoft Office Excel 2020 and Statistica 10 (StatSoft, Inc.).
Results
The groups were homogeneous in age, gestational age at delivery, total weight gain, fetal measurements, and newborn weight: 4,200 g versus 3,850 g ($P > 0.05$). GDM occurred nearly twice as often in Group 2 (32%) compared to Group 1 (18%). The incidence of delivery complications was 1.5 times higher in patients with BMI $\geq$25 kg/m^2 (59%) than in those with BMI $<$25 kg/m^2 (28%) ($P < 0.05$). A strong correlation existed between maternal weight before and after pregnancy. In Group 2, a significant correlation was observed between pre-pregnancy BMI and BMI before delivery ($r > 0.79$; $P < 0.05$).
Conclusion
Higher risks of complicated delivery and GDM were identified in the higher BMI group, despite initial homogeneity. Other predictors of macrosomia were not found, necessitating further research. Comprehensive preconception preparation for overweight and obese patients may improve fetal metabolic programming.
Keywords
obesity, pregnancy, macrosomia, gestational diabetes mellitus.
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P115

Alexithymia and anxiety-depressive disorders in patients with hypothyroidism and the importance of control in a south american hospital using two scales

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Introduction
Hypothyroidism, a prevalent endocrine disorder, significantly affects patients' psychological well-being. Among its psychological manifestations, alexithymia—difficulty identifying and expressing emotions—has been linked to adverse mental health outcomes. Additionally, anxiety and depressive disorders frequently coexist with hypothyroidism, complicating the clinical picture and affecting treatment adherence. Understanding the prevalence of these conditions is vital for comprehensive treatment strategies.
Objective
To analyze the prevalence of alexithymia and anxiety-depressive disorders in patients with manifest hypothyroidism, both newly diagnosed and pharmacologically compensated.
Materials and Methods
This open comparative study involved 100 patients with hypothyroidism, divided into two groups: newly diagnosed manifest hypothyroidism (Group 1; $n = 50$) and pharmacologically compensated hypothyroidism (Group 2; $n = 50$). The study was conducted in 2022. Both groups were comparable in gender, age, body mass index, etiology of hypothyroidism, and comorbidities. Alexithymia was assessed using the Toronto Alexithymia Scale (TAS), while anxiety and depression levels were evaluated using the Hospital Anxiety and Depression Scale (HADS).
Results
A personality profile of alexithymia was identified in 52 patients, with 60 exhibiting anxiety and/or depression. Patients with alexithymia reported significantly more complaints ($P = 0.003$) than those without. A positive correlation was found between TAS and HADS scores ($P < 0.05$). More than half of the patients in both groups showed symptoms of anxiety and/or depression, with no significant differences between groups ($P > 0.05$).
Conclusion
High prevalence rates of alexithymia, anxiety, and/or depression were observed in both groups, indicating a need for targeted psychological support in hypothyroid patients to improve their quality of life and treatment satisfaction.
Keywords
hypothyroidism, alexithymia, anxiety, depression.
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P116

Nutrition and resilience in geriatrics: evaluating the role of diet in latin american patients

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Introduction
This study investigates the effect of a resilience diet on age-related vitality and functional capacity in geriatric patients.
Objective
To evaluate how a resilience diet impacts vitality and functionality in geriatric patients.
Methodology
A retrospective, comparative, and controlled study was conducted in a South American hospital from 2021 to 2023. A total of 106 patients were included and divided into three groups (vegetarians, traditionalists, and resilience). The resilience group followed a specific diet for six months. Vitality was measured using the MIIRM scale, while functional capacity was assessed through a visual analog scale (VAS), physical tests, and scales for anxiety, depression, and cognitive status.
Results
The resilience group showed a significant improvement in age-related vitality (from 15.2 $\pm$ 1.9 to 20.1 $\pm$ 1.3 points) and functional capacity compared to the vegetarian and traditionalist groups. Improvements were observed in hand strength, physical functioning, and levels of anxiety, depression, and cognitive status ($P < 0.05$).
Conclusion
The resilience diet, which is rich in plant-based proteins and fish while low in red meats, significantly enhanced the vitality and functionality of geriatric patients, suggesting that an adapted diet may promote healthy and functional aging.
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P117

Unravelling the mystery: a case of hirata's disease with an elusive trigger

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A 63-year-old gentleman presented with multiple episodes of unsteadiness of gait that had started over the preceding 1 week, associated with reduced consciousness. His medical background included TIA, hypertension and dyslipidaemia, taking clopidogrel, amlodipine and atorvastatin. He did not report any preceding illness, or any new medications. He was brought to the emergency department where examination was unremarkable, and so was his biochemistry. Neuroimaging and ECG were normal. Capillary blood sugar was 2.3 mmol/L coupled with low ketones. Despite being given glucose supplements, the low capillary blood glucose readings would recur, going as low as 1.4 mmol/l. His cortisol values, TFTs, and coeliac serology were unremarkable, HbA1c was 37 mmol/mol. Simultaneous serum insulin levels were found to be 4957 mU/l, C-peptide levels were 1759 pmol/l, and sulfonylurea screen was negative. Contrast CT of his abdomen was normal. EUS was undertaken to confidently rule out an insulinoma, and this was normal as well. He was empirically started on diazoxide and the panel of anti-insulin antibodies came back positive. The hypoglycemic episodes gradually started reducing, and he ultimately came off diazoxide after 7 months and remained normoglycemic thereafter. This case highlights an uncommon presentation of a rare condition, in the absence of any known trigger. Development of Hirata's disease (Insulin Antibody Syndrome) involves the formation of insulin-IAA complexes. IAA prevent the binding of insulin to its receptor in the postprandial phase. Insulin is then released from the complexes, causing hypoglycemia. Drugs associated with IAS are mostly

sulfhydryl-group drugs, which act as haptens. They interact with the disulphide bonds of insulin, potentiating its immunogenicity. Viral infections can be triggers for the development of IAS. Since IAS usually is a self-remitting disease, the management involves dietary modifications. Pharmacological therapy includes drugs that reduce pancreatic insulin secretion and immunosuppressive agents.

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P118

Efficacy of liraglutide (Saxenda) for weight loss in pre-diabetes: an audit of patients in a weight-management clinic in a district general hospital

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Background
Glucagon-like peptide 1 (GLP-1) agonists have been used in treating type 2 diabetes and, more recently, in promoting weight loss in high-risk obese patients without diabetes. This audit aimed to assess the effectiveness of Saxenda (Liraglutide 3.0 mg) on clinical parameters of patients in a Weight Management Clinic in a District General Hospital in the UK and determine the impact of the national shortage of Saxenda on these patients.
Methods
A total of 19 patients who attended the clinic between 2022 and 2023 and were treated with Saxenda in line with NICE guidelines were included. Data on weight, BMI, HbA1c, lipids, and co-morbidities were collected from clinical records before and after starting Saxenda to evaluate its efficacy and detect weight regain following the drug shortage. T-tests were used to compare the findings.
Results
The mean baseline characteristics (range) were as follows: weight 130.0 kg (92.7–171.0), BMI 44.97 kg/m^2 (31.70–60.59); HbA1c 41.4 mmol/mol (28-47). These patients were at high cardiovascular disease risk with 12/19 diagnosed with cardiac co-morbidities. Following Saxenda, significant weight loss of -9.58 kg or 7.37% (3.15%–27.35%; $P < 0.001$); a significant BMI reduction was observed: -3.52 kg/m^2, $P < 0.05$. There was a borderline significant reduction in HbA1c levels: -2.44 mmol/mol, $P < 0.05$. Minor improvements in cholesterol were observed.
Conclusion
This audit highlights the effectiveness of Saxenda for weight loss in a real-world setting on high-risk pre-diabetic patients with obesity. It also underscores the need for consistent drug supply and better documentation of key clinical parameters in patient records. Recommendations include the reintroduction of Saxenda or an alternative such as Wegovy or Mounjaro alongside creating a standardized template for clinic letters.

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P119

A case of atezolizumab and bevacizumab induced type 1 diabetes mellitus and myocarditis

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Background
Checkpoint inhibitors like atezolizumab and bevacizumab show promise in treating hepatocellular carcinoma (HCC) but may cause immune-related adverse events (irAEs), impacting various organs. We present a 71-year-old male who developed severe irAEs, leading to Type 1 Diabetes Mellitus (DM) presenting with diabetic ketoacidosis (DKA), and myocarditis.
Case Presentation
A 71-year-old man presented with drowsiness, confusion, agitation, and peripheral edema five days after his first cycle of atezolizumab and bevacizumab. He has past medical history of HCC, liver cirrhosis, tonsillar cancer, deep vein thrombosis, hypertension and hypothyroidism. His medications included bendroflumethiazide, finasteride, thyroxine, tamsulosin, and nystatin. His investigations revealed metabolic acidosis with low bicarbonate, ketonemia, and hyperglycemia consistent with DKA. His other blood tests showed elevated troponin, BNP, C-reactive protein, deranged liver function tests, and acute kidney injury. An electrocardiogram showed a new right bundle branch block. He was initially managed with intravenous antibiotics for sepsis and the DKA was treated as per hospital guidelines, leading to the diagnosis of immunotherapy-induced Type 1 Diabetes Mellitus. He was switched to a basal-bolus insulin regimen once DKA resolved. His echocardiogram showed reduced left ventricular ejection fraction of 41%, along with global hypokinesis and impaired diastolic function. He was reviewed by cardiology team. These changes were attributed to immunotherapy-induced myocarditis and a follow-up was arranged. The oncology team also reviewed his case and started him on Methylprednisolone (1 mg/kg, later 2 mg/kg), which improved his condition.
Conclusion
This case underscores the need for early recognition and rapid, multidisciplinary intervention in managing immune-related adverse events. High-dose corticosteroids remain the cornerstone of treatment for irAEs. Although the patient stabilized, the potential for long-term complications, including the progression of his cardiomyopathy and the management of his new-onset diabetes, will require ongoing monitoring and care.

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P120

Audit on albumin to creatinine ratio measurement in outpatient diabetes clinic of our lady's hospital navan, co meath ireland

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Introduction
As per the American Diabetes Association guidelines published in March 2022, ACR should be measured in all patients with type 1 diabetes with duration of ≥ 5 years and in all patients with type 2 diabetes regardless of treatment. In patients with diabetes with deranged RFTs or reduced EGFR, ACR should be checked twice per year.
Aim
we sought to identify the standard of care delivered in our secondary care centre against the recommendations of American diabetes association.
Methods and Results
Between December 2023 and January 2024, 42 patients attended our diabetes outpatient services including type 2 DM 36(85.7%). Mean HbA1c was 59.11 $\pm$ 15.8 mmol/mol. 22 (52.3%) patients were on ACE or ARBs and 14 (33.3%) were on SGLT-2 inhibitors. 23 (54.76%) of the patients had ACR taken in last year. 11 (26.1%) had either abnormal ACR or reduced EGFR, of which 3 (27.2%) had ACR samples taken twice per year.
A Re-Audit
Was conducted in May 2024 to July 2024, post education of doctors as well as engagement with phlebotomy services to improve the collection of ACR samples. 48 patients including 36(75%) with type 2 DM. Mean HbA1c was 62.7 $\pm$ 17.7. 36(75%) were on ACE or ARBs with 19(39.5%) on SGLT-2 inhibitors. 39(81.3%) had their ACR taken over last year. 16(33.3%) patients had either abnormal ACR $\geq$3.3 g/mol or reduced EGFR $\leq$ 60 mL/min/1.73, of which 8(50%) had their ACR taken twice per year.
Conclusion
We have demonstrated the improvement in measurement of ACR in our patients with the help of education and engagement with our phlebotomy services.

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P121

A case of IGF-2 secreting retroperitoneal fibroma, lack of hypoglycaemic awareness at presentation, and the role for continuous glucose monitoring (CGM)

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A 72 year old man was admitted with chest-pains and leg and abdominal swelling and was diagnosed with significant coronary artery disease. He was incidentally noted by nursing staff to have episodes of irritability and drowsiness associated with low capillary glucose. His lowest laboratory blood glucose was 1.8mmol/L which was contemporaneous with signs rather than symptoms of hypoglycaemia. Resolution of signs was prompt when glucose normalized thus fulfilling Whipple's triad. Abdominal ultrasound demonstrated a large abdominal mass confirmed with CT with the mass connected to the retroperitoneum, pancreas, stomach and mesentery. Blood testing associated with laboratory glucose $<$ 2mmol/L were as follows: insulin $<$3.0mU/l, C-peptide 1.1ug/L and 3-OHbutyrate $<$0.1mmol/l. Urinary sulphonylurea screen was negative. Samples analyzed by Royal Surrey peptide lab were as follows: IgF1 8.9nmol/l (5-25nmol/l), IGFBP-3 2.1 mg/L (2.6-6.3 mg/l). IGF-2 199.3nmol/l and IgF2:IGF1

ratio 22.4 (<10). His hypoglycaemia became more frequent requiring hospital readmission. He was given a sensor for CGM, with hypoglycaemia alarm set at 4.5mmol/L and connected to remote access. He had coronary artery bypass grafting followed by open abdominal surgery and his hypoglycaemia resolved post operatively. Histopathology was of a 21x20x15 cm lesion weighing 3.5 Kg, composed of spindle cells, consistent with a fibrous tumour. Mitotic count was 2/10 HPF, margins were not clear (R1) and the lesion was classified as high (~70%) risk for metastasizing. IGF2 is secreted by mesenchymal and epithelial tissues, and associated with fibrous tumours causing hypoglycaemia and suppressed IGF1, growth hormone and insulin. His prescription for CGM was outside of NICE guidelines but this has facilitated his outpatient followup especially given his hypoglycaemic unawareness. Lack of hypoglycaemic awareness at presentation is a characteristic feature of such tumours (both islet-cell and non-islet cell) and so there may be a niche but important role for CGM in management of these complex cases.

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P122

Evaluation of acute release of cholecystokinin from human duodenal i-cells in response to free fatty acids in a co-culture model

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The I-cell is one of the critical human enteroendocrine cells essential in modulating digestion and appetite by releasing cholecystokinin (CCK). The transcriptome analysis of mouse and human I cells reveals the expression of several G-protein coupled receptors that can be activated in the presence of different free fatty acids and based on mouse enteroendocrine cell lines and preliminary data in our group from human duodenum-derived organoids, different free fatty acid receptors stimulate CCK secretion through intracellular calcium rise. However, little is known about whether the direct effect of fatty acids in human I-cells can stimulate CCK release in short-term effects. Therefore, this study aims to evaluate the acute CCK release dynamics in response to different fatty acids in human organoid-derived I-cells through the use of a biosensor assay employing CCK1R transfected HEK293 cells loaded with Fura2 to enable Ca2+-elevation monitoring as a proxy in response to CCK released from nearby cells. For this study, the plasmid expressing CCK1R and a red fluorescent protein 'mCherry' in a bicistronic message under a eukaryotic promoter was transfected transiently into HEK-293 cells using transit-293. Live-cell calcium imaging experiments were performed using the ratiometric calcium indicator Fura-2. We confirmed the responsiveness of the biosensor cells by perfusing them with CCK (100 nM), whereas they were unresponsive to KCl (70 mM), which will be used as a control stimulant for CCK release from I-cells, as we already know that this triggers Ca2+-elevation in I-cells and stimulates secretion assessed over longer time frames (2h) by an LC-MS/MS assay. Future work will now use the new biosensor to monitor CCK release from Venus-labeled I cells in co-culture, and different stimuli will be tested in co-cultured and isolated biosensor cells. This study deepens our understanding of the physiological processes of I-cells and holds promise for drug development.

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P123

Abstract Withdrawn

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P124

Gaps in coeliac screening upon diagnosis of type 1 diabetes in sligo university hospital

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People with type 1 diabetes are at increased risks of developing other autoimmune conditions. This includes coeliac and autoimmune thyroid disease. The prevalence of coeliac disease is 1 in 100 people however in type 1 diabetes the prevalence increases up to 9%. As these cohort of patients are at a higher risk it is crucial to screen for coeliac disease. The American diabetes association (ADA) guidelines recommend screening for coeliac disease soon after diagnosis and within 5 years thereafter. The aim of this audit was to determine if adult patients with type 1 diabetes were screened for coeliac disease within 5 years of diagnosis as per the ADA guidelines. This retrospective study occurred in October 2023. All patients with type 1 diabetes attending Sligo University Hospital were included in the study. Data including demographics, duration of diabetes and date of last coeliac screening was obtained from Prowellness diabetes database. Coeliac screening compromised of Anti-tTG and IgA. 584 patients were included in the study. 56% were males and remaining 44% females. Ages ranged from 18-79 with average age of 28. 20% ($n = 121$) had coeliac screening performed within the time period 2022 to 2023. 2.4% ($n = 14$) had screening done within 5 years of diagnosis of Type 1 diabetes. Of the 14, 1 patient tested positive for coeliac disease within 4 months of diagnosis of type 1 diabetes. Studies have shown that diagnosis of coeliac disease in type 1 diabetes usually occurs within 5 years. Results of this audit highlights poor screening for coeliac disease within 5 years of diagnosis in Type 1 diabetes and need to increase physician awareness. Coeliac disease can complicate treatment of type 1 diabetes due to increase morbidity and mortality. Further research is warranted to determine necessity for screening beyond first 5 years of diagnosis.

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P125

Management of HHS in line with JBDS guidelines. an audit on the current practice in manchester royal infirmary

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Introduction
We audited the management of HHS based on JBDS guidelines.
Methods
Data was collected from January 2023 to August 2024 and 19 patients with glucose ≥30 mmol/l, serum osmolality ≥320 mOsm/kg, and absence of significant ketoacidosis (pH ≥7.3 / bicarbonate ≥15 mmol/l) were identified.
Results
Only 58% (n 11) had Osmolality calculated and documented in the notes to make the diagnosis. In addition to osmolality 68% (n 13) had documented PH, Blood glucose and ketone levels. 63%(n12) had at least 1 litre of 0.9% normal saline in first hour. In first 6 hours 26% (n 5) had had hourly documentation of fall in osmolarity (targeted at 3-8mOsmol/kg/hr). Where the aim was not achieved, insulin was commenced after 1 hour at 0.05 units/kg/hr for 89% (n 17). 100% (1 patient) had their fluid changed to 0.45% saline when Osmolarity had increased despite correct fluid. 75% (n 3) were commenced on Dextrose or had their insulin reduced when capillary blood glucose (CBG) <14 mmol/L & 25% (n 1) didn't have dextrose/insulin reduced. 94% (18 patients) had either VRII or Subcutaneous insulin prescribed by 24 - 72 hours when their Biochemistry Sodium, CBG/osmolarity had normalised. 100% (3 patients) with osmolarity >350 mosm/kg, Na > 160mmol/l; K > 6 or < 3.5 mmol/l; GCS <12 or abnormal AVPU had review by ITU or decision about their escalation made.
Conclusion
Despite JBDS guidelines having been around for several years, there remains potential areas for improvement in care. Calculating osmolality, fluid management and monitoring of response to treatment were areas identified for improvement. PDSA cycle of educational meetings on the diagnosis & management of HHS have been planned.

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P126

The impact of type 2 diabetes mellitus on postoperative outcomes in cardiovascular surgery: a retrospective study from Uzbekistan

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Introduction
The prevalence of T2DM exceeds 9% of the adult population, while cardiovascular disease accounts for approximately 52% of all deaths, highlighting the urgent need for tailored perioperative strategies for these high-risk patients. Although T2DM patients are known to face greater risks of adverse outcomes after cardiovascular surgeries, more research data needs to improve local and global diabetes management. In our study we analysed postoperative outcomes in patients with T2DM undergoing coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI).
Materials and methods
Data of 200 patients (100 with T2DM and 100 without) who underwent CABG and PCI in American Hospital in Tashkent, Uzbekistan between 2018 and 2023 were gathered and analysed and compared among those with and without T2DM also according to type of surgery. We mostly pointed in patients age, gender, pre and postoperative surgery complications, heart rate, SAD, DAD, glycemia and HbA1c level, inflammatory markers such as CRP.
Results
Among the 100 patients undergoing CABG and 100 undergoing PCI, T2DM patients showed significantly higher fasting (1.4x) and postprandial (1.6x) glycemia levels, HbA1c (1.4x), and CRP (1.54x) compared to non-diabetics (all $P < 0.05$). HR, SAD, and DAD were also elevated in the T2DM group. Postoperative outcomes and mortality rates were similar across CABG and PCI groups; however, T2DM patients were 1.7 times more likely to experience complications (odds ratio = 1.7, $P < 0.05$). Elevated CRP and preoperative HbA1c correlated with poorer postoperative indicators, underscoring the need for targeted perioperative management in diabetic patients.
Conclusions
Postoperative outcome and mortality rate were comparable in CABG and PCI group and showed significant differences between with and without T2DM and have 1.7 times higher complications. Pre and postoperative level of CRP, HbA1c were found indicator of poor outcome in those patients.

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P127

Case report: hypoglycaemia caused by unintentional gliclazide ingestion

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Background
Gliclazide has a high propensity to cause hypoglycaemia when taken by subjects who do not have diabetes.
Case Report
A 69-year-old man presented with symptoms compatible with hypoglycaemia (sweating, lethargy, faintness). He had known hypertension, chronic kidney disease 3b, and osteoarthritis, but was not on any regular medications apart from amlodipine. Initial observations showed a capillary blood glucose (CBG) of 2.4 mmol/l. He was given 200 ml of 10% glucose intravenous, however, a repeat CBG was 1.8 mmol/L and blood ketones 0.4 mmol/l. The patient had no past history of diabetes mellitus, bariatric surgery, had not been fasting and reported no use of any herbal remedies. There was no diabetes history in any household members nor medical or nursing contacts. The patient had no previous episodes of hypoglycaemia. He was admitted to further manage his hypoglycaemia. A laboratory glucose, insulin, c-peptide and sulphonylurea screen were sent. His hypoglycaemia failed to improve with oral glucose - blood glucose rose briefly to 7.4 mmol/l, before dropping to 1.6 mmol/l. He required IV 10% glucose infusion for 16 hours to maintain euglycaemia, but thereafter was euglycaemic on a normal diet. Laboratory work up showed cortisol 362nmol/l, TSH 0.39 mIU/l, FT4 16.4 pmol/l. Laboratory glucose of 1.6 mmol/l confirmed severe hypoglycaemia and c-peptide was inappropriately raised at 3,397 pmol/l (ref 366-1465 pmol/l). He was observed for 2 days and had no further hypoglycaemic episodes. His blood sulphonylurea screen later returned positive for gliclazide (Diamicron). There was no known source of this. We have contacted his community pharmacy to ensure that there had not been a medication dispensing error.
Conclusion
This case emphasises the need for vigilance when investigating atypical causes of hypoglycaemia and for timely completion of relevant blood tests within the narrow time frame of true hypoglycaemia.

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P128

A quality improvement project (QIP) to assess the measurement of blood ketones during intercurrent illness in patients with type 1 diabetes during pregnancy

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Background
Ketosis during pregnancy can lead to serious maternal and fetal complications in patients with Type 1 Diabetes, including risk of miscarriage or still birth for the fetus and risk of maternal mortality. This project evaluates the prevalence of ketone testing in pregnant women with Type 1 Diabetes presenting to the emergency department (ED), the incidence of ketonemia and the associated pregnancy outcomes.
Methodology
A retrospective study was conducted from September 1, 2023, to August 31, 2024, involving 20 ED visits by 13 pregnant women with Type 1 Diabetes. Data, provided by the Business Intelligence team and anonymized for confidentiality, included maternal illness visits during pregnancy, blood ketone measurements, glucose readings, and pregnancy outcomes. The analysis focused on assessing whether appropriate actions were taken for levels exceeding 1.0.
Results
Among the 20 visits, ten women reported feeling unwell, six experienced per vaginal bleeding, three had musculoskeletal symptoms, and one presented with shortness of breath. Blood ketone levels were assessed in only 8 visits (40%),. Of those tested, 5 had ketones <1.0, and three had ketones >1.0. Four women had multiple ED visits, raising concerns about recurrent admissions. The three patients with elevated ketones were managed according to protocols, leading to one readmission with a premature birth at 36 weeks; two others experienced miscarriage.
Conclusion
The findings underscore the urgent need for enhanced monitoring of blood ketones in pregnant women with Type 1 Diabetes during illness.
Actions
Recommendations include prenatal educational reinforcement on ketone monitoring in illness among patients, enhancing communication among healthcare providers, and establishing clear protocols in ED and maternity settings. Educational initiatives, including posters and training sessions, are underway to address these barriers.

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P129

Does AMY1 copy number correlate with metabolic-associated fatty liver disease?

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Background
Metabolic-associated fatty liver disease (MAFLD) is the hepatic manifestation of metabolic syndrome. MAFLD's most severe form is metabolic dysfunction-associated steatohepatitis (MASH). The current gold standard for identifying MASH is histological assessment via invasive liver biopsy. Non-invasive biomarkers are urgently needed to facilitate diagnosis. Genome wide association studies identified copy number (CN) variants in the salivary amylase gene AMY1 as influencing metabolic phenotypes. Low CN levels associate with increased BMI and visceral adipose tissue, whereas high CN levels associate with a favourable metabolic profile. Our aim was to explore correlation between hepatic AMY1 CN and MASH. Through establishing an association, AMY1 CN extracted from non-invasive salivary samples could be used as a risk stratification biomarker in MAFLD.
Method
Liver tissue samples and anonymized patient demographic data, were collected from patients transplanted for MASH cirrhosis and donor liver specimens not used for transplantation collected at the Queen Elizabeth Hospital in Birmingham.

Deoxyribonucleic acid was extracted from MASH ($n = 26$) and healthy donor livers ($n = 26$), and assessed for hepatic AMY1 CN by droplet digital polymerase chain reaction.
Results
The baseline characteristics of the two populations revealed a difference in mean age, prevalence of diabetes, bilirubin (umol/l) and ALT (iu/l)($P < 0.05$), but no difference in body mass index and sex distribution($P > 0.05$). The mean AMY1 copy number in the MASH cohort was 7.04 ± 2.85 and in the donor cohort was 6.70 ± 2.26. The difference in CN was not significant ($P = 0.63$).
Conclusion
Our a priori hypothesis, of a correlation between AMY1 CN and MAFLD severity is not supported by the data from our *in vitro* study. The relatively low number of liver samples included limits any firm conclusions. Future studies should explore with greater power any evidence for a biological causal pathway that implicates AMY1 CN variance in the pathogenesis of MAFLD.

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P130

The obesogenic impact of the 5:2 diet in mice

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Despite its popularity, the physiological impact of the 5:2 diet (2 non-consecutive fast days and 5 normal feeding days) in mice remains unclear. We have previously reported that while this fasting strategy accelerates skeletal growth in both sexes, it only reduces weight in males. To advance our understanding of its broader metabolic impact, adolescent (7-week old) male and female C57BL/6J mice received standard rodent chow in an *ad-libitum* or 5:2 pattern for 24 days. While 5:2 diet-fed mice induced rebound overeating on feeding days, neither sex showed significant cumulative hyperphagia. Tibial epiphyseal plate width (EPW), an index of skeletal growth rate, and marrow adipocyte size were elevated by 9% and 31% in males ($P = 0.027$; 0.038). Proportionate inguinal white adipose tissue (WAT) mass increased in 5:2-fed males and females by 37% and 22% respectively ($P = 0.006$, 0.034), with a 17-20% elevation in adipocyte size ($P < 0.05$). Neither gonadal nor retroperitoneal WAT were significantly affected. Proportionate interscapular brown AT (BAT) was elevated by 37% in both sexes ($P = 0.0001$). Gas chromatography with flame ionisation detection revealed parallel increases (11-35%) in the relative amounts of saturated (C14:0; C16:0; C18:0; C20:0) fatty acids (FAs) in BAT in males and females ($P < 0.05$) and reductions (12-35%) in mono- and poly-unsaturated FAs (C16:1n9; C20:1n9; C20:4n6) including essential FAs (C18:1n7; C18:2n6 and C18:3n3) ($P < 0.05$). In contrast, while hepatic essential FA content (C18:2n6; C18:3n3) was reduced and C20 omega-6 (C20:3n6) FA content was increased (17%) in both sexes ($P < 0.01$), saturated FA (C18:0) content was only increased (25%) in males ($P = 0.037$). Thus, the 5:2 diet induces a surprising combination of sex-independent and sex-specific effects. The increase in subcutaneous WAT and interscapular BAT mass suggests improved heat retention in both sexes, accompanied by a broader preferential storage of saturated FAs. However, as a weight loss strategy, the 5:2 diet is only effective in males.

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P131

Elevated cardiometabolic disease risk in males compared to females is not explained by differences in fasting and postprandial insulin secretion and clearance

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Background
Plasma insulin concentrations reflect the balance between insulin section and clearance. Reduced insulin clearance is a common feature of obesity and contributes to hyperinsulinemia, a cardiometabolic disease (CMD) risk factor. Although there are sex-related differences in CMD risk, it remains unclear if sex differences in fasting and postprandial insulin kinetics exist under physiological conditions.
Aim
To investigate whether there are sex differences in fasting and postprandial insulin kinetics and their relationship to CMD risk factors.
Methods
Following an overnight fast, 19 male (51 ± 5yr, 28.3 ± 3.7 kg/m^2) and 20 female (53 ± 6yr, 26.3 ± 3.9 kg/m^2) individuals underwent a 4h mixed-meal feeding study. Intrahepatic triglyceride content (IHTG%) was quantified by MRI/S. Plasma metabolites, pancreatic islet hormones, and the contribution of gluconeogenesis to fasting plasma glucose were assessed. Prehepatic insulin secretion and clearance mathematically modelled and CMD risk was approximated using plasma low-density-lipoprotein (LDL) cholesterol.
Results
Compared to age and BMI matched females, males had a greater ($p < 0.01$) waist-hip ratio, IHTG%, HOMA-IR and fasting LDL-cholesterol. Despite this, males and females had similar postprandial increases in plasma insulin, which corresponded to similarly increased insulin secretion rate (ISR; males:142 ± 68 pmol/min/m^2, females:126 ± 75 pmol/min/m^2) and decreased insulin clearance rate (ICR; males:1.26 ± 0.46 L/min/m^2, females:1.42 ± 0.63 L/min/m^2). Fasting and postprandial glycaemia, and fasting glucose derived from gluconeogenesis did not differ between sexes. A stepwise linear regression model revealed sex was the only significant predictor for the variance in LDL-cholesterol ($p = 0.01$; adj. $R^2 = 0.14$) in our cohort. A partial correlation showed that when controlling for sex, time-averaged ICR and ISR were not correlated with LDl.
Conclusion
Although males display markers of increased insulin resistance compared to females, postprandial glycaemic control and insulin kinetics were comparable. Our findings suggest that differences in CMD risk in age- and BMI-matched males and females are not explained by postprandial insulin kinetics.

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P132

Creating a predictive model for type 2 diabetes improvement post bariatric surgery based on urine-based protein biomarkers

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Introduction
Bariatric surgery can result in substantial weight loss and type 2 diabetes (T2DM) remission, yet predicting those that will attain T2DM improvement can be challenging with 40-80% variability in remission. Current methods to predict successful bariatric outcomes are limited. Therefore, we aimed to investigate the use of pre-surgical urine samples as a non-invasive method to detect biomarkers and predict and/or monitor T2DM improvement, allowing stratification of patients to improve bariatric outcomes.
Methods
Urine samples were collected from female Caucasian participants (age $= 52.7 \pm 1.39$; body mass index $= 41.6 \pm 1.09$; $n = 40$) undergoing bariatric surgery at baseline (pre-surgery) or 6-months post-surgery. Mass spectrometry (MS) was used to assess protein data, identifying 2557 proteins across all samples, and Amica software was used to determine differences in those who improved their T2DM status based on HbA1c ($n = 19$), and those that didn't ($n = 15$). Machine learning techniques, in the form of a swarm of neural networks, were undertaken to interrogate MS data and identify key proteins.
Results
MS identified 57 differentially expressed proteins ($P < 0.05$) in pre-surgery urine samples between these groups, with differential pathways including immune response and peptidase activity. In addition, neural network analysis used 20 models to identify key proteins that were stable across multiple models. The most stable protein in these models, indicating it had most impact on T2DM status improvement, was immunoglobulin-like cell surface receptor for CD47, with the chance of this being a false result less than 3.25x10^-38.
Discussion
These analyses indicate that pre-surgery urine samples may exhibit a different protein profile based on post-bariatric T2DM outcomes, including key proteins which could be used as biomarkers to predict T2DM status improvement post-surgery. This highlights the use of urine biomarkers as an additional method to stratify bariatric surgery patients to offer more personalised support and improve success rates.

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P133

Weight loss trajectories with a targeted prescribing pathway for liraglutide 3 mg using multiple stopping rules: findings from the STRIVE study

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Background
The STRIVE study was a 2-year, multicenter, open-label, randomized controlled trial assessing the clinical effectiveness of a targeted prescribing pathway for liraglutide 3 mg with multiple stopping rules (intervention) compared to standard care (control), in specialist weight management services.
Aim
This ad hoc sub-analysis examined the weight loss (WL) trajectories with the application of different stopping rules for liraglutide 3 mg in the intervention arm.
Methods
The trial enrolled 392 participants with a BMI $\geq$35 kg/m^2 and at least one obesity-related complication. Of these, 260 participants randomized to the intervention arm and received liraglutide 3 mg, with stopping rules applied at 16 weeks ($\geq$5% WL), 32 weeks ($\geq$10% WL), and 52 weeks ($\geq$15% WL). Participants meeting all three stopping rules continued liraglutide 3 mg for an additional 52 weeks.
Results
- Those not passing the $\geq$5% WL stopping rule at 16 weeks (mean WL 3.1%), achieved 1% WL at 104 weeks.
- Participants not meeting the $\geq$10% WL stopping rule at 32 weeks (16 weeks mean WL 7.1%, 32 weeks 6.7%), achieved 1.4% WL at 104 weeks.
- Those not meeting the $\geq$15% WL stopping rule at 52 weeks (16 weeks mean WL 9%, 32 weeks 11.3%, 52 weeks 10.1%) managed 5.6% WL at 104 weeks.
- Participants meeting all three stopping rules at 52 weeks (16 weeks mean WL 11.5%, 32 weeks 14.7%, 52 weeks 17.1%) achieved 11.4% WL at 104 weeks.

Conclusion
Participants who passed all three stopping rules showed a trend toward greater WL compared to the other groups from the first 16 weeks. Weight regain occurred in those who stopped liraglutide 3 mg due to stopping rules. While those who continued liraglutide 3 mg after passing all rules achieved $\geq$10% mean WL at 104 weeks, they too experienced weight regain.

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P134

Diabetes as a risk factor for pregnancy outcome in HPV-affected pregnancy

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Pregnancy is a unique state in which a balance of immune tolerance and suppression is necessary to protect the fetus without compromising the mother's health. Human papillomavirus (HPV) is a common viral infection mainly transmitted through sexual contact, and it can infect the placenta to increase the inflammatory response in the mother, affecting pregnancy outcomes. The objectives of this research are to evaluate diabetes as a risk factor on the effect on clinical course in pregnancy and maternal outcome in pregnant women with HPV infection and to evaluate the impact on neonatal health in terms of adverse clinical effects.

Methodology
The prospective cohort study was done in a tertiary care institution for two years. The study included 250 pregnant women who attended the antenatal clinic for routine check-ups. Written informed consent was obtained from each participant. Participants were asked to complete a detailed questionnaire. HPV DNA was detected using a hybrid capture assay (marketed as Digene HC2 high-risk HPV DNA test, Cat. No./ID: 5199–1220). The cohort was divided into two study groups: 1) those who were HPV positive and 2) those who were HPV negative. SPSS20 (IBM Corporation; NY, USA) was used for statistical analysis of all data.
Results
Out of 228 pregnant women who were followed for their outcome, 27.63% (n = 63) of pregnant women were found positive for the HPV DNA test. In comparing the HPV-positive (n = 63) and HPV-negative (n = 165) groups using chi-square tests, The HPV-positive participants were more likely to have additional morbidities (54%) compared to HPV-negative participants (32.1%). The pregnancy outcome was impacted by more decisions for emergency operative delivery, the preterm onset of labour and babies with lower birth weights.
Conclusion
In summary, the study revealed valuable insights into the relationship between HPV infection during pregnancy and maternal and neonatal health outcomes.

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P135

Ghrelin signaling regulates the sex-specific metabolic impact of ultradian feeding patterns in mice

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Ultradian rhythms of metabolic hormone secretion govern biological activity and are themselves regulated by temporal patterns of feeding behaviour. Despite these well-established phenomena, the broader metabolic impact of temporal feeding patterns remains a major unanswered question in nutritional science. Using an automated CLAMS-based feeding system, we have shown that nocturnal grazing (GR) had no impact on cumulative food intake (cF/I) or body weight gain (ΔBW) in male and female C57BL6/J (WT) mice (*vs ad libitum*-fed (AL) animals). In contrast, while cF/I in nocturnal meal-fed (MF) male WT mice was only 88% of that in AL males (P=0.1036), this was exaggerated in GHSR-null males (reduced by 15%; P=0.0082). ΔBW was also reduced by 62% in MF GHSR-null females (*vs* AL GHSR-null females; P=0.0099). Although GR did not affect skeletal growth rate (tibial epiphyseal plate width (tEPW)) in males, MF accelerated skeletal growth by 13% (P=0.0166). However, in females GR and MF reduced tEPW by 13% and 15% (P=0.0158; 0.0029). These effects were absent in GHSR-null mice. GR increased retroperitoneal white adipose tissue (WAT) mass in male and female mice (by 84% and 41%; P=0.0146, 0.0219), with no significant effect on gonadal WAT mass. Inguinal WAT mass was elevated only in males (by 37%; P=0.032). These effects were abolished in GHSR-null mice. Neither GR nor MF significantly affected interscapular brown AT (BAT) mass. Thus, GR elevates fat mass in ghrelin-sensitive depots in both sexes, while ghrelin maintains orexigenic drive in MF males, promoting skeletal growth. In contrast, interruption of AL feeding in females inhibits skeletal growth, but MF only leads to weight loss in the absence of GHSR activation. Our data imply that the contemporary shift from regular meals to less structured feeding may impair male growth outcomes and elevate fat mass.

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P136

Does anaemia worsen outcomes of diabetic ketoacidosis? a nationwide retrospective cohort study

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Background
Diabetes mellitus (DM) is a critical global health crisis, characterised by rising prevalence and severe complications that strain healthcare systems. Diabetic-ketoacidosis (DKA) is the most severe complication of DM. Anaemia can worsen tissue hypoxia in DKA, trigger inflammatory pathways, disrupt fluid-electrolyte balance, and alter pharmacokinetics of medications. While the role of anemia in diabetes has been studied, its impact on DKA hospitalisations, a common reason for

admissions in DM, remains largely unexplored. This study analyses the effects of anaemia on DKA hospitalisation outcomes.
Methods
The National Inpatient Sample database (2016-2020) was analysed using ICD-10 codes to identify adults hospitalised with DKA, with the cohorts stratified by anaemia prevalence. Categorical variables were compared using chi-square test, while continuous variables were assessed with t-test, considering p-value < 0.05 significant. Multivariate regression analysis evaluated the impact of anaemia on DKA hospitalisation outcomes, adjusting for relevant confounders and hospital characteristics.
Results
A total of 2,068,114 DKA hospitalisations were identified, with 21.85% having anaemia. DKA patients with anaemia were older compared to those without (50.60 vs 43.83 years). Among anaemic patients, 55.02% were females. DKA hospitalisations with anaemia had worse outcomes (Table) and resulted in increased resource utilisation, marked by a longer stay of 3.89 days (7.85 vs 3.96) and higher hospitalisation costs by $52,003 (95,828$ vs 43, 825$).

Table 1: Comparison of Outcomes of DKA hospitalizations with and without anaemia

	% with and without anaemia (p-value)	Adjusted Odds Ratio for confounders (95%-Confidence Interval)	P value
Mortality	4.40, 2.38 ($P < 0.001$)	1.10 (1.04-1.15)	<0.001
Hypoglycemia	0.21, 0.12 ($P < 0.001$)	1.58 (1.24-2.01)	<0.001
Acute-kidney-injury	54.32, 39.87 ($P < 0.001$)	1.45 (1.42-1.48)	<0.001
Hypokalemia	24.11, 20.87 ($P < 0.001$)	1.27 (1.24-1.30)	<0.001
Acute-respiratory-distress-syndrome	0.74, 0.29 ($P < 0.001$)	1.58 (1.39-1.80)	<0.001

Conclusion
This study underscores the significant impact of anaemia on DKA hospitalisations, highlighting the need to address anaemia to improve clinical outcomes and optimise resource utilisation.

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P137

Delayed diagnosis of vasopressin resistance (nephrogenic diabetes) after cessation of treatment with lithium

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Lithium is an effective mood disturbance treatment. Endocrine side-effects include hypothyroidism, hypercalcemia and vasopressin resistance. The latter can resolve on cessation of treatment but may be permanent.
Case Report
A 67 year old female was transferred from a psychiatric unit with deteriorating clinical (anorexia, weight loss and decreased conscious level) and biochemical status: sodium 173 mmol/l, potassium 4.6 mmol/l, urea 22.2 mmol/l, creatinine 193 umol/l, calcium 2.77 mmol/l, plasma osmolality 351 mmol/kg and urine osmolality 148 mmol/kg. Treatment with lithium modified-release 400 mg od for 15 years had stopped 2 months earlier. Dehydration with acute kidney injury due to decreased fluid intake was diagnosed. Vigorous fluid resuscitation corrected biochemical abnormalities with return to the psychiatric unit. Four months later a similar episode occurred with the same treatment and outcome. A further episode 3 months later was attributed to dehydration secondary to primary hyperparathyroidism: calcium 2.94 mmol/L and PTH 4.7 pmol/l. Treatment with cinacalcet and IV fluids improved calcium with only a transient improvement in sodium resulting in endocrine referral. The latter diagnosed unrecognised vasopressin resistance leading to the clinical and biochemical abnormalities. This was confirmed with untreated urine volumes of 3.5 L/24h and raised copeptin level of 33 pmol/l coincidental with sodium 167 mmol/l, plasma osmolality 361 mmol/kg and urine osmolality 205 mmol/kg. Treatment with cinacalcet was stopped and consistently normal biochemical levels ensued with urine volumes of approximately 2 L/24h on treatment with acetazolamide 500 mg bd.
Conclusion
(1) patient had mild vasopressin resistance decompensated with decreased oral fluid intake when unwell; (2) relatively mild polyuria secondary to vasopressin resistance can result in severe hypernatremia and (3) clinicians of all specialties need to be aware that nephrogenic diabetes insipidus can occur post lithium treatment.

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P138

Using contrast enhanced ultrasound to visualise the gastrointestinal response to nutrients

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The prevalence of obesity and related comorbidities is rising globally, with gastrointestinal systems heavily implicated in its pathophysiology. Obesity is an inflammatory state causing disruption of vessel structure and endothelial function. Nutrient-sensing mechanisms enable glucose uptake and secretion of anorectic hormones, potentially contributing to metabolic disease. Changes to postprandial blood flow in obesity are unclear and may be visualised using contrast-enhanced ultrasound (CEUS). This in-vivo study aimed to optimise and use CEUS to quantify the effect of glucose on duodenal blood flow in lean and obese mice. In a repeated measures experimental design, glucose solution (100% w/v, 5ml/kg) or vehicle control (5ml/kg) were administered by oral gavage ($n = 11$) or intraduodenal infusions ($n = 7$) into lean and diet-induced obese C57BL/6 mice. Ultrasound images were acquired using a microbubble contrast agent while under general anaesthesia. Microbubble intensity was representative of blood flow, which was measured by processing ultrasound acquisitions. CEUS enables non-invasive, non-ionising, visualisation of gut microvasculature to a resolution of 10um. In lean mice administered glucose or vehicle via oral gavage, there was a trend for glucose to evoke greater hyperaemia in the duodenum, whereas this trend was not evident in obese mice, potentially indicating a dampened nutrient response in obesity. Initial non-significant decreases in blood flow were observed following both infusions, suggesting either initial vasoconstriction, perhaps in response to shock, or effects of gut distension distorting the density of perfused blood vessels. However, overall, there were no significant differences found between the effects of glucose and vehicle control on duodenal hyperaemia. This study demonstrates the potential utility of CEUS as a method of visualising microvasculature and changes in blood flow to the gut. We demonstrate a potentially dampened glucose-sensing ability in obese mice and present a rationale for future research in understanding nutrient-sensing mechanisms and their role in metabolic disease.

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P139

Unmasking the challenges: hypoglycaemia and its effects on lymphoma hospitalisations

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Background
Hypoglycaemia in lymphoma is well-documented and can result from Warburg effect, pituitary/hepatic infiltration, chemotherapy side-effects, and glyceraldehyde-3-phosphate dehydrogenase overexpression. It disrupts cellular signalling pathways of growth and apoptosis, affects insulin secretion—which may support lymphoma cell survival—and impairs immune function, especially in T-cells and natural-killer cells. This complex interplay triggers inflammation, facilitating tumour progression. This study analyses the impact of hypoglycaemia on in-hospital outcomes of lymphoma.
Methods
The National-Inpatient-Sample-database (2016-2020) was utilised to identify lymphoma hospitalisations, stratified by hypoglycaemia prevalence based on ICD-10 codes. Categorical variables were analysed using chi-square tests, while continuous variables were assessed through t-tests, significance threshold set at $P < 0.05$. Multivariate regression analysis determined how hypoglycaemia affects lymphoma hospitalisations, adjusting for relevant confounders, sociodemographics and hospital characteristics.
Results
1,485,770 lymphoma hospitalisations were identified, with 8,765 cases of hypoglycaemia. The mean age was similar for both groups (64.64 years for hypoglycemic and 64.47 years for non-hypoglycemic). Among those with hypoglycemia, 44.5% were females. Racial distribution was 63.05% white, 19.01% black, and 9.98% Hispanic ($P < 0.001$). Lymphoma patients with hypoglycemia experienced greater resource utilisation, with an average increased length of stay by 3.53 days (10.37 vs 6.84) and costs by $51,325 (139,353$ vs 88,028$). Multivariate regression analysis revealed worse outcomes for lymphoma hospitalisations with hypoglycemia, as detailed in the table.

Table 1: Impact of hypoglycaemia on lymphoma hospitalizations

	% with and without hypoglycaemia (p-value)	Adjusted-Odds-Ratio for confounders (95%-Confidence Interval)	P-value
Mortality	29.86, 4.74 ($P < 0.001$)	8.43 (7.33-9.69)	<0.001
Infections	32.57, 11.01 ($P < 0.001$)	3.70 (3.25-4.21)	<0.001
Metabolic-acidosis	37.82, 8.10 ($P < 0.001$)	6.61 (5.84-7.49)	<0.001
Tumour-lysis	10.49, 1.91 ($P < 0.001$)	5.66 (4.64-6.91)	<0.001
Disseminated-intravascular-coagulation	4.90, 0.45 ($P < 0.001$)	10.67 (8.14-13.98)	<0.001

Conclusion
Hypoglycaemia significantly impacts lymphoma hospitalisations, leading to increased resource utilisation, longer hospital stays, and poorer patient outcomes. Optimal management of hypoglycaemia in lymphoma patients is essential for high-value care and improving clinical results.

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P140

Super-resolution ultrasound imaging to visualise changes in pancreatic microvasculature in a mouse model of type ii diabetes

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Microcirculatory deterioration can occur early in the development of diabetes and structural changes in the capillary beds are well reported. High levels of insulin have been found to damage blood vessels and, particularly in type 2 diabetes (T2D), are linked to cardiovascular diseases such as hypertension. Therefore, we hypothesised that capillary beds surrounding the islets of Langerhans would also be affected by these vascular changes during the onset and progression of disease. With the use of super-resolution ultrasound (SRUS) it is possible to obtain high resolution (10um) structural and dynamic data on the microvasculature, including blood vessel coverage, vessel diameter, and blood velocity. For this study, we used polygenic T2D Tally Ho mouse model, in which males typically develop diabetes spontaneously around 8 to 10 weeks of age. Fasted male Tally Ho mice were anaesthetised and intravenously infused with a microbubble (MB) contrast agent (790ul/min/kg, IV) while images of the pancreas were acquired. Post processing of the data enabled us to locate and track individual MBs flowing through the microvasculature of the pancreas. These imaging sessions were performed on a weekly basis before and during the onset of glucose intolerance. Fasted blood glucose measurements were also taken on a weekly basis to monitor the progression of T2D. Control mice which did not develop diabetes showed no change in blood flow in the pancreas. Mice that developed diabetes showed a significant negative correlation between blood glucose levels and a pancreatic blood flow. These preliminary results suggest a relationship between a deterioration of the microcirculation in the pancreas and a disruption in glucose homeostasis. SRUS imaging could be used as a non-invasive tool to longitudinally follow the effect of T2D on the microvasculature of the pancreas and provide insight into the mechanisms of the disease and potential drug targets.

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P141

A retrospective evaluation of inpatient referrals to Endocrinology for hyponatraemia at a tertiary hospital

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Introduction
Hyponatraemia is a common electrolyte disturbance in hospital inpatients and a frequent reason for referral to Endocrinology. Hyponatraemia is a marker for an underlying pathology and fluid status rather than a diagnosis per se. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) occurs as a complication of several medical presentations. The aim of this retrospective audit was to assess inpatient referrals of hyponatraemia to the Endocrinology team and identify ways to reduce workload using the **RCP Referring wisely** document.
Methods
Hyponatraemia referrals received via the electronic referral system over a 6-month period (January-June 2024) were analysed. Clinical judgement on aetiology of hyponatraemia was derived based on a comprehensive review of these referrals.
Results
$n = 76$ (18% of total referrals received) Sodium at referral: Mild: 130-135mmol/L (2.6%) Moderate: 125-129mmol/L (40.8%) Severe: <125mmol/L (56.6%). Mean time of referral following onset of hyponatraemia: Day 6 (between day 1 to day 25). Referring departments: Medical wards (73%), surgical wards (26%), intensive care (1%). Hyponatraemia blood screening panel prior to referrals: 59% were performed. Likely cause of hyponatraemia: Drug induced (27.6%) SIADH (26.3%) Fluid overload (13.2%) Dehydration (13.2%) Unclear cause (10.5%) Multifactorial (7.9%) Primary endocrine pathology (1.3%).
Conclusion
This audit demonstrates that over half of inpatient referrals for hyponatraemia to Endocrinology had a drug/fluid balance precipitant. These could have been avoided by use of the comprehensive Trust guidelines. A systematic diagnostic approach, by the primary team (majority from physician sub-specialties), is warranted to determine the aetiology of hyponatraemia. In view of the various non-endocrine causes of hyponatremia and the higher prevalence during inpatient stay, there is a need to follow Referring wisely RCP guidance stating referral to Endocrinology for '*Symptomatic or severe hyponatraemia or where diagnostic doubt exists*'. This is pertinent when majority of the causes for hyponatraemia is not due to a primary endocrinopathy.

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P142

Findings from the introduction of genetic testing for rare causes of obesity in an NHS weight management service

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Background
Genetic testing technology has improved considerably in recent years and is now more widely available. In the UK, obesity genetic testing is currently available from the NHS Genomic Medicine Service, or the Rare Obesity Advanced Diagnosis (ROAD) programme. We aimed to enable patients living with obesity the ability to access this genetic testing if they were eligible and interested in exploring this aspect of their care.
Methods
In February 2023 we introduced ROAD genetic testing (a panel of 79 genes and 1 chromosome region) in our regional adult medical obesity clinic. All patients provided written informed consent. Decisions to offer genetic screening were based on: BMI >40 kg/m^2 ($n = 48$, 98.0%), early onset in childhood ($n = 42$, 85.7%), family history ($n = 11$, 22.4%), features of hyperphagia ($n = 6$, 12.2%) or developmental delay/learning disability ($n = 6$, 12.2%).
Results
We performed 60 tests (23 buccal swabs, 37 saliva) in 49 patients (11 repeats, 2 pending). Patients were majority female ($n = 31$, 63.3%) with mean age 35.3 $\pm$ 1.4 yrs, weight 155.9 $\pm$ 5.3 kg and BMI 55.3 $\pm$ 1.6 kg/m^2. Pathogenic variants were detected in 8 patients (17.0%), with heterozygosity in *PCSK1* ($n = 3$), *POMC* ($n = 1$), *MC4R* ($n = 1$) and ch16p11.2 deletion syndrome ($n = 3$) reported. Variants of unknown significance (VUS) were reported in a further 19 (40.4%) patients. In 20 (42.6%), no pathogenic variants explaining the clinical phenotype were detected.
Conclusion
Aberrations in genes proposed to regulate appetite is common in the medical obesity clinic. Identification may provide patients with an explanation for their weight gain, facilitate testing of family members and enable access to obesity pharmacotherapy in research/treatment pathways. However, VUS detection is likely to be more common with ROAD than the NHS Severe Early-Onset Obesity panel (a smaller panel of 33 genes associated with obesity). Further study on predicting response to obesity treatments based on genotype is needed.

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P143

Successful and prompt management of 'severe hypertriglyceridaemia' in a patient with new onset diabetes

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Introduction
Hypertriglyceridaemia is common and can be managed safely by treating the underlying cause like poorly controlled diabetes, profound hypothyroidism, obesity, alcohol excess but severe hypertriglyceridaemia (>5.6mmol/l) poses high risk of complications including pancreatitis, venous thromboembolism (VTE) and long-term cardiovascular complications. Urgent management is extremely important to reduce the above risks.
Case report
A 49-year-old man with a history of well-controlled asthma, heavy smoking, and alcohol excess admitted with osmotic symptoms (increased thirst and urination) and a year-long history of glove and stocking numbness and tingling. On examination, he had central adiposity with a body mass index of 31.4 kg/m^2. No clinical features of endocrinopathy like Cushing's or acromegaly. His clinical picture was consistent with new-onset type 2 diabetes mellitus given an HbA1c of 135. He was noted to have severe hypertriglyceridemia with hypercholesterolaemia, as mentioned below. There were no clinical features of familial hypercholesterolaemia like tendon xanthoma or xanthelasma.
Investigations
Baseline investigations including full blood count, bone profile, C-reactive protein, renal functions, thyroid functions, coagulation profile, B12, folate, and amylase levels were normal but mild asymptomatic hyponatraemia (124 mmol/l). However, he had severely lipaemic serum with triglyceride levels of 63 (<1.7 mmol/l) and total cholesterol of 21.5 (<5mmol/l).
Management
He was successfully managed with a variable-rate insulin infusion (VRIII) at 0.05 units/kg/hour, 5% dextrose (100-150 ml/hour), and a high-dose prophylactic low molecular weight heparin, in addition to a low-calorie and fat-free diet.
Learning points
1. It is extremely important to acutely reduce severe hypertriglyceridemia to alleviate the risk of pancreatitis and VTE. 2. Severe hypertriglyceridaemia can be successfully managed with VRIII without requiring plasmapheresis in majority of cases. 3. High dose VTE prophylaxis is equally important to reduce the risk of VTE secondary to hyperviscosity from hypertriglyceridemia.

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P144

Diabetes mellitus and endometrial cancer: risks and underlying mechanisms

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Introduction
Diabetes mellitus (DM), particularly type 2 (T2DM), has become a significant global health issue, with rising rates linked to increased risks of various cancers, including endometrial cancer (EC). Research increasingly suggests a connection between DM and EC, indicating that DM may not only elevate the risk of EC development but also worsen its prognosis. Metformin, an anti-diabetic medication, is under exploration as a potential preventive and therapeutic agent for EC, highlighting the value of treatments targeting glucose metabolism in mitigating EC risks. Studies show that hyperglycemia is an independent risk factor for EC, with individuals with DM twice as likely to develop EC compared to non-diabetics. This heightened risk may stem from high-glucose environments, which promote the growth and invasiveness of EC cells. Although the exact biological mechanisms linking DM to EC are not fully understood, the need for effective prevention and early intervention through glucose regulation is increasingly emphasized as an essential area for future therapeutic developments.
Materials and Methods
Published data over the past two years from sources such as MEDLINE, EMBASE, PubMed, and Research Gate were systematically analyzed to understand the association between DM and EC.
Results
Findings reveal a strong association between EC and T2DM. T2DM significantly raises the risk and mortality rate of EC, with a 4.9% increased risk of EC identified even in early-stage DM patients. Type 1 diabetes is also associated with elevated EC risks, confirming DM as an independent factor for EC mortality. Biological Mechanisms: Insulin resistance and hyperinsulinemia influence endometrial cells, while signaling pathways such as PI3K and MAPK/ERK, facilitated by chronic inflammation markers like TNFα and IL-6, contribute to EC development.
Conclusion
This research advances our understanding of the DM-EC link, proposing antidiabetic therapies as promising options for EC management and inspiring future research directions in this field.

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P145

Dietary modification prior to bariatric surgery leads to marked improvement in glycaemia during continuous glucose monitoring

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Background
Prior to gastric bypass surgery, patients undertake a 2-week low-calorie diet (LCD) of 800-1000 kcal per day. This aims to consume liver glycogen and fat stores, thereby shrinking the liver to facilitate laparoscopic access to the stomach. The impact of this diet on glycaemic control in those with type 2 diabetes has not been clearly defined.
Methodology
Seven patients with Type 2 Diabetes and obesity (mean age 54 ± 8 years) participating in a longitudinal prospective study underwent 7-day continuous glucose monitoring (CGM) whilst on a LCD in preparation for bypass surgery. Routinely, during the diet SGLT2 inhibitors are stopped and insulin doses are reduced. Seven controls (mean age 53 ± 12 years) matched on age and pre-operative HbA1c underwent CGM whilst on their normal diet. CGM data was analysed using EasyGV Calculator v.10. Pre-diet oral hypoglycaemic and GLP1 analogue usage were similar between groups. However, four patients within controls were on insulin, compared to one patient on the diet. Results are stated as mean±SD.
Results
Average HbA1c was 62 ±10 mmol/L in the diet group vs. 61 ±9 mmol/mol in controls (P = 0.865). The average blood glucose on the diet was significantly lower at 7.8 ±1.3 mmol/L compared to 10.1 ±2.3 mmol/L in controls (P = 0.045). The diet groups spent on average 86.1% in range between 3.9 – 10.0 mmol/l, this was significantly greater than the average of 55.0% in the controls (P = 0.018). Of note, 6 of 7 patients in the diet group had TIR >70% and 4 of 7 > 90%, compared to 2 and 0 in the control group, respectively.
Conclusion
For patients with diabetes and obesity, a 14-day low calorie diet represents a feasible option for rapid non-pharmacologic glycaemic control pre-operatively, that could have potential benefits throughout the whole perioperative period.

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P146

The correlation between gestational diabetes and the development of autism spectrum disorders: a cross-sectional study

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Introduction
According to the World Health Organization (WHO), autism affects 1 in 100 children. Nevertheless, the possible risk factors have not been extensively studied. Emerging evidence suggests that gestational diabetes mellitus (GDM) may adversely affect

neurodevelopment, potentially increasing autism spectrum disorder (ASD) risk. This study investigates the association between GDM and autism-related behavioral markers in offspring.
Material and Methods
Using cross-sectional survey data based on M-ChartRF and questionnaire assessing prenatal condition, we analyzed maternal health metrics, including gestational blood glucose levels, alongside autism-related behaviors in children. The sample comprised 300 dyads aged 16-30 months, with variables focused on GDM exposure and subsequent child behavioral indicators. Additionally, we conducted a comprehensive review of existing literature on PubMed, MEDLINE, Scopus, and Google Scholar to support our findings, examining studies on the relationship between maternal diabetes and neurodevelopmental outcomes in offspring. Key studies were selected to provide a robust scientific foundation for our analysis and interpretation of survey data.
Results.
Preliminary linear regression analysis demonstrates a statistically significant association between maternal prepartum hyperglycemia and the manifestation of ASD-related behaviors in offspring. Specifically, 36.4% of toddlers born to mothers with prepartum hyperglycemia are classified as at moderate risk for ASD. In comparison, only 13.9% of toddlers born to mothers without elevated blood glucose levels exhibit moderate to high risk for ASD. Consequently, maternal hyperglycemia is associated with a 2.6-fold increase in the risk of autism spectrum disorder in offspring.
Conclusion.
Findings underscore the significance of maternal glycemic regulation during pregnancy as a potential factor influencing ASD-related behaviors, supporting further exploration of prenatal glucose management's role in neurodevelopmental outcomes.
Key words.
Autism spectrum disorder, Gestational Diabetes, neurodevelopment, glucose.
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P147

Obesity delays onset of lactation and causes mammary mitochondrial dysfunction independently of insulin resistance

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Physiological onset of lactation occurs 24-72 hours after childbirth and is characterised by increased mammary cell metabolism to support milk synthesis. Obesity is associated with delayed lactation onset and causes mitochondrial dysfunction in metabolically active tissues. We hypothesised that obesity may impair lactation through adverse effects on mammary mitochondria. To investigate this, we recruited $n = 27$ obese pregnant women (mean BMI = 34 ± 0.7 kg/m^2) intending to breastfeed, following informed consent, and compared them to $n = 87$ matched controls (BMI < 25 kg/m^2) during postpartum days 1-5. First, we assessed the timing of lactation onset, through participant self-reporting of milk coming in, and found that obese mothers had delayed lactation onset compared to controls (3.4 ± 0.1 *vs* 2.8 ± 0.1 days postpartum, $P < 0.001$). We assessed if this is associated with altered mammary metabolic gene expression. RNA sequencing was performed on mammary cell RNA isolated from postpartum day 1-5 milk samples ($n = 11$ obese mothers and $n = 62$ controls). Gene expression analysis revealed significant downregulation (>0.8-fold decrease in obese *vs* control, $P < 0.05$) of mammary genes encoding mitochondrial complex I (*NDUFA2*, *NDUFA12*), complex III (*UQCRC2*), complex IV (*COX1*, *COX3*), ATP synthase (*ATP6*, *ATP8*), and mitochondrial translation initiation and transcription factors (*MTIF3*, *TFB1M*), consistent with mammary mitochondrial dysfunction. We then investigated if this was caused by insulin resistance, which is reported to induce mitochondrial dysfunction in tissues such as skeletal muscle. We assessed the plasma leptin/adiponectin ratio (LAR), a non-fasting insulin resistance measure, and compared the transcriptome of $n = 22$ insulin-resistant (LAR > 3) with $n = 38$ control (LAR < 1) mothers. This showed an inflammatory mammary phenotype in insulin-resistant mothers with increased expression of pro-inflammatory cytokine receptors e.g. *IL6R* (1.7-fold increase, $P < 0.05$) and enrichment of inflammatory processes. However, mitochondrial gene expression was not altered in insulin-resistant mothers. Thus, our findings indicate that obesity may cause mammary mitochondrial dysfunction and delayed lactation onset by insulin-resistance independent mechanisms.

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P148

Postgraduate doctors-in-training's limited knowledge and practice in the assessment and management of inpatients with diabetes and frailty may contribute to suboptimal outcomes

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Introduction
People with diabetes and frailty require less intensive treatment of hyperglycaemia. Previous study has shown low rates of HbA_{1c} assessment and deintensification for people with diabetes and frailty. PGDiT is important in the inpatient management of people with diabetes and frailty. This study aims to assess the knowledge and management practice amongst PGDiT in managing people with diabetes and frailty and how this translates to patients' clinical outcomes.
Methods
Three cross-sectional survey-based studies were conducted on PGDiT at the beginning of each 4-month rotation. Survey questions incorporated knowledge of HbA_{1c} goals and on PGDiT deintensification practice in people with diabetes and frailty who are overtreated with blood glucose lowering medication. These were coupled by two cross-sectional data collection on patients' outcomes conducted during the same period including HbA_{1c} assessment and rates of deintensification.
Results
PGDiT survey: 160 PGDiT responded to the survey. 80.0% ($n = 128/160$) of PGDiT reported that they knew the target HbA_{1c} in patients with diabetes and frailty. However, only 32.8% ($n = 42/128$) of these correctly indicated the target HbA_{1c} for such patients. PGDiT deintensification practices were lower than expected and several barriers of inpatient deintensification were identified. Patients' clinical outcomes: 198 patients with diabetes and moderate-severe frailty were included in our analysis [Median age 80 years (71-87) with median CFS of 6 (6-7)]. For patients who did not have their HbA_{1c} assessed in the last 6 months preceding admission, only 18.1% ($n = 13/72$) had it assessed during admission. In patients who are overtreated, deintensification rate was 29.7% ($n = 22/74$).
Conclusion
Our audit shows limited knowledge and management practices amongst PGDiT in the management of inpatients with diabetes and frailty that may contribute to low inpatient deintensification rate. Interventions are needed to improve patient outcomes and a model of care consisting of appropriate inpatient multidisciplinary team input to reduce treatment inertia.

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P149

Early weight loss from injectable pharmacotherapies in a person-centred multidisciplinary weight management service show comparable outcomes to the STEP-1 trial

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Background
Phase 3 trials of glucagon-like peptide-1 receptor agonists (GLP-1RA) and glucose-dependent insulinotropic polypeptide (GIP)-based therapies have demonstrated clinically important short term weight loss (WL) in people living with obesity. Little prospective data exists showing efficacy of these medications in real world or clinic settings. We present real world 6-month outcomes for use of these medications prescribed through a tier 3 specialist weight management service (SWMS).
Methods
The Tier 3 SWMS at Leicester, Leicestershire and Rutland is a 3-year person-centred pilot commissioned through the local Integrated Care Board. Referrals were paused ($n = 593$) when the agreed pilot capacity was reached. The service commenced Jan 2024. We present efficacy data for the first patients receiving MDT-supported pharmacotherapies (Wegovy and Mounjaro reserved only for people with type 2 diabetes as per current NICE guidance)) who have completed a minimum 6-months of treatment. Weight outcomes collected through clinic or primary care at 3 and 6

months and reported on electronic patient records. Completer and last observation carried forward analyses performed.
Results
Demographics include: 77.3% female with mean age of 47 years and with 57% belonging to White British ethnicity. Mean bodyweight and BMI were 128.5 kg and 45.8 kg/m^2, respectively. There were an average of 2.7 co-morbidities per patient. Compared to the STEP-1 trial, we report 10.2% WL (Wegovy: 10.9% $n = 23$, Mounjaro: 8.8%, $n = 13$) at the end of the first 6-months versus 10.4% (Wegovy) in the STEP-1 trial. Completers ($n = 32$) had 10.2% WL whilst including those ceasing treatment or missing data at 6 months ($n = 36$) had 9.9% Wl. Initial data show that clinical trial outcomes are replicated in the real world when delivered through a SWMS.
Conclusion
WL, discontinuations and complication outcomes of injectable GLP1-RA and GIP at 6 months in a Tier 3 SWMS were comparable to the STEP-1 trial.

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P150

Familial partial lipodystrophy presenting as type 1 diabetes: the importance of accurate diagnosis

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Background
Congenital lipodystrophy is an uncommon genetic disorder, with an incidence of less than one in a million globally. It involves a lack of subcutaneous adipose tissue, leading to the abnormal accumulation of fat within internal organs, especially the liver, which can result in complications like cirrhosis, hypertriglyceridemia, and insulin resistance, eventually causing diabetes. Here, we discuss a case of familial partial lipodystrophy (FPL), initially mistaken for Type 1 Diabetes Mellitus (T1DM).
Case Report
A 32-year-old Caucasian female was first referred to the lipid clinic for eruptive xanthomas and a triglyceride level of 67. Her HbA1c was elevated at 94 mmol/mol. She had no major medical history other than excessive alcohol intake (40-50 units/week) and a parent with T2DM. Despite a BMI of 20.7, she was placed on a T1DM regimen with basal-bolus insulin, though she required unusually high doses (over 150 units/day) given her weight of 61 kg. Physical examination showed fat loss in her limbs and prominent shoulder musculature. Additional tests, including elevated C-peptide levels and negative diabetes auto-antibodies, suggested an alternate diagnosis. Genetic testing confirmed FPL, and the patient was referred to the National Severe Insulin Resistance Service, where she began metreleptin therapy. After starting metreleptin, both her blood glucose and insulin requirements decreased.
Conclusion
This case underscores the importance of not defaulting to a T1DM diagnosis when clinical features are atypical, especially with negative auto-antibodies. The patient's complex diabetes resulted from insulin resistance due to FPl. Metreleptin, a human leptin analog, proved effective in improving glycemic control in this context.

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P151

Subcellular control of skeletal muscle Mono- and Poly- ADP-ribosylation by glucocorticoids

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Compartmentalised regulation of NAD^+ is intrinsic to key processes including cellular metabolism, and tissue differentiation. Using NAD^+, the post-translational modification ADP-ribose is applied to proteins altering their biological activity. Our recent work established ADP-ribosylation in skeletal muscle to exist beyond the nuclear compartment and impact the critical steroid hormone class, glucocorticoids. Here, we hypothesised that like NAD^+, ADP-ribosylation is compartmentalised and its interplay with glucocorticoids also occurs in a subcellular-specific manner. ADP-ribosylation occurs in two variants, a single ADP-ribose subunit (mono-ADP-ribosylation) or branched multiple ADP-ribose units (poly-ADP-ribosylation). These occur independently and are distinct, but both are poorly understood. In whole muscle cells (C2C12s), we show the synthetic glucocorticoid, dexamethasone (1μM) to inhibit poly-ADP-ribose levels (0.61 fold change $\pm$ 0.13 sem, $P < 0.01$; $n = 8$) and conversely, induce mono-ADP-ribosylation (1.34 $\pm$ 0.20, $P < 0.0001$ $n = 6$). In parallel, dexamethasone increases cellular NAD^+ significantly (20% increase over vehicle control, $P < 0.02$; $n = 8$). This demonstrates the rate-limiting nature of NAD^+ and poly-ADP-ribosylation, but not the mono-variant. Subcellular fractionation of C2C12s reveals poly-ADP-ribosylation is absent from the cytoplasm but detected in microsomes, mitochondria, and nuclei. We find Mono-ADP-ribosylation in all compartments examined. Furthermore, with immunoblotting, poly-ADP-ribose is decreased in mitochondria (0.75 $\pm$ 0.08) and nucleus (0.85 $\pm$ 0.07) and increased in microsomes in the presence of dexamethasone ($P < 0.05$; $n = 3$). Interestingly, mono-ADP-ribosylation is significantly elevated in all the fractionated organelles in response to dexamethasone (nucleus: 1.61 $\pm$ 0.30; mitochondria: 2.37 $\pm$ 0.68; microsomes: 3.36 $\pm$ 1.18; cytoplasm: 3.28 $\pm$ 1.14). These findings not only highlight the struggle between cellular compartments for NAD^+ but also the capacity to produce poly- and mono-ADP-ribosylation. Moreover, these two post-translational modifications shift in a compartmentalised specific manner as a response to exposure to glucocorticoids. Our findings suggest ADP-ribosylation is a common but poorly understood mechanism involved in affecting steroid hormone signalling in skeletal muscle.

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P152

Diabetic ketoacidosis guidelines have been poorly adopted and implemented in the UK, with an associated lack of improvement in outcomes

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Aims
The Joint British Diabetes Society-Inpatient (JBDS-IP) group recommends reducing the fixed rate intravenous insulin infusion (FRIII) rate from 0.1 to 0.05 units/kg/hour when blood glucose falls less than 14 mmol/L to reduce the risk of hypoglycaemia and hypokalaemia associated with the acute management of diabetes-related ketoacidosis (DKA). We aimed to evaluate trends in complications and outcomes associated with implementing the revised JBDS-IP guidelines for DKA management.
Methods
We performed a retrospective review of DKA admissions from October 2021 to March 2023 across five hospitals in the United Kingdom that manage DKA using JBDS-IP guidelines. Data on demographics, complications and outcomes were collated. We studied the rate of uptake of FRIII reduction across time in all hospitals. We measured the time difference between the first instance of blood glucose reaching 14 mmol/L during DKA to the initiation of 10% dextrose and the FRIII reduction to 0.05 units/kg/hour.
Results
We identified 753 DKA admissions across five hospitals. In DKA episodes where FRIII rate reduction guidelines were adopted, there was a significant lag between starting 10% Dextrose and FRIII rate reduction when blood glucose became <14 mmol/l (median [IQR] hours – all episodes: 0.5 (0.1 – 1.8) vs 3.2 (0.7 – 6.5), $P = 0.00001$)). There was no significant reduction in hypoglycaemia (16.5% vs 13.8%, $P = 0.344$) in episodes that adopted FRIII reduction. There was a trend for longer duration of DKA episodes [hours] (23.7 (13.6 – 31.8) vs 16.2 (10.8 – 24.4), $P = 0.060$) and total units of FRIII administered during DKA episodes (152.7 (81.3 – 254.3) vs 115.8 (64.7 – 192.8), $P = 0.085$) in those with hypoglycaemic events vs those without.
Conclusions
Our study shows that there is suboptimal adoption of the guidelines. Further work is required to understand the barriers and facilitators involved in the safe implementation of guidelines.

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P153

Corticosterone induces less metabolic dysregulation than cortisol in male and female mice, independent of ABCC1

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Management of adrenal insufficiency primarily involves hydrocortisone (cortisol) replacement, yet dosing challenges and the increased risk of adverse cardiovascular complications persist. Preliminary evidence suggests another endogenous glucocorticoid, corticosterone, does not induce the same adverse cardiometabolic effects as cortisol. We hypothesised this protection results from selective export of corticosterone, but not cortisol, from metabolic tissues by the transmembrane transporter ABCC1 (ATP-binding cassette Subfamily C Member 1). We used a murine model to i) compare the metabolic effects of corticosterone and cortisol treatment; ii) to assess the effect of *Abcc1* deletion; and iii) to identify potential sexually-dimorphic responses. Adult (8-12 weeks) male and female mice lacking *Abcc1* (ABCC1-KO) or wild-type (WT) littermates were adrenalectomised and administered either corticosterone or cortisol in drinking water (25μg/ml) for 5 weeks. Body composition (TD-NMR) was measured between 3-4 weeks and metabolic parameters (insulin tolerance, HOMA-IR) between 4-5 weeks. In male mice, corticosterone but not cortisol treatment revealed significant genotype effects on body composition, with KO mice displaying reduced fat-mass and increased lean-mass compared to WT mice. In contrast, female mice displayed reduced weight gain in response to cortisol compared to corticosterone, independent of genotype. Steroid treatment or genotype had no effect on body composition. In male mice, metabolic measures including HOMA-IR and insulin tolerance were exacerbated in cortisol- compared to corticosterone-treated mice, but no genotype effects were observed. Similarly, in female mice, cortisol induced greater insulin intolerance than corticosterone, independent of genotype effects. However, HOMA-IR was not different in female mice between glucocorticoid treatments. This study demonstrates that in both male and female mice, chronic glucocorticoid treatment with cortisol induces greater whole-body insulin resistance than corticosterone, an effect independent of changes in body weight or composition. Contrary to our hypothesis, ABCC1 does not confer protection from corticosterone-induced metabolic dysregulation, but exerts steroid sex-specific effects on adiposity.

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P154

Exploring the pleiotropic function of miR-10b in the regulation of adipogenesis

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Adipogenesis is a highly organized series of events that facilitates the healthy expansion of adipose tissue, beginning during embryogenesis and continuing throughout life. White adipogenesis protects against lipotoxicity, influencing insulin resistance and obesity-related comorbidities, while brown adipogenesis increases energy expenditure, counteracting weight gain. Recently, there has been a significant increase in interest regarding adipocyte differentiation, particularly focusing on the interplay between microRNAs (miRNAs) and the transcriptional cascade that governs adipogenesis and metabolic dysfunction. This study aims to identify miRNAs regulating white and brown adipocyte differentiation and define miRNA action in a stem cell model of adipogenesis. Small RNAseq analysis of primary mouse brown and white adipocytes (WAs) identified miR-10b to be upregulated in mature brown adipocytes (BAs). We generated two model systems: 1) immortalized brown pre-adipocytes treated with miRNA inhibitors and 2) CRISPR/Cas9 KO of miR-10b in E14 mouse embryonic stem cells (ES). Both cell models were differentiated to mature adipocytes. To unravel the pathways that are affected by miR-10b depletion, a transcriptomic analysis was performed at key time points. Both cell models demonstrated that miR-10b depletion severely compromised differentiation into mature adipocytes, evidenced by a lack of lipid droplet accumulation and decreased adipogenic gene expression. We hypothesize that miR-10b-5p directs ES towards the mesoderm lineage, facilitating commitment to pre-adipocytes by controlling GATA6 and its downstream target BMP2. Notably, this mechanism appears unaffected in BA. 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 BA and decreased with miR-10b-5p upregulation in WA. Our research highlights the pleiotropic regulatory role of miR-10b-5p during adipogenesis. Understanding the miR-10b-mediated mechanism in adipocyte commitment and differentiation may aid in developing adipose tissue-engineering strategies for cellular therapies for lipodystrophy and obesity.

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P155

Effectiveness of a pragmatic prescribing pathway with multiple stopping rules for liraglutide 3 mg in people with and without diabetes: a post-hoc analysis of the strive study

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Background
Previous studies suggest that individuals with obesity and type 2 diabetes (T2D) may lose less weight with liraglutide 3 mg compared with those without diabetes. The STRIVE study, a 2-year, randomised controlled trial, evaluated the effectiveness of a targeted prescribing pathway for liraglutide 3 mg with multiple stopping rules versus standard care in specialist weight management services (SWMS).
Aim
This sub-analysis compared the effectiveness of the targeted prescribing pathway for liraglutide 3 mg on weight loss (WL) between individuals with or without T2D.
Methods
The STRIVE study recruited 392 participants with BMI >35 kg/m^2 who presented to SWMS. Participants were randomised 2:1 to the intervention (targeted prescribing pathway for liraglutide 3 mg, $n = 260$) or control (standard care, $n = 132$) arm. In the intervention arm, stopping rules were applied at 16 weeks ($\geq 5\%$ WL), 32 weeks ($\geq 10\%$ WL), and 52 weeks ($\geq 15\%$ WL). Diabetes status at baseline was available for 259 participants.
Results
In the intervention arm, 67.1% (102/152) of participants without T2D and 74.8% (80/107) with T2D passed the $\geq 5\%$ WL stopping rule (16 weeks, $P = 0.343$). At 32 weeks, 42.8% without T2D (65/152) and 44.9% with T2D (48/107) passed the $\geq 10\%$ WL rule ($P = 0.916$). At 52 weeks, 20.4% without T2D (31/152) and 21.5% with T2D (23/107) passed the $\geq 15\%$ WL rule ($P = 0.977$) and continued liraglutide 3 mg for another 52 weeks. At 52 and 104 weeks, the mean difference in % WL with the targeted prescribing pathway versus standard care was similar between people with and without T2D (-4.4% vs -5.9% at 52 weeks; -3.4% and -4.4% at 104 weeks; p for interaction = 0.377 and 0.532, respectively).
Conclusion
There were no differences in passing the stopping rules or % WL between people with and without T2D with the targeted prescribing pathway for liraglutide 3 mg, suggesting similar effectiveness of the pathway regarding WL for both groups.

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P156

Improving inpatient hypoglycemia management: a study of risk factors, timing, and protocol adherence in diabetic patients

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Background
Inpatient hypoglycemia, defined as a blood glucose level below 4 mmol/l, poses a substantial risk to diabetic patients, increasing morbidity and extending hospital stays. This study combines data from two audit cycles at a district general hospital

to identify factors contributing to hypoglycemia, particularly during high-risk nighttime hours.
Aim
This study aims to evaluate the timing, frequency, and management of hypoglycemic episodes in hospitalized diabetic patients, assessing associations with risk factors like renal impairment, HbA1c levels, and adherence to management protocols.
Method
A total of 122 hypoglycemic events were analyzed across two audit cycles. Data included patient demographics, diabetes type, timing of episodes, AKI presence, HbA1c levels, and protocol adherence. Statistical analyses were conducted using chi-square tests for categorical variables and t-tests for continuous ones.
Findings
Results indicate that 60% of hypoglycemic events occurred between 8 PM and 8 AM, a statistically significant association ($\chi^2 = 9.34$, $P < 0.05$). AKI was also significantly correlated with hypoglycemia incidence ($\chi^2 = 7.28$, $P < 0.01$), underscoring renal impairment as a major risk factor. Higher HbA1c levels showed a marginal, though statistically insignificant, increase in recurrent hypoglycemia risk ($t = 1.96$, $P = 0.06$). Protocol adherence was suboptimal, with 68% of cases achieving timely blood glucose rechecks and little improvement between cycles ($\chi^2 = 0.89$, $P = 0.35$).
Conclusion
This study highlights the need for targeted training on hypoglycemia management, particularly during nighttime hours and in patients with concurrent AKI. Next steps include implementing protocol improvements to reinforce adherence, increasing staff training on hypoglycemia risks, and establishing proactive monitoring for high-risk patients, particularly during off-peak hours. Routine audits and feedback loops are recommended to support continuous improvement in inpatient glycemic management, with the ultimate goal of reducing hypoglycemic events and enhancing patient safety.

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P157

Metabolic fatty liver disease present high risk in the development of diabetes complications

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Introduction
Liver have a crucial role in the body metabolism, especially in maintaining of carbohydrates level. Type 2 Diabetes Mellitus (T2DM) frequently accompanied Metabolic Fatty Liver Diseases (MAFLD) which has impact on the development of the diabetes complications. We studied relationship between diabetes microvascular complications according to presence of MAFLD.
Material and methods
134 patients with T2DM admitted to Hospital of Republican Specialised Scientific Practical Medical Centre in Uzbekistan were observed and body weight, BMI, total blood count, fasting and postprandial glycemia, HbA1c, ALT, AST, bilirubin, blood lipids level were measured, liver ultrasound were performed. Data were compared according to presence and absence of MAFLD.
Results
MAFLD were detected in 52% of patients with T2DM. MAFLD have relationship with body weight, BMI, fasting glycemia, HbA1c, blood triglycerides, LDLP level. Moreover, diabetic microvascular complications such as retinopathy, nephropathy were presented in higher degrees in MAFLD group, DR3 seen in 34% vs 13% and CKD with uremia were detected in 26% vs 6% and suggested about role of the MAFLD in the development and progression of chronic diabetes complications. Calculated Fib4 score were significantly higher in MAFLD group. Interestingly, among patients on insulin therapy daily dosage of insulin, as well as short acting and long acting insulins were calculated and compared, where insulin dosage were significantly higher in MAFLD group and suggested about iits impact on glycemic control and microvascular complications.
Conclusion
MAFLD involved into pathogenesis of microvascular complications of T2DM by affecting glycemia, HbA1c, blood lipids level, where early detection and management is crusial for future management.

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P158

Diabetic risk assessment in secondary schoool students in ondo state south west, Nigeria

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Background
Diabetes mellitus is a global health concern of major public health importance affecting people of all ages, including adolescents. The prevalence of diabetes has continued to rise significantly among young individuals. And the incidence of type 2 diabetes is increasing more rapidly in adolescents and young adults than in other age groups and in some regions more type 2 than type 1 diabetes mellitus is being diagnosed in prepubertal children, teenagers, and young adults.
Objective
This is to to determine 10 year risk of developing type 2 DM using an interviewer administered Finland Diabetic Risk Score (FINDRISC score) among secondary school students age 10-19 years.
Method
This is a cross-sectional study conducted among 1067 students from three secondary school age 10-19 years selected using a multistage sampling from 72 public secondary schools. Four risk factors for diabetes were assessed, namely, overweight/obesity, impaired fasting blood glucose (IFG), hypertension and family history of diabetes. Data was analyzed using SPSS.
Result
Overall the prevalence of one or more DM risk factors is about 15%, 3% of the students were overweight/obese, 3% were also had impaired blood glucose. 10% had family history of DM and 2% were hypertensive. Logistics recession analysis shows that female students were 30% less likely to be at risk of DM compared to their male counterpart. Students not taking fruits and vegetable everyday had 37% odds of having DM risks compared to those taking daily and those who did not engage in daily exercise had 17% increased risks of DM although not statistically significant.
Conclusion
The significant risk factors identified in this study were family history of DM, oveweight/obesity, hypertension and impaired fasting blood glucose. Early screening for diabetic risks in younger school children could lead to to early detection of diabetes and its risks

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P159

Integrated placental multi-omics identifies potential molecular pathways due to maternal B12 deficiency

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Almost 2 billion adults in the world are overweight, and obesity linked metabolic disorders are a worldwide health concern affecting about one-third women of reproductive age. Obesity during pregnancy can increase the risk of complications for both mother and the baby leading to risk of metabolic diseases by programming *in utero* events. Vitamin B12 (B12) has a potential epigenetic role that could influence placental dysfunction and fetal metabolism. Here, we aim to identify epigenetically regulated genes and miRNAs due to B12 deficiency through comprehensive integrated multi-omics on placenta. We integrated differentially methylated regions (from RRBS-seq), differentially expressed genes (from RNA-seq) and differentially expressed miRNAs (from sRNA-seq) in placental tissues ($n = 50$) from pregnant women (PRiDE cohort) with deficient (<220 pmol/l) and sufficient (>220 pmol/l) levels of B12 adjusting for clinical covariates including maternal age, fetal sex and body mass index. The study identified 2,565 hypomethylated and 2,792 hypermethylated regions in gene promoters associated with B12 deficiency. Furthermore, 270 and 46 differentially expressed genes and miRNAs were identified respectively. Integrative analysis of differentially methylated regions, differentially expressed genes and miRNAs revealed 13 genes (GYPC, NTRK2, EVA1C, DMTN, PRLHR, HYAL1, ZBTB16, PMIS2, CGB5, LYPD3, LHX3, FAM167A, FTCD) and 11 miRNAs (mir-373, miR-3940, miR-5708, miR-1299, miR-18b, miR-219b, miR-3667, miR-4664, miR-4784, miR-5683, miR-6859) due to B12 deficiency during

pregnancy. Further enrichment analysis identified glycosaminoglycan degradation, one carbon pool by folate and histidine metabolism as the top deregulated pathways. These findings potentially can unravel the molecular mechanisms associated with maternal B12 deficiency in placenta. This study also highlights the significance of integrative multi-omics approach for in-depth characterisation of epigenomic and transcriptomic signatures in human placenta associated with metabolic risks.

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P160

Development of a novel LC-MS/MS method to profile multiple steroids in rodent plasma and tissue

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Valuable in endocrine studies, reliable quantification of multiple steroids remains an analytical challenge. The steroidogenic pathway contains many similar and same mass steroids and without separation prior to detection then this can affect the number of steroids that can be confidently measured in a sample. We developed an LC-MS/MS approach that relies upon isotopically labelled internal standards to track steroids and confirm retention times. A calibration curve covering 0.0025 – 100 ng/mL was prepared. The method allows simultaneous profiling of up to16 steroids including progestogens, androgens, glucocorticoids, mineralocorticoids and estrogens and applied it to rodent samples of both plasma and tissue in rodents of different ages and sex. A Waters I-Class Acquity UPLC system fitted with a Kinetex C18 (150 x 2.1 mm; 2.6 um) column with a mobile phase of water and methanol with 50 uM ammonium fluoride to encourage negative ion formation at 0.3 mL/min was used to separate steroids, with positive and negative ionisation through polarity switching on a Sciex QTrap 6500+ mass spectrometer. Plasma samples were extracted using supported liquid extraction in 96-well format on an SLE200 extraction plate. We assessed varying volumes, with reliable quantitation in 10 uL up to 100 uL, with corticosterone detectable in as little as 10 uL but 100 uL profiling the majority of steroids in the method, depending on the age and sex of the rodents. The method was validated in plasma according to bioanalytical guidelines, and applied to over 100 mouse and 100 rat plasma samples. This LC-MS/MS method was also used to analyse homogenates of rodent tissue (10-50 mg), extracted through phosopholipid depletion plates. The method succesfully detected up to 14 steroids in the tissue homogenates and allowed profiling of steroids both circulating and in tissue in individual rodents.

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P161

Does nutritional deficiency exist in women with severe hyperemesis gravidarum and contribute towards adverse metabolic outcomes

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Background
Hyperemesis Gravidarum (HG) describes severe nausea and vomiting in pregnancy resulting from increased pregnancy hormones (notably hCG and GDF-15). Children born to women with severe HG have increased risk of subsequent cardiometabolic disease. We hypothesis that this may relate to a period of catch-up growth in growth restricted babies secondary to maternal nutrient deficiency.
Aims
a) describe HG-associated fetal outcomes in a UK population b) determine whether nutrient status is associated with adverse outcomes.
Methods
CogStack, a Natural Language Processing system, identified severe HG-pregnancies between 2011-2023. HG-patients were compared to controls using data and stored samples from a non-intervention screening study. First trimester nutrient assays were performed at the Cambridge Nutritional Biomarker Laboratory and correlated with adverse outcomes.
Results
Cogstack identified 2741 patients with the term 'hyperemesis' on their hospital electronic record system. 881 were confirmed to have severe HG after review of their hospital records and were compared to 54,045 women from the background South-East London population. HG-women were more likely to be of black ethnicity compared to white (39.2% vs 17.0%, $P < 0.00001$); no differences in age, body mass index, parity or past medical history were determined. HG-pregnancies were associated with fetal growth restriction (FGR) (18.0% vs 12.1%, $P = <0.00001$) in all ethnicities. Differences in gestational diabetes rates were not found. HG-patients had lower vitamin B6 (38.2 vs 16.6nmol/l, $P < 0.001$), 25(OH)D3 (58.8 vs 42.9nmol/l (<0.001), fat-soluble vitamin concentrations ((lutein and zeaxanthin (0.58 vs 0.45, $P < 0.001$) and b-carotene (0.93 vs 0.72, $P = 0.005$)). Linear regression revealed that low iron ($P < 0.01$), vitamin B6 ($P = 0.02$), vitamin D ($P < 0.0001$) and fat-soluble vitamin concentrations (both $P = 0.02$) correlated with FGR.
Conclusion
This is the first study to correlate nutrient status in HG-women with adverse outcomes. Future work will focus on nutrient status and outcomes with respect to endocrine parameters, ethnicity and birthweight.

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P162

Impact of intermittent cold exposure on the function of brown adipose tissue in paediatric MASLD

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Paediatric obesity is a significant global health issue, associated with metabolic dysfunction-associated steatotic liver disease (MASLD). The only current non-invasive treatment is lifestyle change, which succeeds in 25% of cases, highlighting the need for new interventions. Research suggests that activating brown adipose tissue (BAT) can reduce hepatic lipids through non-shivering thermogenesis (NST). Additionally, white adipose tissue (WAT) can transition to a BAT-like phenotype, a process termed 'beiging'. Since BAT is more prevalent in children and young people, activating it, alongside increasing WAT beiging in this population, may provide significant health benefits. Intermittent cold exposure (ICE) can activate BAT in humans, making it a promising treatment strategy. We hypothesise that 1 hour of ICE using a 6°C liquid cooling vest will activate BAT in MASLD patients and healthy controls. Nine MASLD and thirteen control participants aged 8-16 were recruited. Vital signs and metabolic parameters were measured to assess ICE-related changes. Skin temperature was monitored during treatment, with thermal images and MRI scans taken pre- and post-ICE to evaluate BAT activation. Results indicated significant differences in ICE responses between MASLD and control participants, and between sexes. Male MASLD patients showed a decrease in fasting blood glucose ($P = 0.0365$), and a significant decrease in sternum skin temperature ($P = 0.0006$), with their BAT-associated supraclavicular temperature remaining consistent, suggestive of BAT activation. However, thermal imaging revealed decreased supraclavicular temperature. Female controls showed an ICE-induced decrease in sternum skin temperature ($P = 0.0328$), but maintained their supraclavicular temperature, indicating BAT activation; this was not seen in female MASLD patients. MRI data indicated an ICE-induced reduction in fat fraction among controls ($P = 0.0033$), associated with NST. ICE was tolerable and acceptable to participants. These preliminary findings suggest a greater ICE response in controls and sex differences. More participants are needed to better understand potential clinical implications of ICE for paediatric MASLD.

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P163

Determinants of hepatic steatosis and increased liver stiffness in late pregnancy: analysis of 3000 women using transient elastography

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Background
Steatotic liver disease (SLD), a metabolic and hepatic disorder, is increasingly prevalent among reproductive-age women. Pregnancy can unmask maternal predispositions to future diseases, providing an opportunity to influence lifelong health. Understanding the relationship between SLD and pregnancy may enable early identification of at-risk women. This study aimed to investigate maternal and gestational factors associated with hepatic steatosis and increased liver stiffness in the third trimester.
Methods
3000 pregnant women were recruited between 35+0- and 36+6-weeks' gestation at the Harris Birthright Research Centre (London, United Kingdom). Exclusion criteria were chronic liver disease, alcohol intake >14 units/week pre-pregnancy and multifetal gestation. A FibroScan® was used to quantify Controlled Attenuation Parameter (CAP) and Liver Stiffness Measurement (LSM). The 90th percentiles of CAP (246dB/m) and LSM (7.1kPa) were used to define hepatic steatosis and increased liver stiffness, given the absence of gestation-specific reference ranges.
Results
70.2% of participants were White, 15.9% Black, 7.4% South Asian, 1.9% East Asian, and 4.5% of mixed ethnicity. Median age and BMI were 34 years (interquartile range [IQR] 31-37) and 24.4 kg/m^2 (IQR 21.9-28.3), respectively. Factors associated with steatosis were obesity (odds ratio [OR] 11.7, 95%CI 8.01-17.2), overweight (OR 2.71, 95%CI 1.85-3.99) and maternal weight gain (OR 1.03, 95%CI 1.01-1.06). Increased LSM was associated with type 1 diabetes mellitus (OR 19.5, 95%CI 4.06-104), obesity (OR 1.94, 95%CI 1.3-2.87), previous fetal growth restriction (OR 2.43, 95%CI 1.19 – 4.62), previous gestational diabetes (OR 1.98, 95%CI 1.10-3.74), pre-eclampsia (OR 1.8, 95%CI 1.04-2.97), and nulliparity (OR 1.56, 95%CI 1.11-2.20).
Conclusion
Overweight and obese women, those with pre-eclampsia and a previous history of fetal growth restriction or gestational diabetes may benefit from enhanced postnatal surveillance to monitor their hepatic health. Future longitudinal studies should focus on these subgroups to better understand the natural course SLD in pregnancy and the postpartum period.

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Neuroendocrinology and Pituitary

P164

Patient with cystic macroprolactinoma with visual deficit requiring transsphenoidal adenomectomy (TSA)

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Introduction
Cystic prolactinoma, a variant of prolactin-secreting pituitary adenoma, presents ongoing debate regarding the most effective first-line treatment strategies. While dopamine agonists are known to offer considerable clinical improvement and tumor shrinkage, potentially reducing the need for surgery, the optimal approach remains uncertain. We present a patient with cystic macroprolactinoma who had TSA for persistent visual field defect despite excellent biochemical response to dopamine agonist treatment.
Case
A 26-year-old woman was diagnosed with a 3.3 cm cystic macroprolactinoma following 12 months of galactorrhoea and secondary amenorrhea. Serum prolactin at presentation was 20,193 mIU/L (monomeric prolactin 14,760, ref range 109-557). Her IGF1 was normal 7.4 nmol/l (10.3 – 39.6). She had a left homonymous hemianopia at diagnosis. Her prolactin fell to 7281 mIU/L 6 weeks after initiation of cabergoline. Despite this reduction, her visual field deficit persisted, leading to the decision to offer transsphenoidal surgery (TSA). During TSA, extensive cavernous sinus involvement was noted. The histology found a lactotroph adenoma with strong cytoplasmic cam 5.2 expression, and low proliferation index (MIB1 1-2%). Four weeks post-TSA, her prolactin reduced to 835 mIU/l. Post operative MRI at 3-months showed a reduction in the size of the pituitary adenoma and decompression of optic chiasm. Postoperatively, her visual field deficit improved significantly. Cabergoline treatment was continued for the residual disease.
Discussion
This case highlights the importance of careful consideration of both medical and surgical treatment options in patients with prolactinomas with large cystic components. TSA may be considered as a first line option for cystic macroprolactinomas with significant visual impairment.

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P165

Familial isolated pituitary adenoma probably due to an unknown genetic variant: a report of two brothers

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Introduction
Introduced by Beckers in 1999, familial isolated pituitary adenoma (FIPA) describes families with pituitary adenomas. FIPA are larger, more aggressive tumours, with earlier age of onset compared to sporadic pituitary adenomas. They are non-syndromic (e.g., not part of MEN1, MEN4, Carney complex, McCune-Albright, etc). Pathogenic variants within the aryl hydrocarbon receptor interacting protein (*AIP*) gene have been identified in 10-20% of FIPA families and 50% of growth hormone (GH) producing tumour families. Rarely, duplication of the orphan G protein-coupled receptor (*GPR101)* causes X-linked acrogigantism (GH- and prolactin-producing tumours). The genetic cause for the majority of FIPA families remains unknown. We present two brothers with non-functioning pituitary tumours.
Case
Case-1: A 54-year-old male from a non-consanguineous family presented with reduced libido and erectile dysfunction. Medical history included type 2 diabetes and primary hypothyroidism. Investigations demonstrated mild hyperprolactinaemia and hypogonadotropic hypogonadism. Brain imaging confirmed a 10x9x9mm non-functioning pituitary adenoma, which was managed conservatively. Case-2: A 58-year-old male (brother of case-1) had an incidental 16x20x13mm pituitary macroadenoma discovered during investigation for a stroke. Medical history included primary hypothyroidism. Investigations demonstrated mild hyperprolactinaemia. A non-functioning pituitary adenoma was resected. Subsequent sequencing and dosage analysis of the endocrine neoplasia gene panel (*MEN1, CDC73, AIP, CDKN1B, RET*) revealed no pathogenic variants. The negative *AIP* gene analysis in one brother plus the absence of other tumours or syndromic features in both brothers, confirmed FIPA.
Conclusion
This report emphasises the high frequency of variant-negative FIPA. The genetics of familial and apparently sporadic pituitary tumours is ongoing and new candidate genes have been identified, however, causative evidence is required. Offsprings of affected individuals have a 50% chance of inheriting unknown autosomal dominant variants with reduced penetrance. Detailed family history is important in prompting genetic and clinical screening to achieve early diagnosis and treatment of FIPA.

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Protected characteristics in the UK acromegaly registry – opportunities for improvement

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Background
The UK acromegaly registry (UKAR) was established in 1997 and holds data on 3,568 patients diagnosed with acromegaly. The Society for Endocrinology UKAR steering committee intend to relaunch this initiative. The National Institute for Healthcare Research (NIHR) has an equality, diversity and inclusion strategy. One theme is widening access and participation for greater diversity and inclusion.
Aim
To measure the UKAR dataset against the nine characteristics highlighted by NIHR and protected by the Equality Act 2010.
Methods
The existing UKAR dataset was measured against the nine protected characteristics stipulated in the NIHR strategy. Measures from the Office for National Statistics were used to infer socioeconomic status of the UKAR population.
Results
Data for 3,568 patients were reviewed. There are no specific disability data held in the registry. Age is available for 3,500 (98%) patients. Ethnicity is available for 2,286 (64%) and 2,179 (95%) of these patients were white. Sex is available in 3,495 (98%) with 1,720 (49%) of these patients being female. Gender is not documented for any patients. No data are available with regards sexual orientation, marriage/civil partnership status or religion/belief. Pregnancy data are rare (46/3,358, 1%) and not systematically collected in the registry. There are no data regarding socio-economic status. When considering Office for National Statistics data, the UKAR centres tend to lie in global cluster C (17/32, 53%) and economic cluster A (20/29, 69%); associated with low healthy life expectancy, low employment rate and low income.
Conclusion
The UKAR is a significant rare disease resource; however, when measured against the NIHR equality, diversity and inclusion strategy, it is suboptimal. Direct socioeconomic data are not available and ethnicity data indicate a lack of diversity. These characteristics must be systematically collected in future UKAR recruitment to make the dataset as diverse and representative as possible.

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Routes to diagnosis of pituitary neuroendocrine tumour: a 20 year analysis

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Pituitary neuroendocrine tumours (PitNETs) have a spectrum of clinical manifestations and patients often present to various specialities before receiving a diagnosis. Symptoms can overlap with those of other, more common conditions. The aim of this study is to explore how the diagnosis of PitNET came to be made in a regional cohort of patients with PitNETs ultimately managed *via* neurosurgical intervention. Cases of surgically-managed PitNETs were identified by searching SNOMED codes within histopathological archives. Clinicopathological data were collected retrospectively as part of an audit within the Belfast Health and Social Care Trust; approval number 6057. From 01/01/2000-19/07/2023, 537 adult patients underwent a first surgery for PitNET in Northern Ireland. Data were available for 520 patients in whom the referral source leading to diagnosis was known. Two hundred and twenty-three patients (43%) were female. Median age at diagnosis was 54 years (range 18–85 years). Median diagnostic delay was 2 years (range 0–25 years). Patients with PitNETs were referred from 27 different sources. The most common sources of referral were general practice in 162/520 (31%), ophthalmology 74/520 (14%), emergency medicine 48/520 (9%), optician/optometry 45/520 (9%) and neurology 37/520 (7%). In only 6% was the diagnosis of PitNET first queried by endocrinology. A higher proportion of those who had apoplexy were referred from emergency medicine compared to non-emergency medicine practitioners ($p < 0.001$). Patients with macro-PitNETs were more likely to be referred by ophthalmology/optician/optometry compared to micro-pitNETs ($p < 0.001$). Those with macro-PitNETs were also more likely to have diagnosis of cataract or glaucoma compared to those with micro-PitNETs ($p = 0.043$). These data demonstrate the diagnostic delay and widespread routes of diagnosis associated with PitNETs. Patients with PitNETs encounter a range of clinical services in their journey to pituitary surgery. Raising awareness of these tumours across all clinical disciplines could reduce diagnostic delay.

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Association of slipped capital femoral epiphysis with pituitary macroadenoma, apoplexy, and panhypopituitarism

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Introduction
In general population, slipped capital femoral epiphysis (SCFE) is a rare hip condition, characterized by posteroinferior displacement of femoral epiphysis from metaphysis through an open physis. This commonly occurs in adolescents with average age at onset being 13.5 years in males and 12 years in females. There are several risk factors, including obesity; calcium disorders; genetic disorders (Marfan syndrome, Down syndrome); and endocrine disorders (hypothyroidism, hypogonadism, growth hormone deficiency, panhypopituitarism, hyperparathyroidism, and pituitary tumours). Our case is a 19-year-old gentleman who was initially diagnosed as left SCFE, treated with in-situ fixation, 7 weeks later, developed pituitary apoplexy and panhypopituitarism secondary to a pituitary macroadenoma.
Case presentation
A 19-year-old gentleman initially presented with limping and left groin pain, was diagnosed as left SCFE. In-situ fixation was done by orthopedics team. 7 weeks later, presented with severe headache, and vomiting. Found to have pituitary macroadenoma with apoplexy, panhypopituitarism, smaller and younger appearance than his age with lack of secondary sexual characteristics. Hydrocortisone, levothyroxine, and testosterone replacement (Testogel) were commenced. Then reviewed in Endocrine clinic and a bone age assessment was performed, which showed a delayed bone age. Adjusting testosterone replacement from Testogel to injection helped him to achieve adult height and secondary sexual characteristics.
Discussion
Although the exact pathophysiology of SCFE is not well understood, patients who first presented with SCFE in post-adolescence need evaluation as endocrinopathies are the most common causes in these atypical age groups from delayed epiphyseal fusion. Our gentleman might have developed SCFE from his pituitary macroadenoma, which later became evident as pituitary apoplexy associated with panhypopituitarism.
Conclusion
All delayed-onset SCFE should be evaluated for endocrine disorders pre-operatively to prevent adrenal crisis during the fixation procedure. Similarly, patients with known endocrine abnormalities who report hip, or groin pain should be evaluated for SCFE regardless of their age.

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Low-dose tolvaptan for the treatment of SIADH-induced hyponatraemia: a meta-analysis and systematic review of the efficacy and safety

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Background and aims
Tolvaptan at the current licensed dose of 15 mg is highly efficious in the treatment of hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone (SIADH), but there is a significant risk of over-correcting and therefore the possibility of osmotic demyelination syndrome (ODS). We aimed to investigate the efficacy and safety of both initial and subsequent doses of sub-15 mg, and review the effects on quality of life, length of stay and also side effects.
Method
Systematic searches were performed across six databases. Our keywords and Medical Subject Heading (MeSH) search terms included: '*hyponatremia OR hyponatraemia AND (SIADH OR Syndrome of Inappropriate ADH Secretion OR syndrome AND of AND Inappropriate AND ADH AND secretion) AND tolvaptan*'.
Findings
18 papers were available for data extraction. When tolvaptan was administered at an initial dose of below 15 mg, data could be extracted for 495 patients. The mean increase in sodium within 24 hours was 7.2 mmol/L (CI 6–8.4 mmol/l). 31% had an overcorrections of $\geq$ 10 mmol/L with an initial dose of 7.5 mg tolvaptan (CI 15-53%). Over-corrections of $\geq$ 12 mmol/L was seen in only 10% of patients (CI 3-20%). Assessment of subsequent doses suggests that continued use of sub-15 mg is effective and safe, with the increment in sodium being smaller compared to the initial dose and much reduced chances of over-correcting compared to the initial dose. There was insufficient evidence to comment on side effects and the effects on length of stay and quality of life.
Interpretation
Our analysis supports the use of sub-15 mg as the initial dose of tolvaptan. If the basal sodium is $\geq$ 125, or if the patient is frail or has risk factors for ODS, then 3.75 mg should initially be trialled. In other cases, 7.5 mg is sufficient. 7.5 mg can be given for subsequnt doses.

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Measurement or arginine-stimulated copeptin in the diagnosis of arginine vasopressin deficiency

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The biochemical investigation of suspected arginine vasopressin deficiency (AVPD, formerly cranial diabetes insipidus) has historically been with water deprivation and its effect on serum and urine osmolality. The test is lengthy and unpleasant for patients and is demanding of staff time. It often yields indeterminate results due to impairment of the concentrating ability of the renal medulla where osmotic pressure across the distal convoluted tubule and collecting duct has been diminished due to 'washout' caused by high volume urine output over time. Thus diagnosis is often not aided by this investigation and is made clinically on the basis of symptoms, history and the ruling out of other potential aetiologies. The measurement of copeptin, a cleaved peptide fragment from the arginine vasopressin (AVP) prohormone, offers a novel alternative biomarker for AVP (in)sufficiency. Provided here is the data from Plymouth Hospitals NHS Trust (PHNT), accumulated over 3 years, obtained from the osmotic stimulation (by L-arginine hydrochloride) of copeptin in patients in whom a diagnosis of AVPD was suspected. The protocol is a modified version of that proposed by Winzeler *et al*. Copeptin is measured at baseline and at 30-, 45-, 60-, 90- and 120-minutes post infusion. Biochemical outcomes are considered along with clinical details to support or refute diagnoses. A total of 20 patients have undergone this test. 6 patients had copeptin levels below the 60-minute threshold at which sufficiency is considered and are receiving treatment with DDAVP. The remaining 14 patients had a diagnosis of primary polydipsia or were normal. The experience of PHNT is that this is a reliable test offering diagnostic certainty.

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A rare presentation of pituitary cushing's disease in a patient with lynch syndrome

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Introduction
Pituitary tumours especially Cushing's disease is extremely rare to present in Lynch syndrome. The pathophysiology behind the disease is complex and patients with MSH 2 variant tend to have aggressive tumours in the form of corticotroph carcinomas or invasive non-functional pituitary adenomas.
Case Report
62-year-old gentleman known to have Lynch syndrome (MSH-2 variant) was waiting for reversal of his stoma due to right hemicolectomy for colonic malignancy done in late 2023. He later presented to emergency around April 2024 with worsening of heart failure. He was offloaded with diuretics which unmasked his cushingoid features. On examination, he is afebrile, with blood pressure of 140/80 mm Hg, pulse of 100/min. His bloods showed refractory hypokalaemia. His random cortisol was 700 nmol/l with testosterone of 2.9 nmol/l, FSH of 0.7 iu/L and LH of $<$0.1 iu/l. He was subjected to 24 hours urinary cortisol which showed elevated cortisol levels of 358 nmol/24 hrs and 578 nmol/24hrs on two occasions. He had later undergone low dose dexamethasone suppression test which yielded a level of 391 nmol/l showing biochemical evidence of Cushing's syndrome. His ACTH level was also high 168 ng/L which was unusual. His MRI pituitary revealed pituitary mass of 1.5 x0.7x1.1 cms. He had PET scan which showed no evidence of any ectopic tumour or metastatic disease. He was discussed in pituitary MDT with outcome of Transsphenoidal hypophysectomy. He underwent the operation with postop cortisol level $<$ 50 nmol/l showing recovery. Histological report confirmed corticotroph adenoma.
Conclusion
The link between Pituitary Cushing's disease and lynch syndrome is rare and only few case reports have showed its existence. One report showed evidence of MSH-2 variant lynch syndrome with corticotroph carcinoma. Ours was a benign pituitary corticotroph adenoma with no evidence of any metastasis.

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Therapeutic effects of aqueous soursop seed extract on the hypothalamo-pancreatic axis in an aluminum chloride-induced alzheimer's disease rat model

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The tropical fruit Annona muricata, commonly known as soursop, possesses notable medicinal properties, including antioxidant and anti-inflammatory effects. This study looks at how aqueous soursop seed extract affects the hypothalamo-pancreatic axis in a rat model of Alzheimer's disease (AD) caused by aluminium chloride. It shows how neurodegeneration and metabolic dysfunction are linked. Alzheimer's disease is associated with pancreatic islet cell dysfunction and disrupted insulin signalling, indicating a potential metabolic component in neurodegenerative processes. In this study, rats were given 100 mg/kg of aluminium chloride to induce AD. The rats were then split into three groups: the control group (Al), the soursop-treated group (Al + Soursop), and the standard treatment group (Al + Std, receiving 100 mg/kg of donepezil).d Alzheimer's disease (AD) experienced significant weight loss ($P > 0.05$), significantly elevated blood glucose levels, and reduced insulin concentrations ($P > 0.05$), indicating pronounced pancreatic dysfunction. Treatment with soursop seed extract reversed these metabolic disturbances. Furthermore, oxidative stress was marked by increased lipid peroxidation, as shown by higher levels of malondialdehyde (MDA), along with a significant drop in antioxidant enzyme activity (superoxide dismutase, SOD) in both the pancreas and hypothalamus. However, administration of soursop seed extract effectively mitigated these oxidative markers, highlighting its potential in countering the detrimental effects of oxidative stress in this neurodegenerative model.

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Atypical presentation of sheehan's syndrome: pancytopenia as a diagnostic clue

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Introduction
Sheehan's syndrome (SS) is a rare but important cause of hypopituitarism, typically triggered by postpartum hemorrhage and pituitary necrosis. It often

remains underdiagnosed, particularly in developing countries, due to limited access to proper obstetric care and the prevalence of home deliveries. This case report underscores the importance of recognizing atypical presentations of SS, such as pancytopenia, which can aid in early diagnosis and prompt management.
Case Presentation
A 40-year-old female presented with symptoms of acute abdomen and was initially diagnosed with acalculous cholecystitis. However, further history-taking revealed significant postpartum hemorrhage 18 years prior, raising suspicion of Sheehan's syndrome. Subsequent investigations confirmed panhypopituitarism, including deficiencies in thyroid, adrenal, and gonadal hormones. Additionally, the patient presented with pancytopenia, an uncommon hematological manifestation of SS.
Discussion
Sheehan's syndrome is often associated with nonspecific symptoms, leading to delays in diagnosis. In this case, the patient's acute abdomen symptoms were due to secondary adrenal insufficiency related to panhypopituitarism. The co-occurrence of pancytopenia and hyponatremia added complexity to the diagnosis. Following hormone replacement therapy, the patient showed significant clinical improvement, highlighting the critical role of early detection and treatment.
Conclusion
Sheehan's syndrome remains a significant yet underdiagnosed cause of panhypopituitarism in developing regions. Rare manifestations such as pancytopenia are often overlooked, further complicating diagnosis. This case emphasizes the need for increased clinical awareness of SS in patients with unexplained hematological abnormalities, especially in areas with high rates of postpartum hemorrhage. Early diagnosis and appropriate hormone replacement can greatly improve patient outcomes and prevent long-term complications of this underrecognized condition.

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Incidental pituitary macroadenoma in primary hypothyroidism: a case report

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Introduction
In primary hypothyroidism, thyrotroph hyperplasia can occur due to high thyrotropin releasing hormone (TRH) from loss of negative feedback to hypothalamus. Pituitary thyrotroph hyperplasia can mimic macroadenoma on imaging, but it is reversible with thyroid hormone replacement.
Case
A 34-year-old lady with multiple sclerosis presented atypical headaches and was found to have incidental pituitary macroadenoma measuring 10 x 16 x 10 cm on MRI scan. She had primary hypothyroidism since the age of 15 treated with Levothyroxine 175 mcg/d. She had recently gained 6 kg in body weight over six months and had menorrhagia. Her visual perimetry and range of eye movements were normal. Thyroid profile at presentation found free T3 $<$1.64 (2.63-5.7 pmol/l), free T4 $<$5.15 (9.01-19.05 pmol/l), TSH $>$100 (0.35-4.94 mIU/l) suggesting under-replacement. She was noted to have high TSH for more than 18 months. Her anti Thyroid Peroxidase antibody level $>$2000 IU/ml. Her prolactin was 177mU/L (109-557), and her cortisol was completely suppressed after overnight 1 mg dexamethasone. Her gonadotrophins and oestradiol level were also in range. Following improved compliance and dietary change with treatment for three months, she had free T3 3.80, free T4 18.10 pmol/l and TSH 1.06 mIU/l. Her weight and menstrual cycles improved, and a follow-up pituitary scan six months later showed a reduction in macroadenoma size, with the pituitary gland returning to normal size and a slightly convex superior profile. This confirms that thyrotroph hyperplasia is reversible with six months of adequate thyroid hormone supplementation.
Conclusion
High TSH had been found to be correlated to pituitary enlargement, and may be a feature at new presentation of primary hypothyroidism as well as those with chronic under-replacement. Reduction in pituitary size is common after thyroxine replacement. Patients should avoid unnecessary surgery and have follow-up scans to confirm resolution instead.

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Treatment of pituitary adenoma with lanreotide: what effect on carbohydrate metabolism (a case report)

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Introduction
Lanreotide is a somatostatin analogue used in the treatment of acromegaly and pituitary adenomas expressing growth hormone (GH). We report a case of decompensated diabetes following the introduction of Lanreotide in a patient treated for a pituitary macroadenoma expressing GH.
Case report
A 64-year-old patient with a non-secreting pituitary macroadenoma, revealed by headaches and blindness of the left eye. The patient underwent surgery, and the immunohistochemical study demonstrated 80% positive labelling of the anti-GH antibody. The postoperative evaluation revealed that the macroadenoma persisted, with visual damage to the right eye. The decision was taken to treat the patient with Lanreotide on a medical basis. The patient's preoperative work-up had revealed diabetes, and he was put on metformin. After three months of treatment with Lanreotide, the patient was admitted with an acid-ketotic decompensation without any precipitating factor. The patient was put on insulin therapy and Lanreotide was maintained in view of the endocranial improvement, with regular monitoring of glycaemic control during follow-up.
Discussion
The abnormalities in carbohydrate metabolism induced by somatostatin analogues are due to the inhibition of insulin and glucagon secretion by pancreatic β and α cells. This occurs via binding to somatostatinergic receptor subtypes, which in turn leads to the inhibition of incretin secretion. It should be noted that hyperglycaemia and diabetes are more frequent during treatment with Pasereotide, occurring early during the first three months of treatment. The effect of Lanreotide is minor and cases of induced diabetes are rare. It is therefore recommended that patients taking somatostatin analogues are monitored closely in terms of their carbohydrate parameters (self-monitoring of blood glucose levels, HbA1c at six weeks and then every three months), with treatment adapted according to blood glucose control.

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Vasopressin-associated hyponatraemia: to suspend desmopressin or not to suspend, a management conundrum?

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Arginine Vasopressin Deficiency (AVP-D) a rare endocrine disorder has a reported prevalence of 1 in 25,000 individuals. Central AVP-D is the most common form resulting from deficiency of the hormone AVP secreted from posterior pituitary gland. In the case of desmopressin-associated hyponatremia, majority of surveyed endocrine registrar trainees favour its cessation (67%), which may lead to serious consequences. Can using reverse osmolality theory assist in the management decision-making? A 27-year-old man was admitted in A&E unit with 2-day history of new onset headache, poor concentration, leg cramps and vomiting. He was diagnosed with partial central AVP-D as a 10-year-old, treated with desmopressin but lost to follow up at 18-years old. He had recently been active in a gym and started to drink 4 litres of water with high protein diet as part of his fitness regimen. On examination, he was normotensive, euvolemic with normal neurological and systemic examination. Initial serum sodium was 117. Random serum cortisol was 22 nmol/l but had adequate short Synacthen test result. The rest of his anterior pituitary hormone panel was unremarkable. Desmopressin was initially withheld by admitting doctor and he developed polyuria ($>$5L over 24-hours). Due to his symptomatic acute hyponatraemia, a single dose of hypertonic saline (2.7% 150 ml in 30 minutes) was given with close monitoring of fluid balance. Repeat sodium increased rapidly to 127 mmol/mol within 2 hours and Dextrose5% water infusion was given together with desmopressin. His urine osmolality after hypertonic saline showed a reversed urine osmolality pattern. There was a resolution of symptoms and biochemical parameters upon discharge. Learning points: 1. Theory of using reverse urine osmolality pattern in predicting patients at risk of osmotic diuresis and need for desmopressin continuation. 2. Hypertonic saline remains the recommended treatment option in patients with severe symptomatic hyponatraemia with continuation of desmopressin.

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Syndrome of inappropriate antidiuretic hormone secretion (SIADH) as a rare presentation of pituitary infiltration in acute myeloid leukaemia with central nervous system (CNS) relapse

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Introduction
The overall incidence of pituitary involvement in leukaemia is reported to be 0.6%, and it is considered extremely rare in Acute Myeloid Leukaemia (AML) with unknown frequency. Literature search identified few published cases of pituitary AML involvement causing hypopituitarism and Arginine Vasopressin deficiency (AVP-D), but there are no case reports of SIADH.
Case Presentation
29 years male presented with tonic-clonic seizures and euvolemic hyponatremia with sodium of 122mmol/l, and biochemistry supporting SIADH (plasma osmolality 258 mmol/kg, urine osmolality 318 mmol/kg, urine sodium 28 mmol/l). He has underlying complicated AML diagnosed 2 years earlier and he underwent allogenic stem cell transplantation 3 months prior to presentation. His pituitary MRI showed enhancing lesion infiltrating sella and suprasellar cistern, with nodular enhancement within infundibulum and right side of hypothalamus. His posterior pituitary bright spot was absent, but he had no symptoms of AVP-D. His lumbar puncture showed blast cells, confirming CNS infiltration. His pituitary profile showed raised prolactin 2867mu/l (56-278), testosterone 5.3nmol/l (10-27.6), LH 2.6iu/l (1.2-8.6), and FSH1.1iu/l (1.3-19.3), normal IGF-1and thyroid function. His cortisol was considered reasonable at 363nmol/l and he did not require hydrocortisone cover. His imaging was in keeping with leukemic pituitary infiltration. He was treated with cytarabine-venetoclax chemotherapy and intrathecal cytarabine, followed by cranio-spinal and pituitary radiotherapy. He showed immediate clinical, radiological and biochemical response to treatment within two weeks including rapid reduction in pituitary mass, normalization of sodium and prolactin and recovery of hypothalamic-pituitary-gonadal (HPG) axis in 4 months.
Discussion
Mechanism of SIADH and hyperprolactinemia in our case is likely due to infiltration of pituitary stalk, with hyperprolactinemia causing HPG axis suppression. This is the first case report of co-existing AML, SIADH, and partial hypopituitarism reflecting the importance of coordination between Endocrinology, Haematology and Pituitary MDT to promptly diagnose and treat such cases.

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Bisoprolol induced hyperhidrosis and elevated 5-hydroxyindoleacetic acid (5-HIAA) levels: a case report

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Beta-adrenergic receptor blockers are widely used to manage conditions including cardiovascular disease, migraines, and hyperthyroidism. Drugs like bisoprolol have demonstrated prognostic benefits in heart failure. Given their broad use, awareness of both common and rare adverse effects is essential. We present a case of bisoprolol-induced hyperhidrosis with elevated 5-hydroxyindoleacetic acid (5-HIAA) levels. A 78-year-old man with a history of atrial fibrillation, overactive bladder and haemorrhoids presented to the outpatient clinic with excessive sweating that worsened over two years. His medications included bisoprolol, edoxaban, atorvastatin, and ramipril. Hyperhidrosis episodes lasted up to 30 minutes, occurring daily, sometimes worsened with spicy food. He reported flushing but denied palpitations, dyspnoea or weight loss, gastrointestinal or urinary symptoms. He reported weight gain of 8 kg over the past two years, had a 60-pack-year smoking history, but abstained from alcohol and caffeine. Physical examination showed no signs of parkinsonism or thyroid dysfunction. Initial investigations ruled out tuberculosis, aortic regurgitation, and endocarditis. Biochemical testing revealed an elevated 5-HIAA level of 507 µmol/24 h (reference range: 0.2–118 µmol/24 h), with normal chromogranin A, thyroid function tests, plasma metanephrines, renin-aldosterone levels, and gut peptides. Following an unremarkable CT thorax/-abdomen/pelvis, an octreotide scan demonstrated focal uptake in the pancreatic head. MRI identified a possible small peripancreatic nodule but no definitive lesion explaining his symptoms was found. Surveillance was recommended after multidisciplinary review. Discontinuation of bisoprolol was subsequently followed by normalisation of 5-HIAA levels and marked symptom improvement. A follow-up MRI showed no evidence of the previously noted lesion. Lifestyle advice was provided with cardiology referral for alternative rate control therapy. Beta-blocker-induced hyperhidrosis is rare, with prior reports primarily linked to non-selective beta-blockers. This case highlights the unusual association of bisoprolol with hyperhidrosis. To our knowledge, there are no previous cases reported in the literature.

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Unveiling the unseen: diagnostic challenges of a false-negative copeptin test in arginine vasopressin deficiency – a case report

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Arginine vasopressin deficiency (formerly known as central diabetes insipidus, or CDI) is an endocrine disorder characterized by insufficient secretion of arginine vasopressin (AVP), also known as antidiuretic hormone (ADH). This deficiency leads to impaired renal water reabsorption, resulting in significant polyuria and polydipsia. Copeptin, the C-terminal segment of the AVP precursor, has emerged as a promising biomarker for diagnosing AVP deficiency. We present the case of a 41-year-old male who presented with severe polyuria, polydipsia, and hypernatremia. Due to the strong suspicion of AVP deficiency, severe symptoms, and copeptin test taking 3 weeks to be processed, desmopressin treatment was started empirically while awaiting copeptin results, leading to significant improvement in symptoms and sodium levels. The copeptin level eventually returned at 22.6 pmol/l, above the diagnostic cut-off ($\leq$4.9 pmol/l) for AVP deficiency. Further testing during hypertonic saline infusion test again showed elevated copeptin levels of 19.8, 21.3, and 22.6 pmol/l. Although copeptin results were pointing towards nephrogenic diabetes insipidus, there was a strong clinical suspicion of AVP deficiency, hence a water deprivation test was conducted. The initial urine osmolality was 78 mOsm/kg despite a serum osmolality of 320 mOsm/kg. After desmopressin administration (2 mg IM), urine osmolality increased to 884 mOsm/kg, confirming AVP deficiency. Retrospective copeptin measurement during the water deprivation test showed a level of 12.2 pmol/l. We plan to monitor the copeptin levels every three months to see if the levels eventually drop below 4.9 pmol/l. The laboratory confirmed that copeptin results were accurate with no assay interference. This case highlights the limitations of copeptin testing, particularly in early cases or partial AVP deficiency. Despite high Copeptin test diagnostic accuracy of 97%, confirmatory testing such as water deprivation test should be considered when clinical judgment doesn't align with the test results.

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P180

Central hypoadrenalism as an endocrine manifestation of CHARGE Syndrome

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Background
CHARGE Syndrome characterised by **c**oloboma, **h**eart defects, choanal **a**tresia, **r**etarded growth and development, **g**enital hypoplasia, and **e**ar abnormalities, is a rare, autosomal dominant disorder with wide genetic and phenotypic variability and a strong association with mutated chromodomain helicase DNA-binding protein (CHD7). Endocrine conditions known to be associated with this syndrome include hypogonadotropic hypogonadism, growth failure, growth hormone deficiency and hypothyroidism. Severe cortisol deficiency is uncommon and is usually diagnosed in childhood. We present a patient with CHARGE syndrome who presented with ACTH deficiency and hypoadrenalism at the age of 37.
Clinical Case
A 37-yr old woman with CHARGE Syndrome and chronic asthma presented in 2023 with symptoms of severe fatigue. She had the typical phenotypic manifestations of the condition. Random cortisol 11 years prior to this presentation was 621 nanomoles per l. The patient had required only one course of rescue steroids for an acute exacerbation of asthma in the 12 months preceding this presentation. Tests during this assessment were consistent with central hypoadrenalism with a low baseline cortisol of 31 nanomoles per l. Synacthen test showed a flat cortisol increment with a peak cortisol level of 107 nanomoles per l. Serum ACTH was $<$ 2 nanograms/litre. IGF 1 was normal at 22.8 nmoles per L (normal range 9-31) The pituitary gland was structurally normal on MRI scan. The patient was initiated on steroid replacement therapy with hydrocortisone with symptomatic improvement.

Discussion
Central hypoadrenalism is a rare endocrine manifestation of CHARGE Syndrome. Due to the rarity of the syndrome, an awareness of adrenal insufficiency as an associated endocrinopathy is critical to ensure that patients with CHARGE syndrome are screened periodically for hypoadrenalism to ensure prompt diagnosis and treatment to improve long term health outcomes.

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P181

Dexamethasone on induction for pituitary surgery does not affect day 5 cortisol measurement

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Background
Early morning cortisol levels are commonly used to assess hypothalamo-pituitary-adrenal (HPA) axis function following transsphenoidal pituitary surgery (TSS). Inadequate HPA axis recovery can result in secondary adrenal insufficiency (SAI), a potentially life-threatening complication, requiring glucocorticoid replacement therapy. This need is assessed using early morning postoperative cortisol levels. However, this may be affected by peri-operative dexamethasone administration. Dexamethasone is a long-acting synthetic glucocorticoid that is frequently utilised to decrease post-operative nausea, vomiting and pain. Dexamethasone use will transiently suppress the HPA axis, the extent of which is unknown.
Methods
This is a retrospective cohort study of 71 consecutive patients who underwent TSS at Charing Cross Hospital between 2019 and 2023. The postoperative cortisol level and respective glucocorticoid replacement status of patients who were administered dexamethasone were compared to those who were not. The ability of Day 5, Day 2/3 and Day 4-7 cortisol readings to predict SAI were compared using Receiver Operating Characteristics curves. Samples were analysed using Abbott immunoassays. Dexamethasone was administered to 34 of these patients while the remaining 37 were not given dexamethasone.
Results
Dexamethasone on induction of general anaesthesia showed no significant impact on Day 5 cortisol levels or the need for replacement glucocorticoid therapy. Day 5 (AUC = 0.9645 95% CI 0.9027-1) and Day 4-7 (AUC = 0.8679 95% CI 0.7614-0.9743) cortisol provided better predictive value for SAI compared to Day 2/3 samples (AUC = 0.8095 95% CI 0.5864-1).
Conclusion
Day 5 cortisol levels have the highest predictive value for SAI and are not significantly affected by the use of dexamethasone on induction.

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P182

Metastatic breast carcinoma presenting as metastasis into an occult non-functioning pituitary adenoma

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Pituitary metastasis is a rare complication of advanced malignancy. Tumour metastasis to a pituitary neuroendocrine tumour (PitNET) is a rarer phenomenon. We present a case of breast carcinoma with metastasis to an occult non-functioning pituitary adenoma (NFA). A 69-year-old female presented with acute bitemporal hemianopia. She had a history of breast cancer diagnosed 21 years ago (ER2 positive, HER2 negative), with disseminated sclerotic skeletal metastatic disease identified 3 years prior. Cross-sectional imaging indicated stable disease. Pituitary MRI revealed a macroadenoma with cystic degeneration, suprasellar extension, and optic chiasmal compression. Endocrine evaluation showed mild disconnection hyperprolactinaemia (656mU/l) and inappropriately low gonadotrophins for the postmenopausal state. There were no clinical features of an underlying endocrinopathy. Corticotroph and thyrotroph function was preserved. Pre-operative assessment and radiological characteristics were in keeping with an incidental non-functioning pituitary adenoma. Endoscopic transsphenoidal decompression of the sellar mass was undertaken with improvement in vision. Histopathological evaluation showed a non-functioning pituitary neuroendocrine tumour, with a Ki-67 labeling index of 5-6%. The pituitary adenoma was infiltrated by metastatic breast carcinoma, showing an estrogen receptor quick score of 8/8, a progesterone receptor quick score of 0/8, and was HER2 negative. The patient subsequently received stereotactic radiotherapy (25 Gy) to the pituitary area in five fractions. Pituitary metastases are rare and account for about 1% of all operated pituitary masses and $<1\%$ of all intracranial metastatic lesions. Pituitary metastasis can involve both the anterior and posterior lobes, but the neurohypophysis is mainly involved. This case highlights the importance of considering the possibility of metastasis to pituitary neuroendocrine tumours (PitNETs) when evaluating sellar tumours in patients with existing metastatic disease as preoperative differentiation of pituitary metastasis from NFA can be difficult. Prompt operative intervention and involvement of multidisciplinary teams can salvage vision and potentially improve cancer prognostic outcomes.

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P183

Introducing macimorelin stimulation testing for adult growth hormone deficiency in a UK centre

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Background
The diagnosis of Adult Growth Hormone Deficiency (AGHD) requires confirmation with a Growth Hormone (GH) stimulation test, traditionally either an Insulin Tolerance Test (ITT) or Glucagon Stimulation Test (GST). These tests are often poorly tolerated, labour-intensive, and may have limited diagnostic accuracy. Macimorelin is an oral Ghrelin receptor agonist that potently stimulates GH release. The Macimorelin Stimulation Test (MST) is well-tolerated and highly accurate in diagnosing AGHD, with sensitivity and specificity comparable/superior to ITT, the current gold standard test. MST is less resource-intensive (shorter test duration with fewer blood tests). We piloted MST as an alternative to GST for suspected AGHD.
Results
24 patients (13 female; 11 male; average age 50y; range 19-76y) underwent MST for AGHD evaluation between January and August 2024. All tests were completed successfully, with no inconclusive results. The average patient stay for MST was 1.5-2 hours, compared to a minimum 5-6 hours for GST. Average patient satisfaction scoring for MST was 8.8/10 ($n = 11$). 2 of 3 patients who had previously undergone GST rated MST more favourably. The other found them equivalent. All adverse events ($n = 8$; 32.3%) were mild and consistent with the known safety profile of Macimorelin, not requiring post-test care. Compared to GST, MST was found to be less demanding of staff and endocrine bedspace time, allowing multiple tests to be booked per day, thus improving access and reducing waiting times for ADGH testing and other endocrine investigations.
Conclusions
Macimorelin Stimulation Testing represents a valuable alternative to ITT and GST for the diagnosis of AGHD. Our pilot confirms that it is well-tolerated, highly accurate, and less resource-intensive than ITT or GST. The adoption of MST as a first-line test may improve patient experience, optimise endocrine testing unit operations, and enhance access to AGHD diagnosis.

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P184

A rare complication of secondary radiation-induced sarcoma following pituitary irradiation: A case report

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Background
Radiation-induced sarcoma (RIS) in the sella is a rare but serious complication following radiotherapy for pituitary tumors.
Clinical Case
A 43-year-old patient with recurrent extra-sellar pituitary macroadenomas underwent trans-sphenoidal surgery (TSS) in 2006 and 2016 due to optic chiasm compression. Initial histology showed gonadotroph staining with a KI index of 2%. After a residual tumor was found in the right cavernous sinus, the patient received adjuvant stereotactic radiosurgery (SRS) of 12.5 Gy in 2016. Post-

operative tests revealed suboptimal growth hormone (GH) and testosterone levels, leading to treatment with Genotropin SC and Tostran 2% gel. Seven years later, in 2023, the patient presented with headache, double vision, and right third nerve palsy. MRI a few months earlier had shown empty sella with a small residuum. Repeat MRI indicated a large sellar and suprasellar mass compressing the optic chiasm, causing bony erosions and extending into the right cavernous sinus, distally displacing the internal carotid artery. Given the stability of the disease for seven years, the aggressive nature of the new mass was unexpected, especially in the light of the earlier routine follow-up MRI scan. An emergency endoscopic TSS was performed for decompression and maximal resection. Histology revealed spindle cell sarcoma. CT TAP excluded metastases. Post-operative MRI indicated a residual mass measuring 12 x 17 x 29 mm in the pituitary fossa. The multidisciplinary team (MDT) initiated adjuvant chemotherapy, with three cycles of Doxorubicin and Ifosfamide so far. Follow-up MRIs show continuous reduction in residual tumor size with persistent suboptimal cortisol, testosterone, thyroid, and GH responses requiring hydrocortisone, Thyroxine, and Nebido.
Conclusion
This case exemplifies secondary sarcoma following pituitary irradiation. Strict follow-up and high suspicion after previous irradiation treatment is recommended for early diagnosis and management.

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P185

Investigation of cancer specific DNA changes using oxford nanopore technology (ONT) and more traditional sequencing technologies in the surveillance of patients with neuroendocrine neoplasms

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Background
Circulating tumour DNA (ctDNA) found in the plasma or serum of individuals with cancer presents a non-invasive means of accessing tumour DNA. This 'liquid biopsy' facilitates the examination of various DNA aspects including fragmentation, chromosomal alterations, sequence mutations, and epigenetic modifications. Aberrant methylation of specific promoter regions tends to be a consistent hallmark of cancer. This consistency makes ctDNA methylation amenable to design a clinical assay for neuroendocrine neoplasm.
Subject and Design of study
We plan investigate samples from patients with neuroendocrine neoplasm (NEN) with germline mutation and sporadic mutations and NENs of unknown primary origin. This will be a longitudinal, observational, cohort, pilot study.
ctDNA methylation via Oxford Nanopore sequencer
Nanopore sequencing is the only sequencing technology that offers real-time analysis for rapid insights in fully scalable formats, and can analyse native DNA or RNA, and sequence any length of fragment to achieve short to ultra-long read lengths. We aim to isolate cell-free DNA from 4 ml of blood plasma using the MagMAX Cell-free DNA Isolation Kit on the Kingfisher Flex instrument. For Library preparation we will follow an established Oxford Nanopore Technique protocol using Ligation Sequencing Kit V14 (SQK-LSK114) chemistry, using 10 ng cfDNA input to load on PromethION Flow Cell. In individual patients, change in ctDNA methylation analysis over time will be plotted and compared against change in disease burden on imaging and changes in current biomarker performed as per usual care, using RECIST criteria and, depending on data generated, sensitivity analysis will be completed.
Conclusion
There is limited information on the clinical utility of DNA methylation analysis in the detection and surveillance of NETs. We hope to use third generation nanopore sequencing to investigate circulating DNA methylation to establish if this correlates to disease activity in patients with NENs and will publish our results next year.

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P186

Living on the edge! five years without cortisol in nelson's syndrome

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Introduction
In severe Cushing's disease, first-line treatment is transsphenoidal surgery, with repeat surgery or radiotherapy if remission is not achieved, and medical management if necessary. If these options fail, bilateral adrenalectomy is considered. Nelson's syndrome is defined as continuous secretion of ACTH by pituitary tumour after adrenalectomy. Discontinuing hydrocortisone risks adrenal crisis but may also stimulate the growth of corticotrophinoma.
Case Report
A 36-year-old male diagnosed with Cushing's disease at age 10 underwent transsphenoidal adenomectomy in 2002 and pituitary radiotherapy in 2003, both failing to achieve remission. Bilateral adrenalectomy followed in 2006, with hydrocortisone and fludrocortisone replacement. Lost to follow-up in 2011, he re-presented in 2021 with hyperpigmentation, hypertension, pre-diabetes, obesity, and obstructive sleep apnoea, off hydrocortisone for five years without adrenal crisis. Imaging identified a growing pituitary macroadenoma (14x18 mm), larger than in 2011 (7x6 mm), and a CT showed an 18 mm adrenal remnant. His ACTH was 436 ng/l, and cortisol was 335 nmol/l after 20 hours without hydrocortisone. Following a failed Synacthen test, hydrocortisone and fludrocortisone were resumed. In 2022, a second transsphenoidal surgery confirmed a corticotroph PITNET. Post-operative MRI showed a 10x8 mm residual tumour near the optic chiasm, making further radiosurgery unsafe. Persistently elevated ACTH and repeated Synacthen test failure (cortisol 248-330nmol/l) indicated ongoing adrenal insufficiency despite functional adrenal tissue. He remains under annual MRI and biochemical monitoring.
Conclusion
This case demonstrates that even after five years without hydrocortisone, an adrenal crisis may not occur if even a small volume of functional adrenal tissue remains. It highlights the complexity of Cushing's disease and the need for strict specialist MDT follow-up.

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P187

Re-establishing the UK acromegaly registry (UKAR): a patient-centered survey of priorities and expectations

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Background
The **UK Acromegaly Registry (UKAR)**, established in 1997 to collect comprehensive data on acromegaly and gigantism, is currently on hold. A Patient and Public Involvement and Engagement (PPIE) Survey was conducted from 15 August to 30 September 2024 via Pituitary Foundation communication channels to gather views on the potential re-opening of the registry, focusing on patient preferences regarding data collection and registry functionalities.
Methods
The UKAR steering group developed a ten-question PPIE survey, which was refined using the NHS readability tool to ensure accessibility. It was distributed to approx. 9,300 individuals via the Pituitary Foundation newsletter and social media, reaching approximately 27,000 people. Responses were received from 67 participants, with nearly 96% being patients diagnosed with acromegaly or gigantism. The survey focused on prior awareness of the UKAR, support for its reactivation, preferences for data inclusion, and patient expectations from the registry.
Results
Among the 67 respondents, 3 were healthcare professionals. A significant portion (73.1%) were unaware of the UKAR prior to the survey. Despite this, there was strong support (86.6%) for reactivating the registry. The key data areas that patients deemed essential for inclusion were treatment history (98.5%), treatment efficacy (95.5%), and the impact of the condition on their quality of life (83.6%). On exploring communication preferences, most respondents (86.6%) preferred to receive the registry's updates online. Additionally, 53.7% expressed interest in using a mobile app for future communications. Regarding data updates, 51.5% of participants wanted their information updated annually, while 21.2% preferred updates triggered by changes in their health.
Conclusion
This survey shows considerable patient endorsement for the reactivation of the UKAR. Patients emphasised the need to include treatment data, quality-of-life

measures, and research input. The insights gathered will guide the development of a modernised, patient-centred UKAR that enhances research, improves clinical care, and fosters patient engagement.

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P188

Two cases of pituitary metastasis with varied presentations

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Background
Pituitary metastasis is a rare but life-threatening condition. Patients typically present with visual symptoms, AVP deficiency (diabetes insipidus), and hypopituitarism. We report a couple of cases of pituitary metastasis with varied presentations.
Case 1
A 52-year-old male presented with frontal headaches, polydipsia, visual disturbances, and extreme fatigue. Biochemistry was consistent with hypopituitarism including AVP deficiency; Pituitary MRI revealed a suprasellar pituitary lesion (1.7x1.6x1.4 cm), compressing the optic chiasm. He was started on hydrocortisone, levothyroxine, and desmopressin. Within two weeks, he presented with worsening headaches and confusion. A repeat MRI showed a heterogeneous lesion with a distorted contour & 1 cm size increase. CT CAP revealed a 5 cm lung mass, confirmed on histology as non-small cell lung cancer. He underwent pituitary debulking surgery, followed by chemotherapy. Histology confirmed pituitary metastasis from lung primary. The prognosis remains poor due to lack of treatment response.
Case 2
A 61-year-old female with a recent diagnosis of non-small cell lung cancer presented with left arm weakness. A CT head showed cerebral metastasis. She was hypotensive and hyponatraemic, with blood tests confirming hypopituitarism but no overt evidence of AVP deficiency. She was started on hydrocortisone and levothyroxine. An MRI of the pituitary confirmed pituitary metastasis characterized by an intrasellar focal signal abnormality measuring 11 x 14 x 14 mm with a very thin surrounding layer of residual pituitary tissue. An MDT-led decision was made to start her on palliative radiotherapy.
Learning points
1. Pituitary metastasis should be considered as a differential diagnosis if AVP deficiency is part of the initial clinical presentation. 2. Cancer patients with extreme fatigue should be screened for hypopituitarism and have a low threshold for pituitary scanning to rule out pituitary metastasis. 3. Pituitary metastasis bears poor prognosis and can have variable degree of hormonal deficiencies, with or without AVP deficiency.

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P189

Idiopathic hypophysitis presenting with amenorrhea: a case report

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Background
Hypophysitis, an inflammatory disorder of the pituitary gland, is a rare but significant cause of hypopituitarism. It is often challenging due to its non-specific symptoms and can mimic other suprasellar pathologies. This report presents a case of idiopathic hypophysitis in a young woman, managed with medical therapy and closely monitored for clinical and radiological outcomes.
Case Presentation
A 29-year-old female presented with secondary amenorrhea of 8-month duration. Initial endocrine evaluation revealed hyperprolactinemia (1591 mIU/l), secondary hypogonadism (FSH 3.6 IU/l), preserved cortisol response to synacthen stimulation and central hypothyroidism (FT4 9.4 pmol/l, TSH 1.5 mIU/l). MRI revealed a 13x10 mm homogeneously enhancing suprasellar lesion involving the pituitary stalk, suggesting differential diagnoses of craniopharyngioma or an inflammatory aetiology like hypophysitis.
Management and Outcome
Tumor markers and serum ACE were negative, and a CT TAP excluded systemic malignancy. Following a pituitary multidisciplinary team (MDT) review, the diagnosis was deemed most consistent with idiopathic hypophysitis based on MRI findings, particularly stalk involvement extending into the third ventricle. She commenced prednisolone at 60 mg/day, which led to marked clinical and radiological improvement. One month post-steroid therapy, MRI showed a reduced lesion size (12×9 mm), with further decrease to 10x9 mm after six months. Prednisolone (60 mg/day) was started, resulting in radiological improvement. Follow-up MRI one month post-steroid therapy showed a reduction in lesion size (12×9 mm). Further imaging in 6 months demonstrated continued improvement, with the lesion now measuring 10×9 mm.
Conclusion
This case underscores the efficacy of early recognition and appropriate medical management of idiopathic hypophysitis. The favourable response to glucocorticoid therapy, evidenced by radiological improvement, supports the inflammatory nature of the condition. A structured multidisciplinary approach remains crucial for accurate diagnosis and optimal therapeutic outcomes in such cases, continued monitoring remains essential to exclude alternative diagnoses.

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P190

Moderate vasopressin deficiency (diabetes insipidus) with severe effects

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An NHS England Patient Safety Alert in 2016 stated 'Risks of severe harm or death when desmopressin is omitted or delayed in patients with cranial diabetes insipidus'. Case Report – 64 year old man with panhypopituitarism (including vasopressin deficiency) secondary to treatment of a craniopharyngioma 18 years earlier presented with a fall. Diagnosis: aspiration pneumonia and IV antibiotics and hydrocortisone were administered. Endocrine management had been elsewhere and the available information did not record treatment with DDAVP. On admission: sodium 142 mmol/l, potassium 3.8 mmol/l, urea 7 mmol/l, creatinine 144 umol/L and eGFR 43 ml/min. Over 5 days there was clinical and biochemical deterioration with sodium 171 mmol/l, potassium 3.8 mmol/l, urea 20.4 mmol/l, creatinine 279 umol/l, eGFR 20 ml/min, plasma osmolality 358 mmol/kg and urine osmolality 501 mmol/kg being attributed to acute kidney injury secondary to sepsis. Add-on copeptin 5.9 pmol/l. An alert from clinical biochemistry led to endocrine review which confirmed he had stopped treatment with intranasal DDAVP 10 mg bd 5 years earlier and compensated for thirst/polyuria by increasing oral fluid intake. Treatment with IM DDAVP and 5% dextrose resulted in clinical and biochemical improvement over 4 days: sodium 137 mmol/l, potassium 4.7 mmol/l, urea 11.9 mmol/l, creatinine 118 umol/L and eGFR 54 ml/min. Clinical status was not maintained and he died of respiratory complications. In conclusion this case confirms (a) a need for patients with vasopressin deficiency to carry cards indicating the diagnosis and the nature of DDAVP as a life-dependent therapy; (b) oral fluid controlled vasopressin deficiency decompensates rapidly on compromised intake and (c) the need for endocrine team input in the management of vasopressin deficiency in acute situations especially when conscious level impaired.

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P191

A case of subclinical acromegaly

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Acromegaly is a rare chronic disease due to sustained and unregulated hypersecretion of growth hormone that develops insidiously and progresses slowly. It may result in a variety of cardiovascular, respiratory, endocrine, metabolic, musculoskeletal, and neoplastic comorbidities. In more than 99% of cases this is due to a benign pituitary growth hormone secreting adenoma. Infrequently acromegaly occurs as a result of ectopic secretion of growth hormone releasing hormone from a peripheral neuroendocrine tumour. 5% of cases are associated with familial syndromes. It can remain undiagnosed for about 10 years with only 50% of patients with somatotroph adenomas revealing distinct phenotypic changes, whereas the other 50% are mostly asymptomatic. We present a case of a 34- year- old female who presented with chronic migraines. She had an MRI head that showed a left sided pituitary incidentaloma measuring 14 x5 x5mm. On endocrinology review, patient did not report any symptoms and there were no clinical manifestations of any hormone excess. Anterior pituitary profile showed a raised IGF-1(88.5 nmol/l) but the rest was normal. OGTT with serial growth hormone measurements also showed unsuppressed GH. This case was discussed in the pituitary MDT and it was decided that patient should have surgery, although there was no current clinical manifestation, but in view of insidious onset and impending manifestations. Transsphenoidal hypophysectomy was done in August 2024. Histology showed pit-1 strongly positive and GH present with 40% positivity, Ki67 3-4% in keeping with a somatotroph adenoma.

Post operatively the headaches resolved, the IGF-1 normalised and OGTT showed suppressed growth hormone, and the AIP gene testing result is awaited.
Conclusion
Early diagnosis and adequate treatment are essential to mitigate excess mortality risk associated with acromegaly. Our case was picked up early due to the incidentaloma, timely referral to endocrinology and pituitary MDT which made early treatment possible.

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Rare case of ectopic cushing's syndrome secondary to metastatic prostate cancer withneuroendocrine differentiation

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55 year old male was diagnosed with prostate acinar adenocarcinoma (wild type BRCA1/2 on somatic testing) in February 2023. PSA at diagnosis- 33.4ug/L and PSMA-PET confirmed widespread nodal and bone metastases. He was treated with combination of androgen deprivation therapy and Darolutamide and Docetaxel chemotherapy. His disease was subsequently controlled with PSA of 0.24ug/l. He presented in July 2024 with abdominal distention, pitting oedema, muscle weakness and exertional breathlessness. He had persistent hypokalaemia and metabolic alkalosis, new hyperglycaemia and hypertension (potassium- 2.1mmol/l, bicarbonate- 34.8 mmol/l, pH- 7.55, HbA1c- 62mmol/mol). CT confirmed progressive disease with multiple new hepatic metastases and there was rise in PSA to 4.3ug/l. His cortisol was 3321nmol/l following a 1 mg dexamethasone suppression test and ACTH- 951ng/L (0-46). Rise in PSA, biochemistry and imaging were in keeping with prostate cancer with neuroendocrine differentiation and ectopic cushing's syndrome (ECS). Due to poor performance and need to commence chemotherapy immediately, histological diagnosis or neuroendocrine imaging were not pursued. Patient was unfit for bilateral adrenalectomy. Medical management with Metyrapone, Metformin and Spironolactone were commenced alongside Cabazitaxel chemotherapy. Abnormal liver function tests precluded addition of ketoconazole. Unfortunately, there was no clinical or biochemical response to two cycles of chemotherapy and Metyrapone dose escalation (ACTH- 2227 ng/l, Cortisol 1428 nmol/l) and patient sadly passed away within two months.
Discussion
Neuroendocrine differentiation can occur in 25-30% of metastatic-castrate resistant prostate cancer with prior use of androgen deprivation therapy and is associated with extremely poor prognosis. Ectopic cushing's syndrome as a paraneoplastic phenomenon in this scenario is very rare and has been described in a small numberof reported cases. Persistent hypokalaemia, hypertension and new hyperglycaemia should alert clinicians to this possibility. Despite aggressive treatment of ECS often requiring a combination of rapid-acting steroidogenesis inhibitors, the overall prognosis remains very poor.

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P193

Whole exome sequencing analysis of germline DNA of 222 patients with pituitary adenomas

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Introduction
Pituitary adenomas can cause severe life-long disease due to abnormal pituitary function. Identifying potentially causative germline variants in young-onset and familial cases is challenging and most cases remain unsolved.
Methods
Whole exome sequencing was performed on blood-derived DNA from 222 samples to identify rare germline disease-causing variants. 67 samples originated from 23 *AIP*-negative families and 99 cases were early-onset pituitary adenoma patients with no known family history. The phenotype-based variant prioritisation software Exomiser was used to curate a list of genes containing potentially contributing variants. Variants were filtered to only include those with an autosomal dominant mode of inheritance (for families) where the variant fully segregated and a heterozygous genotype for singletons, with a minor allele frequency less than 0.001%.
Results and Conclusions
294 genes were found in three or more kindreds, with 39 of these being constrained with a loss-of-function observed/expected upper bound fraction less than 0.5, according to gnomAD, suggesting that these genes have a relatively lower frequency of loss-of-function variants in the general public. Twelve of these genes harboured shared rare variants where the variant itself was found in three or more kindreds, with two containing a shared, loss-of-function variant. While our pipeline has identified genes containing potentially novel disease-causing variants, further work is needed to confirm the presence of these variants by Sanger sequencing and before starting mechanistic studies for disease mechanism.
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Follow-up protocol of sporadic pheochromocytoma patients, a tertiary centre experience

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Introduction
Pheochromocytomas may occur sporadically or associated with identifiable genetic syndromes. Reported recurrence rate in sporadic pheochromocytomas in literature is around 3%. There are no consensus guidelines for follow-up of sporadic pheochromocytoma when genetic mutations have been excluded, with varying opinions by ESE, ES and AACE. We aimed to assess characteristics of sporadic phaeochromocytoma patients in our tertiary centre between January 2000-January 2020. Data was gathered on the following characteristics: Age at diagnosis, Sex, genetic testing, presenting symptoms and histology. Follow-up data included: follow-up duration, modalities used, timing of recurrence and survival data.
Results
64 patients were identified (29 Male, 35 Female). We excluded patients with positive genetics, no local records, and metastatic disease at diagnosis. Age at diagnosis: 18.4-81.2 years. Presenting symptoms were adrenergic (27), adrenal incidentaloma (18) or cardiac symptoms (5). (Insufficient information for 14 patients) On histology review, PASS score was available for 26 patients. Median PASS score was 5 (range 0-10). 18 patients had PASS score ≥ 4, 8 had PASS score < 4. Median follow-up duration was 108 months (range:16 months-389 months). Recurrence was noted in 4 patients, earliest at 41 months and latest 156 months, identified by symptoms (2) and biochemistry (2). Treatments for recurrence included 2 MIBG-therapy, 1 Redo surgery. One patient died prior to treatment. Survival data revealed 11 patients had passed away during follow up period.
Conclusion
This data is in keeping with published data that a small percentage (6%) of patients with sporadic pheochromocytomas will experience recurrent disease. Given the findings, clinical and biochemical surveillance remain reliable ways of identifying recurrence with less frequent imaging. Risk stratifying patients at diagnosis and highlighting at risk groups is important to utilise resources both of those of the patient and NHS.

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P195

An unusual case of left ventricular systolic dysfunction secondary to acromegaly

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Introduction
Elevated levels of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) are a recognised cause of dilated cardiomyopathy in patients with acromegaly. Presentation with acute heart failure suggests late-stage disease with left ventricular (LV) systolic dysfunction being a rare consequence of the underlying acromegaly.
Case Report
A 45-year-old man presented to the emergency department with dyspnoea and was found to have acute decompensated heart failure with no prior background of cardiac disease. Echocardiogram showed LV systolic dysfunction with an ejection fraction of

27%. After cardiology review, he was commenced on heart failure medication. Cardiac MRI showed non-ischaemic dilated cardiomyopathy, significant LV dilatation, severe LV systolic impairment and mid-wall/subepicardial fibrosis. From facial features, a diagnosis of acromegaly was suspected and he was referred to endocrinology. Examination revealed acromegalic facies, with diastema, prominent nasolabial folds and prognathism. Investigations showed IGF-1 of 640 μg/L (74-227) and lack of GH suppression during oral glucose tolerance testing with a nadir value of 1.4 μg/L (<0.3). Pituitary MRI showed a 6 mm hypo-enhancing lesion in the left lateral aspect of the pituitary gland in keeping with a microadenoma. Considering his heart failure, he was started on lanreotide 60 mg monthly prior to surgery with improvement of IGF-1 levels to 273 μg/L eight weeks after treatment initiation and he reported marked improvement in exercise tolerance. He is being assessed by the neurosurgical team for transsphenoidal resection surgery.

Discussion

Despite the cardiac manifestations of acromegaly usually indicating a late diagnosis, cardiac improvement can be achieved with normalisation of IGF-1. Successful treatment with somatostatin analogues can reduce circulating levels of GH and IGF-1 and result in the reversal of cardiac fibrosis. Even greater cardiac recovery is seen with definitive transsphenoidal surgery. Ultimately, the early diagnosis and treatment of acromegaly is key to improving cardiac outcomes.

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P196

Severe refractory hypokalaemia as a manifestation of ectopic ACTH syndrome due to small cell lung cancer-a diagnostic and therapeutic challenge

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Background

Hypokalaemia is a common biochemical presentation caused by increased potassium loss, intracellular shift, or reduced intake. Common causes include diuretic use and gastrointestinal losses. Rarer aetiologies involve sustained activation of mineralocorticoid receptors by elevated levels of circulating cortisol, as seen in Ectopic ACTH Syndrome (EAS).

Case Presentation

A 60-yr old lady presented with severe refractory hypokalaemia (1.8-2.9 mmol/l), psychosis and hypomania. There were no somatic features of Cushing's syndrome. The patient had been diagnosed with small cell lung cancer (SCLC) 3 months prior. Ectopic ACTH secretion from SCLC was suspected in view of hypokalaemia refractory to treatment with intravenous and oral potassium supplements. Investigations showed marked hypercortisolaemia (midnight cortisol 4283 nmol/l), elevated ACTH (120 pmol/l), and a markedly raised ACTH precursor concentration (1712 pmol/l; normal < 40 pmol/l), indicating ACTH-dependent hypercortisolaemia. Low-dose 48-hour overnight dexamethasone suppression test showed unsuppressed cortisol (3658 nmol/l), confirming a syndrome of cortisol excess. Pituitary MRI and adrenal CT were normal. Treatment with Metyrapone was initiated to inhibit steroid synthesis and serum cortisol improved from 3658 to 1345 nmol/l after 9 days of therapy and potassium levels normalized in parallel. Adrenal blockade was combined with rescue Hydrocortisone therapy. The patient was referred for palliative radiotherapy.

Discussion

Ectopic ACTH secretion from a bronchogenic carcinoma may be associated with florid hypercortisolaemia without any somatic features of Cushing's syndrome, due to malignancy induced cachexia. Refractory hypokalaemia in this context is highly indicative of ectopic ACTH-dependent hypercortisolaemia but the diagnosis may be challenging in the non-specialist environment of a general medical ward. ACTH precursors characterize EAS and are disproportionately elevated compared to serum ACTH. Patients with malignancy induced ectopic ACTH secretion and hypercortisolaemia have a uniformly poor prognosis. A high index of suspicion remains the cornerstone of diagnosis.

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P197

Cortical vasculature in polycystic ovary syndrome and associations with circulating testosterone

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Introduction

Polycystic ovary syndrome (PCOS) is a common, multi-system condition often associated with hyperandrogenism. Patients demonstrate increased risk of cardio- and cerebrovascular abnormalities. The exact mechanism for this is unknown but may involve a direct action of testosterone on the cerebrovascular system. The current study investigates multiple cerebrovascular functions in PCOS patients compared to healthy controls and specifically investigates associations with testosterone.

Methods

15 PCOS patients (testosterone mean[SD]=1.39[0.47]nmol/l) and 13 BMI-and-age-matched healthy controls (testosterone mean[SD]=1.13[0.43]) completed an MRI session (Siemens MAGNETOM Prisma 3T scanner). A multi-post labelling delay pseudocontinuous arterial spin labelling (MPLD-pCASL) perfusion scan (maximum TR=5.6s; TE=11s; voxel resolution=3.4x3.4x6.0mm; tag duration=1800; post-labelling delays=250-3000ms in steps of 250ms) assessed regional Cerebral Blood Flow (CBF). A T2-relaxation-under-spin-tagging (TRUST) sequence (TR=3s; TE=3.9ms) estimated global oxygen extraction fraction and cerebral metabolic rate of oxygen. Linear models investigated the amount of vascular function that could be explained by PCOS status or additional testosterone variance.

Results

A significant CBF association was found with PCOS status (χ^2 (1)=52.715; P = 3.856x10^{-13}) and testosterone (χ^2 (1)= 63.987; P = 1.253x10^{-15}). While PCOS status reduced CBF by -6.561ml/100g/min±0.864 (standard error [SE]), additional testosterone variance was associated with an increase of 1.981ml /100g/min± 0.238 (SE) with each 0.1nmol/l increase. Further investigation suggested that both effects occurred globally. Neither had a significant association with any other outcome function.

Conclusion

These results illustrate how PCOS status and testosterone level influence the cerebrovascular system, which occurred globally across cortical and subcortical regions. Any CBF shift would impact oxygen delivery. The opposing directions found in CBF may suggest that factors outside of hyperandrogenism lead to the PCOS status difference, and increased testosterone may actually be protective, at least in this young cohort.

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P198

Upregulation of LKB1-AMPK signalling pathway in sparsely granulated somatotropinomas: a phosphoproteomics based approach

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Background

Based on granularity somatotropinomas are divided into sparsely (SG) and densely granulated (DG). SG shows aggressive clinical behaviour (presentation at a young age, with increased invasiveness, recurrence, and resistance to treatments as compared to DG. Upregulation of LKB1-AMPK pathway can support tumour survival and growth by promoting autophagy and providing an adaptive response to a nutrient-poor microenvironment.

Method

Quantitative mass spectrometry-based phosphoproteomics analysis was performed on SG (n = 4) and DG (n = 4) tumours. Candidates of significantly enriched pathways (cut-off=1.5 fold-change) were considered for validation by immunohistochemistry (IHC) (n = 10; SG=4, DG=6) on tissue microarray in a separate group of samples.

Results and Discussion

Mass spectrometry analysis revealed significant over-phosphorylation of 85 proteins belonging to the LKB1-AMPK pathway (fold enrichment = 1.8, P = 2.2E-09) in SG tumours. Antibody availability guided the selection of four candidates TSC1 Ser1080, AMPKβ Ser108, MAPT Thr548, and ULK1 Ser638 for IHC. Over-phosphorylation of AMPKβ Ser108 (6.0-fold, P = 0.0073) signifies AMPK activation, suggesting metabolic adaptation to energy stress. A substantial increase in TSC1 Ser1080 phosphorylation (9.5-fold, P = 0.01) implies inhibition of the TSC complex, potentially activating mTOR signalling and promoting anabolic processes in SG tumours. Over-phosphorylation of MAPT at Thr548 (3.8-fold, P = 0.02) suggests enhanced cytoskeletal dynamics, potentially facilitating invasion. Although ULK1 Ser638 phosphorylation showed a smaller, nonsignificant increase (1.8-fold, P = 0.54), this trend may indicate autophagic adaptation to metabolic stress. Upstream analysis identified PRKAA1 and GSK3β as regulators of AMPKβ Ser108 and MAPT Thr548, respectively, while mTOR phosphorylates TSC1 Ser1080 and ULK1 Ser638. IHC confirmed increase in mTOR expression in SG tumours (3.5-fold P = 0.01) compared to DG, underscoring mTOR's role in driving tumour growth.

Conclusions
In SG tumours, PRKAA1-mediated AMPK activation, GSK3β-driven cytoskeletal remodelling and mTOR signalling, collectively promote tumour cell survival, growth and invasiveness.

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P199

A rare case of FGF-23-mediated hypophosphataemia secondary to a neurodendocrine tumour

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A 49-year-old male with a history of hypertension, hypothyroidism, obstructive sleep apnoea, and prostatitis presented to the emergency department with a presyncopal episode and tachycardia (140 bpm). Notably, the patient's mother had recently passed away from metastatic small bowel neuroendocrine tumour (NET). Laboratory findings revealed severe hypophosphataemia (phosphate: 0.36mmol/l, calcium: 2.41mmol/l, PTH: 8.7 pmol/l), initially managed with intravenous phosphate. Within a week of discharge, he was readmitted for recurrent hypophosphataemia and discharged on oral phosphate. His medical history included similar admissions with critically low phosphate levels (as low as 0.18mmol/l), previously attributed to diarrhoeal illness. At the endocrine clinic, further investigations showed persistently low phosphate, elevated 24-hour urinary phosphate (82mmol/day), and raised fibroblast growth factor (FGF-23) at 135 IU/ml (reference range: <100). He was prescribed alfacalcidol (0.75 mcg) and sando-phos (6 tablets daily) which stabilized his phosphate levels. Unexpectedly, gallium DOTATATE PET/CT (Ga-68 DOTATATE) imaging revealed a 15mm somatostatin receptor-expressing mesenteric nodal deposit, suggestive of a NET. No primary tumour was identified on somatostatin receptor (SSTR) imaging, contrast enhanced CT or capsule endoscopy. Following discussion at the NET MDT, the patient underwent a small bowel wedge resection and excision of mesenteric nodes, which identified a well-differentiated small bowel grade 1 NET (Ki67 $<3\%$) staged as pT4N1R1. Postoperative phosphate levels stabilized at 0.89mmol/l, allowing him to discontinue alfacalcidol and phosphate supplementation.
Conclusion
To our knowledge, this is the first reported case of tumour-induced osteomalacia secondary to a small bowel NET. It highlights the need to consider tumour-induced osteomalacia in the differential diagnosis, the critical role of somatostatin receptor (SSTR) imaging, and multidisciplinary management in diagnosing and treating NETs with paraneoplastic manifestations.

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P200

Oxcarbazepine (OXC) associated SIADH with adrenocortical insufficiency: learnings from a complex hyponatraemic case with multifactorial aetiology

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Introduction
OXC is a commonly used anti-epileptic drug with a reported prevalence of 29.9% hyponatraemia due to the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). We present a case of a 49-year-old man with refractory epilepsy on OXC who developed severe hyponatraemia following unilateral radical nephrectomy 4 weeks prior for focal renal cell carcinoma.
Initial presentation
He presented with status epilepticus with serum sodium (sNa^+) between 115-120mmol/l. Osmolality studies showed serum 250-262mOsm/kg and urine 328-546mOsm/kg suggestive of SIADH but atypically high urine sodium at 64-112mmol/l. Short Synacthen Test showed a suboptimal 30-minute rise of cortisol level (76 to 395 mmol/l; ACTH normal:22ng/l). Rest of endocrine milieu and MRI brain were unremarkable. Concomitant medications included OXC, Levetiracetam, Perampanel and Citalopram.
Management
Initial management included 1L/day fluid restriction and hydrocortisone. As sNa^+ levels dropped (112 mmol/l), Citalopram was stopped and Fludrocortisone was added despite normal ACTH. Neurology was hesitant to stop OXC due to fear of precipitating seizures but sNa^+ persisted between 115 -120mmol/L and hence Tolvaptan was started at 7.5 mg OD. The latter showed a rise of sNa^+ but plateaued at <125mmol/l. Following neurology consultation, OXC was guardedly weaned down without recrudescence of epilepsy resulting in sNa^+ rising to 130-140mmol/l. Once OXC was completely stopped, Tolvaptan was next weaned down completely with sNa^+ remaining stable at 132-138mmol/l.
Learning Points
SIADH can be challenging especially if there are multiple contributing aetiologies. In this case, the effect of low sNa^+ on precipitating seizures, reticence to stop OXC and adrenocortical insufficiency, all contributed to a complex interplay needing prolonged inpatient stay. This case highlights that clinicians should be alert to OXC side effects and such cases need complex MDT approaches to achieve the best clinical outcome.

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P201

Proinsulin secreting neuroendocrine tumour: diagnostic challenge

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Background
Proinsulinoma is a rare neuroendocrine tumour (NET). Diagnosis is frequently challenging.
Presentation
A 79-year-old female presented with 2-year history of hypoglycaemia symptoms after morning exercise. A diagnosis of reactive hypoglycaemia was made after five-hour glucose tolerance testing (peak glucose 12.3mmol/l; nadir 2.7mmol/L at 210min). Complex carbohydrate supplements and acarbose were commenced but over 18 months symptoms progressed.
Further investigations
A 72h fast was carried out, soliciting spontaneous hypoglycaemia (Table). Concomitant insulin concentration was not consistent with insulin-driven hypoglycaemia, but C-peptide and proinsulin were elevated with a high proinsulin to insulin ratio. HbA1c was low (31mmol/l). Sulphonylurea screen, IGF2 and IGFBP3 were normal. Further fast again provoked hypoglycaemia, high insulin, C-peptide and proinsulin concentration (table) with a low fatty acid (0.8mmol/l) and capillary blood ketone concentration (0.6mmol/l), consistent with insulin-driven hypoglycaemia. Peptidomic analysis (mass spectrometry) identified Chromogranin B and neuroendocrine protein (7B2). Collectively, the biochemistry was most consistent with proinsulinoma.
Localisation studies
CT pancreas (Non-contrast due to contrast allergy), MRI, Tc99m HYNIC-TOC SPECT CT, and endoscopic ultrasound were inconclusive. DOTATATE PET-MR reported a potential lesion at the pancreatic head. All old scans were reviewed, revealing a 5mm hypervascular lesion in the pancreatic tail on post-contrast CT done 7 years ago. Revisiting DOTATATE PET-MR suggested a corresponding lesion. This was confirmed on repeat CT with contrast (with antihistamine cover).
Management
She required diazoxide therapy, followed by laparotomy and enucleation of the NET, with a resolution of hypoglycemia. Histology confirmed grade 1 well-differentiated NET.
Conclusion
A strong clinical suspicion and persistent MDT approach was crucial for identification and management of a slowly evolving proinsulinoma.

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Abstract P201

	Hours into fast(h)	Plasma glucose (mmol/l)	Insulin (pmol/l)	C-Peptide (pmol/l)	Pro-insulin (0-7 pmol/l)	C-Peptide: Insulin	Proinsulin: Insulin
14 Jun 23	20	2	5* <18#	294	8.2	58.8	1.6
14 Sep 23	15	1.9	17	569	13.3	42.7	0.78

*DiaSorin Liaison; # Mercodia

P202

Utility of suvmax threshold for pathological discrimination of incidental fdg-pet pituitary uptake - a united kingdom single centre retrospective analysis

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Background
Positron emission tomography-computed tomography (PET-CT) is essential for cancer staging. Fluorine-18 fluorodeoxyglucose (FDG), marks increased cellular activity as maximum Standardised Uptake Value (SUVmax). Malignancies show elevated FDG uptake, benign conditions (inflammation, benign tumours, post-treatment) also increase avidity. Distinguishing between benign and pathological uptake is critical. Currently there are no UK guidelines for evaluating incidental pituitary uptake on FDG-PET CT scans.
Methods
Retrospective analysis of PET-CT scans at a UK single centre. 88 patients with 'pituitary' mentioned in scan report (January 2017-June 2024) were identified. 20 patients excluded (5- known pituitary tumours, 5- pending investigations, 9- other centre, 1- deceased).
Results
68 patients (mean age 71.6 years; median age 70.5 $\pm$ 13.5 years) (25% females). Secondary imaging- performed in 48/68 patients: (23- MRI Pituitary, 21- CT Head, 3- MRI Head, 1-CT Pituitary) Mean uptake in pituitary incidentaloma: 20.620 $\pm$ 4.819 (range: 4.8 - 57.2), median 31.0 $\pm$ 26.2. Mean uptake in all cases of positive secondary imaging (pituitary adenoma + other pathologies including malignancy): 16.743 $\pm$ 3.799, median 31.0 $\pm$ 26.2 (range: 4.8 - 57.2). Mean uptake in normal secondary imaging: 4.659 $\pm$ 0.262 (range: 2.9 - 9.1), median 6.0 $\pm$ 3.1. Significant difference in SUVmax value ($P < 0.001$) between pituitary incidentaloma vs normal imaging, and in all pathology on secondary imaging vs normal imaging.

Primary malignant condition:

Condition	Patients
Dermatological	n =19 (27.9%)
Respiratory	n =9 (13.2%)
Otolaryngological	n =4 (5.9%)
Urological	n =1 (1.5%)
Endocrine	n =1 (1.5%)
Non-malignant disease	n =8 (11.8%)
Haematological	n =26 (38.2%)

Secondary imaging results:

Results	Patients
Pituitary macroadenoma	n =6 (12.5%)
Pituitary microadenoma	n =3 (6.3%)
Metastatic disease	n =1 (2.1%)
Neurological spread from primary malignancy	n =1 (2.1%)
Indeterminate nodule	n =1 (2.1%)
Osmotic demyelination syndrome	n =1 (2.1%)
Pituitary macroadenoma + metastatic disease	n =1 (2.1%)
Normal	n =34 (70.8%)

Conclusion
We propose that a cut-off SUVmax value of 4.75 (100% sensitive, 61.8% specific) could be used to differentiate between physiological versus non-physiological uptake in the pituitary fossa.

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P203

When a pituitary tumour is not a tumour: inflammatory pituitary lesions - a case series

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Introduction
Pituitary adenomas account for 90% of sellar parasellar lesions. Inflammatory pituitary lesions are rare and can mimic tumours, creating diagnostic challenges. This case series presents five patients referred to our centre as pituitary tumour but were non-tumour inflammatory process mimicking a tumour radiologically. Two had pituitary sarcoidosis, two granulomatosis with polyangiitis (GPA), and one lymphocytic hypophysitis.
Cases
• 57-year-old man with fever, weight loss and hypopituitarism; MRI revealed sellar mass. CT scan showed hilar lymphadenopathy, suggesting sarcoidosis or lymphoma. Following rapid vision loss, intravenous methylprednisolone (neurology and respiratory input) led to vision restoration and lesion shrinkage. At 12 months, on methotrexate, patient remains well.
• 49-year-old woman with acute vision loss and bitemporal hemianopia referred by ophthalmology; pituitary MRI showed large sellar lesion compressing optic chiasm. Urgent decompression and histology confirmed granulomatous lesion; lymph node biopsy revealed sarcoidosis. She was treated with high-dose steroids.
• 50-year-old woman with idiopathic orbital sclerosis causing persistent headache, not responding to azathioprine. Progressively enlarging sellar lesion elevating optic chiasm, MRI features indistinguishable from adenoma. Surgical decompression confirmed lymphocytic hypophysitis.
• 53-year-old male with panhypopituitarism; MRI showed atypical cystic-solid lesion. He was recently diagnosed with GPA, and systemic treatment started. The sellar lesion regressed with high-dose corticosteroids.
• 44-year-old woman with worsening retro-orbital headaches and hypopituitarism; MRI showed sellar lesion, with differentials of sarcoidosis or metastasis. Severe dyspnea and an enlarging pulmonary lesion led to lobectomy which confirmed necrotizing granulomatosis; cANCA-PR3 positivity indicated GPA. Treatment with pulse cyclophosphamide therapy led to lesion shrinkage.
Conclusion
Inflammatory disorders of varying aetiology can affect the pituitary gland. Timely specialist MDT involvement can guide appropriate treatment decisions. Pituitary MRI reports in isolation can be misleading, and therefore a detailed history and assessment is mandatory in patients with rapid-onset visual loss, atypical systemic symptoms and unusual MRI findings.

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P204

Analysis of qualitative patient feedback on a novel pilot model for group education for nutritional/dietary advice and symptom management in neuroendocrine neoplasms (GEDNEN course) in an ENETS centre of excellence

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Background
Group education as a concept in healthcare has mainly been used in diabetes mellitus and health optimisation pre-surgery. In Sheffield ENETS centre of excellence, we have piloted a bespoke course focussing on nutritional and dietary education for patients with neuroendocrine neoplasms (NEN).
Aim
To ascertain if the GEDNEN course is suitable and/or improves general accessibility to experts with specific analysis of qualitative patient feedback.
Methods
This 4-hour face-to-face pilot session included patients with small bowel and non-functional pancreatic NEN group with stable disease. Initial overview was delivered by a NEN consultant, treatments and side effects by a specialist NEN nurse, nutritional needs overview with a practical session delivered by three specialist NEN dietitians. Bespoke and validated pre- and post-course questionnaires were completed by all participants.
Results
There were 15 participants: 10 had small bowel NEN and 5 had pancreatic NEN. 80% of participants had not received specialist education previously. 99% reported they were extremely happy or happy to be in a group session. 100% found the group education useful, with 40% being extremely happy and 60% happy with this. 86% learnt something new. 92% were extremely happy or happy to ask questions freely in the group session. 100% of participants reported that they would attend another group education course in the future. After the course 73% felt extremely happy or happy to manage their NEN related nutritional needs. All patients felt more empowered to manage their NEN dietary health after the course and would recommend the course.
Conclusion
Qualitative feedback in this pilot has shown 100% of patients found it useful and would attend again with 86% learning something new. Overall, the participants thought that the speakers were knowledgeable, very clear and gave an informative and excellent presentation. This is an acceptable form of education.

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P205

The utility and efficiency of cannulated prolactin levels prior to clinical review

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Introduction
Prolactin is assessed for a multitude of reasons in primary and secondary care. Wider testing with non-specific symptoms often yields ambiguous results requiring further confirmation of pathology. Defaulting to magnetic resonance imaging of the pituitary gland has the potential to increase demands on radiology services, waiting times and may result in the detection of incidental findings.
Methods
We organised cannulated prolactin levels for all patients referred with elevated prolactin up to 5000 mU/L without known cause (dopamine antagonist medication, known pituitary disease). We conducted a retrospective review of all data for 12 months on our day unit. All prolactin results, including community referral data, were carried out on the Roche platform with manufacturer reference ranges.
Results
95 patients had cannulated prolactin during the study period (11 male, 84 female). 72 (75%) of these were tested from triage without clinical review. 72% patients were deemed to have a stress response and 62 patients (65%) were able to avoid imaging. Median time from referral to cannulation and diagnostic outcome was 21 days (6-452) and 27 days (12-459) respectively. The minimum prolactin level on cannulation associated with microadenoma was 537 mU/L affirming the need to avoid hard cut-offs at triage for a suspected stress response. Variance in cannulated levels was lower than in those deemed to have a stress response but there was little appreciable difference in variance from primary care referral prolactin data.
Conclusion
Cannulated prolactin levels used straight from referral without clinical review can improve clinic efficiency and reduce patient waiting times whilst also reducing overall cost. Variability of prolactin on repeated community testing may prove useful in future. Further studies looking at other reliable prognostic factors could help narrow testing criteria to ease service pressure.

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P206

Endocrine features of optic pathway gliomas in neurofibromatosis type 1

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A 23-year-old woman was diagnosed with neurofibromatosis type 1 (NF-1) at the age of 7 years. She presented with café au lait patches, axillary freckling, Lisch nodules, and plexiform neurofibromas on her left cheek and in the left paraspinal muscles. Genetic testing confirmed the PV c.7348C > T (Arg2450Ter). At the age of 12 years, MRI identified asymptomatic bilateral optic pathway gliomas (OPGs) affecting both optic nerves and the chiasm. Unusually, over the next decade, imaging showed no signs of progression, and her vision remained unimpaired, with no signs of proptosis or nystagmus. She developed normally through puberty, experiencing menarche at age 14 years, with consistently regular menstrual cycles. However, secondary amenorrhea emerged at the age of 22 after sudden weight gain. At this time MRI of the pituitary gland revealed the existing OPGs and additional exophytic cystic nodules involving the retro-chiasmatic structures, including the hypothalamus. A pelvic ultrasound ruled out polycystic ovaries and showed a thin endometrium. Her hormonal profile indicated hypogonadotropic hypogonadism, with luteinising hormone (LH) at 4.6 IU/l, follicle-stimulating hormone (FSH) at 6.6 IU/l, and oestradiol below 89 pmol/l, with no deficiencies in other pituitary hormones (confirmatory dynamic testing yet to be performed). Endocrine dysfunction due to hypothalamic extension affects 10-20% of individuals with OPGs and NF-1. Notably, the location of the tumours is a stronger predictor of complications than treatment history. Current management guidelines for OPGs depend on whether the tumours affect or threaten vision. OPG glioma occurs in ~15% of patients with NF-1 but is symptomatic 40% of the time. Given these insights, it is important for endocrine teams to recognise the association between OPG, endocrine dysfunction and, more rarely, hypothalamic dysfunction as part of the comprehensive care required for the patient with NF-1.

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P207

Panhypopituitarism associated with recurrent severe anaemia, 15 years post partum. a case report

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Introduction
Panhypopituitarism is characterised by inadequate production of anterior pituitary hormones. It has diverse etiologies, including Sheehan syndrome, defined as anterior pituitary gland necrosis, following significant bleeding post-partum, and may present with non-specific symptoms, making diagnosis challenging. This case captures a delayed diagnosis of panhypopituitarism in a young woman with resultant comorbidities and reduced quality of Life (QOL), and highlights a scenario of both acute and chronic presentation of Sheehan's syndrome, which is rare in available literatures.
Case Presentation
A 37-year-old female teacher, with fatigue, low mood, recurrent blackouts of 11 years duration; and weight loss of 20 kg over five years. Symptoms were severe leading to resignation from her job. She reported postpartum haemorrhage in her last confinement,15years earlier, which was eventually managed definitely by hysterectomy, after receiving 30 units of blood transfusions. Within a 5-year interval, she received multiple blood transfusions, for recurrent anaemia of unknown origin, until referral to Haematology clinic, from where she was referred to endocrinology clinic. Examination revealed a young woman with sallow look, flat affect, pale, bilateral pitting pedal oedema and Positive Woltman sign PR:80b/m, BP:79/56mmhg. PCV 29.5%, TSH: 3.893uIU/ML (0.38-5.33) **FT3**:1.68pg/ml (3.6-6.8), **FT4** 0.63pg/ml (7.2-16.4), **ACTH**: < 5.00 (0-46 pg/ml), 30M cortisol 22.12 (240-618), **60M cortisol** 18.77 (240-618), 90M cortisol 20.36(240-618), **Prolactin** 1.22ng/ml (3.3-26.7). **Brain MRI**: Empty sella turcica A diagnosis of **Panhypopituitarism** (2^0 adrenal insufficiency, 2^0 hypothyroidism, hypoprolactinaemia, growth hormone deficiency) secondary to Sheehan's syndrome, was made. She was commenced on Hormone replacement therapy, and counselled on fertility options. Symptoms resolved, with improved QOL, in 8 months of therapy.
Conclusion
There should be a high index suspicion of panhypopituitarism, especially in treatment-resistant anaemia, among women of reproductive age.

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P208

Unusual presentation of lymphocytic hypophysitis with isolated secondary adrenal insufficiency and normal appearance of pituitary gland in MRI

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Introduction
Lymphocytic hypophysitis is a rare clinical condition with incidence as low as 1 in 9 million cases. It occurs commonly in women during pregnancy and symptoms may continue postpartum. Often, imaging of sellar masses is not sufficient to diagnose the condition and needs undertaking of good clinical history.
Case report
42-year-old female with history of 14 weeks postpartum admitted to emergency with c/o worsening tiredness and fatigue which lasted for few days. She has a history of vomiting associated with headaches for about 7 months. She is not able to breast feed her child and has some menstrual spotting observed a week ago. On examination, she is thin built, and fair skinned with blood pressure of 110/70 mm Hg on lying down, pulse of 75 beats/min. There is absence of skin hyperpigmentation with no associated visual field deficit. Her rest of the examination is within normal limits. Her investigations revealed morning cortisol level of 60 nmol/l with serum Na- 123 mmol/l, serum calcium- 2.7 mmol/l, serum phosphate-1.5 mmol/l, Prolactin-128 miu/l, FSH-5.6 iu/l, LH- 4 iu/l, Oestradiol-819 pmol/l, fT3-3.2 pmol/l, fT4- 12.2 pmol/l, TSH-4.13 miu/l. She was started on IV fluids and hydrocortisone 100 mg IV stat followed by 50 mg intravenous 6^{th} hourly. She felt much better the next day with an improvement in her GI symptoms. Her MRI pituitary on admission revealed normal appearance of the pituitary gland.
Conclusion
Our case presented with clinical features of headaches and vomiting started towards third trimester pregnancy and continued postpartum with symptoms of isolated secondary adrenal insufficiency and normal MRI of pituitary pointing towards diagnosis of lymphocytic hypophysitis as most common cause. This is

unusual as classically LH may present with radiological evidence of pituitary enlargement with or without stalk thickening.

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P209

How can innovative technology improve medication safety for inpatients with arginine vasopressin deficiency?

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Arginine vasopressin deficiency (AVPD) is a disorder of the pituitary gland characterised by an inability to produce antidiuretic hormone (ADH), resulting in the production of large volumes of dilute urine. Untreated, patients with AVPD can develop life-threatening dehydration. Desmopressin is a synthetic form of ADH used to treat AVPD and is considered to be a life sustaining medication in this situation. Between 2009 and 2016 NHS England was made aware of four incidents where omission of desmopressin resulted in severe dehydration and death. In February 2016 NHS England issued a patient safety alert asking for all organisations providing NHS - funded care for treatment of AVPD to take action including: (1) identify if omission of desmopressin for the treatment of AVPD has or could occur (2) consider if immediate action needs to be taken locally. In 2018 the Society for Endocrinology published guidelines for the inpatient management of AVPD. At our organisation since 2016 we have done continuous quality improvement work using the 'Plan-do-study-act' cycle. We have had automated medication dispensing cabinets available (Omnicell®) since 2014 which allow all wards to have 24-hour access to desmopressin. When desmopressin is dispensed from the cabinet an email alert goes out to all endocrinologists in the hospital with the inpatient's details and location, so that they are aware of the admission. The same alert goes out to the nurse who accesses the desmopressin stating 'do not delay administration.' We are working to create an alert on the inpatient EPR so that when desmopressin is first prescribed the same alert is sent out to the ward nurses. Our work has led to a reduction in medication safety incident (DATIX®) reports relating to desmopressin (4 between 2015 and 2018 but none since 2022). We hope to roll out the same technology for other life sustaining medications.

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P210

Functional characterization of AIP gene variants causing gigantism

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Introduction
AIP (Aryl Hydrocarbon Receptor Interacting Protein) predisposes to young-onset growth hormone secreting adenomas. Mutations in the *AIP* gene are known to be associated with young-onset pituitary tumours. The pathogenicity of some *AIP* missense variants is unclear, and this is relevant for clinical genetic counselling.
Aim
This study evaluated the protein stability of *AIP* missense variants identified in patients to determine their pathogenic role.
Method
Site-directed mutagenesis performed using Agilent's QuikChange Kit. Functional evaluation of the *AIP* variants was done by cycloheximide chase assays in HEK293T cells transfected with wild type (WT) and the five *AIP* variants and subsequent immunoblotting. The results were analysed using a one-phase decay equation and the degradation constants of the AIP variants were compared to the WT AIP. We applied ACMG scores (pathogenic (P), likely pathogenic (LP), variant of uncertain significance (VUS), likely benign (LB), benign (B)) and Revel scores (suggesting pathogenic above 0.7). *AIP* variants were also analysed via computational protein stability prediction tools such as DDMut, mCSM and DUET.
Results
The results of the half-life experiments for five *AIP* variants showed that variant c.38T>A (p.I13N) and c.47G>C (p.R16P) have a shorter half-life, while variant c.68G>A (p.G23E) have intermediate and both c.325G>A (p.A109T) and c.491A>G (p.Q164R) variants resembled wild type with long half-lives. *In silico* predictions for all five variants (p.I13N ACMG:VUS, Revel 0.936), p.G23E (ACMG:B, Revel:0.816), p.A109T (ACMG:LB, Revel:0.457), p.Q164R (ACMG:LB, Revel:0.265) and p.R16P (ACMG:VUS, Revel:0.744)) were consistent with the results of the half-life experiment. The variants p.I13N and p.R16P, with shorter half-lives, have significantly higher degradation rates than WT and are predicted to affect protein stability by in silico prediction tools.
Conclusion
The phenotype of the patients, half-life data and in *silico predictions* confirm that the variants p.I13N and p.R16P are most likely to be pathogenic.

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P211

A case of metastatic neuroendocrine tumor with rare secretory evolution and hypoglycaemic crisis

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We present the case of a 69-year-old male with a rare progression of neuroendocrine tumor, initially presenting with hypoglycemia and ultimately leading to multi-organ failure. The patient, an ex-smoker with a history of alcohol use (80 units/month), was incidentally found to have a solid lesion in the pancreatic tail on CT during lung cancer screening. Referred to hepatobiliary team and underwent a distal pancreatectomy. Histology confirmed a well-differentiated neuroendocrine tumor, WHO stage 2, with a Ki-67 index of 10% and no secretory activity. Postoperative imaging showed no residual disease, and the patient recovered well, later developing type 2 diabetes, managed with metformin. Approximately six months post-surgery, the patient presented with hypoglycaemic collapse (blood glucose 1.7 mmol/l). Repeat imaging revealed recurrence in the pancreas and new hepatic lesions. MRI and biopsy confirmed recurrence of well differentiated neuroendocrine tumor with gross hepatic metastasis. Biochemical analysis showed a marked elevated C-peptide (3190 pmol/l) with paired serum glucose of 1.7mmol/l, corresponding with severe, refractory hypoglycaemia requiring continuous dextrose 20% infusion, diazoxide, and octreotide. Surgical intervention was not feasible due to metastatic disease. peptide receptor radionuclide therapy was considered keeping in view non-surgical neuroendocrine tumor but the patient succumbed to sepsis secondary to hospital-acquired infection. This case underscores the rare progression of a non-secretory neuroendocrine tumor into a secretory phenotype, a phenomenon not widely documented. It highlights the importance of ongoing surveillance for functional transformation in neuroendocrine tumors, even after initial presentation as non-secretory, and the significant challenges posed in managing metastatic insulinomas with high hypoglycaemic burden.

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Nursing Practice

P212

What are the barriers to successfully integrating a band 4 associate practitioner (AP) into an endocrine nursing team and how can they be addressed?

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Introduction
We have had an exciting opportunity over the last 6 months to welcome a non-registered AP within our large endocrine nursing team. This is an evolving role, and there are barriers that need to be addressed to ensure its success. Drawing on Benner's Novice to Expert framework and the Society for Endocrinology (SfE) Competency framework, we focused on supporting the AP's development within the team.
Methods
To support the AP, a structured framework was introduced based on the competency framework, which supported a novice transitioning into this role. Having recently

contributed to an aspect of the revised competency framework, I was able to incorporate my learning into the structure. Regular meetings and feedback helped support the change of team culture and the development of the role.
Discussion
I was keen to support the AP in our team, I have a strong interest in mentoring and supporting colleagues to reach their full potential. Feedback from the AP and the wider nursing team have been invaluable to overcome barriers. A barrier I underestimated was the change of culture and educating colleagues, this was overcome with a strong structure and support from the senior nursing team. The strong structure included adapting strategies suitable to the level of competence of the AP and regular meetings. An AP is rich in skills and time, resulting in a high level of patient care delivered with compassion and respect. The extended workforce has resulted in better patient experience and the patient values the continuity of care that an AP can offer. The band 4 role is becoming essential to the NHS workforce, ensuring structured support and resources are essential for success.

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P213

The role of endocrine specialist nurses in modern medicine

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The NHS is an evolving organisation facing huge challenges while still striving to provide best possible patient care. Our Endocrine Specialist Nurses (ESNs) are an integral part of endocrine services. They create links between endocrinologists, surgeons, patients and community services to ensure high quality care for all. A dedicated ESN clinic with direct access to an endocrinologist was set up. The aim was to ensure blood tests, medication titration and patient education were provided in a timely manner to ensure achieving good control. We reviewed the clinical journey of 7 patients who underwent a total thyroidectomy for Graves thyrotoxicosis. Length of stay post op ranged from 1 to 9 days (mean 4.5 days) All patients were discharged on Adcal-D3 Chewable tablets and Alfacalcidol capsules in addition to Levothyroxine. All patients were given an appointment with the ESN for follow up blood tests 3-7 days post op (mean 4.3 days). No patient required re-admission for hypocalcaemia. 5 patients achieved normal PTH and were weaned off both Adcal-D3 and Alfacalcidol and were normocalcaemic within 0-15 days (mean 5 days). 2 patients remained on Adcal-D3 and Alfacalcidol. All 7 patients achieved a normal freeT4 ranging from 14.3 pmol/l to 20.2 pmol/l (mean 17.3 pmol/l). 6 patients were on Levothyroxine 100 mg daily and 1 patient was on 125 mg daily. It took 5 to 13 weeks (mean 8 weeks) to confirm normal thyroid results. Patients were seen 3 to 6 times to achieve both stable calcium and T4 levels over a mean duration of 8 weeks. The ESN endocrine clinic has enabled us to:

- increase outpatient consultant appointment capacity by reducing the number of endocrine clinic follow-up visits.
- improve patient satisfaction, education and care due to direct access to endocrine team.
- reduce the burden on phlebotomy services.

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P214

PEI, PERT & NENs: the impact of PERT shortages and implications for practice

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>Maasberg *et al* (2017) 'demonstrated for the first time that nutritional status is an important independent risk factor for poorer survival' in those with neuroendocrine neoplasms (NENs): it is evident in up to 40%, and can 'increase risk of death 5-fold'. But there are many contributing factors, not least size, site, grade and differentiation of primary tumour, presence / absence of metastases and /or associated hormone syndromes, alongside the impact of treatments. Somatostatin analogs (SSAs) are a first-line treatment for many well-differentiated NENs: however, they can inhibit pancreatic function, which can lead to PEI. The first clinical study to recognise the association between somatostatin-analogs (SSAs) and development of PEI, was published in 2010 by Saif *et al*. The recommended treatment for PEI, is Pancreatic Enzyme Replacement Therapy (PERT). However, for the last 12 months, there has a significant UK supply shortage. A national Patient Safety Alert was issued May 2024 - with clinical guidance being informed by the Pancreatic Society of Great Britain & Ireland (PSGBI) Position Statement June 2024. Current advice centres around dietary modification and dose reduction, if possible, but this not without impact. In a recent survey undertaken by Neuroendocrine Cancer UK, 67% (94/140) of those with NEN-related PEI, have experienced difficulty in obtaining PERT: 37% being without any at all on at least one occasion: with 39% going without eating - if low/no supply available. More than 50% have reported increase in symptoms: 35% diarrhoea, bloating, 10% pain/cramping, 6% weight loss (>3 kgs) and 46% reporting a direct impact on mental health, with 13% unable to leave the house due to symptoms. It is therefore important that HCPs are aware of issues and the guidance available to help support those with NEN-related PEI. Resource links to guidance and advice are available at https://www.neuroendocrinecancer.org.uk/-pert-update/

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Reproductive Endocrinology

P215

Probiotics mitigates ovarian angiogenic disturbance in letrozole-induced PCOS

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Background
Among metabolic/endocrine diseases affecting women in the reproductive years, polycystic ovarian syndrome (PCOS) is well documented as the leading cause of female infertility and several complications including dyslipidemia, and cardiomorbidities, among others. Vascular endothelial growth factor (VEGF) is a proangiogenic marker which plays a crucial role in endothelial dysfunction, including ovarian dysfunction. Probiotics are gut microbiome that regulate metabolic health via epigenetic modulation of histone. Nevertheless, the present study was designed to investigate the beneficial effect of probiotics on aberrant ovarian angiogenesis in a PCOS rat model.
Materials and methods
Eight (8)-week-old female Wistar rats were randomized into four groups, $n = 5$/group. Letrozole administration of 1 mg/kg (*p.o*) for three weeks induced PCOS, thereafter the animals were treated with $2x10^7$ CFU (*p.o*) of probiotics for six weeks.
Results
Rats that received letrozole exhibited obesity, ovarian weight gain, hyperandrogenism, hypoestrogenism, multiple ovarian cysts, and demonstrated an increased level of anti-Mullerian hormone. Animals in this group also demonstrated ovarian lipid accumulation (triglyceride), inflammation (NF-κB, TNF-α), lipid peroxidation (MDA), metabolic stress (elevated corticosterone) and elevated angiogenic factor (VEGF), as well as decreased level of antioxidant defense (NrF2), and HIF-1a. Similarly, a significant decrease in Mfn2 was observed while HDAC2 was significantly elevated when compared with the control group. Interestingly, treatment with probiotics significantly reversed these ovarian metabolic, biochemical and morphological changes.
Conclusion
Collectively, the present result suggests that probiotics ameliorate ovarian angiogenesis with subsequent improvement of ovarian function in the PCOS model. This beneficial effect of probiotics is accompanied by modulation of Mfn2 and suppression of HDAC2.

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P216

Probiotics ameliorates hypothalamic amenorrhea in a rat model of PCOS

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Background
Polycystic ovary syndrome (PCOS) is a common endocrinometabolic disorder affecting women of reproductive age, and is often characterized by hormonal

imbalances, irregular menstrual cycles, and infertility. Hypothalamic amenorrhea has been documented as frequent manifestation of PCOS and is attributed to the cessation of menstruation due to disruptions in the hypothalamic-pituitary-gonadal axis. Beneficial microorganisms, Probiotics, are well known known for improving metabolic health, and have shown promise in restoring hormonal balance as well as enhancing fertility. In this study, we hypothesize that probiotics would ameliorate hypothalamic amenorrhea by modulating hypothalamic kisspeptin and reducing inflammation in a rat model of PCOS.
Methods
Eight (8)-week-old female Wistar rats were grouped into four with $n = 5$. Letrozole administration (1 mg/kg, *p.o.*) for 3 weeks induced PCOS, thereafter the animals were treated with probiotics (2 x 10^7 CFU, *p.o.*) for six weeks, while control animals received distilled water.
Results
The present findings revealed that PCOS animals were characterized by impaired insulin sensitivity, hyperinsulinemia, ovarian dysfunction with evidence of disrupted steroid hormone levels (testosterone/17β-Estradiol) and cystic follicles as well as hypothalamic lipid accumulation, elevated inflammatory markers (NF-kB/TNF-α) and antioxidant depletion (GSH/NrF2), which are accompanied by decreased level of kisspeptin. Nonetheless, administration of probiotics reversed these pathological alterations by enhancement of hypothalamic kisspeptin and suppression of inflammatory response.
Conclusions
Altogether, the present results demonstrated that probiotics significantly ameliorated hypothalamic amenorrhea by mitigating hypothalamic lipid accumulation, suppressed inflammation, and replenished antioxidants. Crucially, probiotics enhanced hypothalamic kisspeptin levels, a key regulator of reproductive function, highlighting their potential as a therapeutic strategy for restoring ovarian function in PCOS.
Keywords
Amenorrhea; hypothalamus; inflammation; Kisspeptin; PCOS; Probiotics.
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P217

The immunomodulatory features of MSC cells derived from human umbilical cord: an in silco based analysis

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Umbilical-Cord mesenchymal stem cells (UC-MSCs) have shown a defined role in regeneration of potential parts of the body through their capability of trilineages differentiation and secretion of immunomodulatory molecules. Also, the physical contact of UC-MSC with immune cells plays critical roles in mediating immunomodulation which create a regenerative microenvironment for tissue repair. In this study, we carried out a bioinformatic analysis of previously published gene expression datasets (two human datasets GSE147114 and GSE220781) (Mishra, Sevak *et al*. 2020, Zhou, Cai *et al*. 2024) to identify the downregulated genes in umbilical cord blood derived MSC (UCB-MSC) and umbilical cord tissue derived MSC (UCT-MSC) cells with their biological processes and pathways. Differentially expressed genes (DEGs) were generated using GE02R while functional enrichment was performed in GSEA and IntAct. The study analysed two human GEO datasets GSE147114 and GSE220781, 1168 and 2428 down-regulated genes were found, respectively. Among these genes, 133 common genes were identified by Venn diagram analysis. GSEA analysis of common genes revealed that these genes were assigned to immune response as well as significantly enriched in translocation of ZAP-70 to Immunological synapse pathway. IntAct interaction analysis showed that Zap70 interact with several genes are associated with the T cell receptor signalling pathway and predominantly linked to immune response. Overall, the featured genes could be exploited as biomarkers to identify immunoregulatory activity of UC-MSCs and thus contributes to MSC-based therapies for various inflammatory diseases.
Reference
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P218

Response to kisspeptin reveals recovery of hypothalamic dysfunction in a woman with reversal of congenital hypogonadotrophic hypogonadism (CHH) with a heterozygous GnRHR inactivating variant

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Congenital hypogonadotrophic hypogonadism (CHH) is a rare genetic disorder with central hypogonadism and pubertal failure. While CHH reversal is rarely reported in women, we present a case of CHH reversal in a woman with a heterozygous *GnRHR* mutation highlighting kisspeptin's role in assessing hypothalamic function. A 15-year-old girl presented with primary amenorrhoea and incomplete puberty. Due to high BMI, clinical hyperandrogenism and insulin resistance, she was initially diagnosed with polycystic ovary syndrome (PCOS) and treated with combined oral contraceptives (COC) resulting in breast development. A aged 21, she remained amenorrhoeic off COC. Her blood tests indicated hypogonadotrophic hypogonadism (HH): LH 0.2 IU/l, FSH 0.3 IU/l, oestradiol <92 pmol/l. She had a normal sense of smell and a normal MRI, leading to a revised diagnosis of CHH. A heterozygous pathogenic variant in the *GnRHR* gene was identified. COC was changed to hormone replacement therapy (HRT) due to hypertension. At 32, off HRT, she remained amenorrhoeic, but her hormonal profiles improved: LH 5.0 IU/l, FSH 8.3 U/l, oestradiol 162 pmol/l. Ultrasound showed normal ovarian morphology with an endometrial thickness 5.8mm. Following a 20 kg weight loss on a GLP-1 agonist, GnRH and kisspeptin challenge tests demonstrated increased LH and FSH responses. She subsequently resumed regular menstrual cycles (oestradiol 800 pmol/l). CHH was diagnosed based on primary amenorrhoea, HH and a *GnRHR* variant. A single heterozygous mutation is typically insufficient to cause CHH suggesting possible oligogenicity. Her robust response to kisspeptin indicated hypothalamic responsiveness, which is inconsistent with CHH suggesting CHH reversal, reported in 20% of cases with *GnRHR* variants. The elevated kisspeptin response compared to healthy women is consistent with decreased hypothalamic function, which could indicate Female Obesity-Related Hypogonadism. This case highlights kisspeptin's utility in assessing hypothalamic function, diagnosing CHH and identifying reproductive recovery.
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P219

Association of bisphenol a (BPA), advanced glycation end products (AGEP), kisspeptin 1 (KISS 1) & melatonin (MT) with PCOS

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This study aims to provide associations of BPA, AGEs, Kisspeptin, and Melatonin with PCOS. The study included 133 PCOS and 65 control females. We measured serum BPA, AGEs, kisspeptin, and melatonin. Statistical differences were derived using Mann-Whitney U, ROC curve, and Spearman's correlation tests. Serum BPA levels were quantified in 109 PCOS and 45 controls. PCOS had significantly higher serum BPA (32.82 vs 21.27 ng/ml, $P < 0.05$). Phenotype D had BPA levels lower than controls. The AUC was 0.7, with sensitivity and specificity ranges 61-62%. The levels of AGEs were quantified in 83 PCOS and 40 controls. The mean levels of AGEs were significantly higher in PCOS (12.08 vs 4.79 ng/ml; $P = 0.0001$). A positive correlation was observed between AGEs and BMI ($r= 0.225$, $P < 0.05$). The AUC was 0.63, with sensitivity and specificity of 58-60%. Serum kisspeptin levels were quantified in 133 PCOS and 65 controls. Serum kisspeptin concentrations were higher in the PCOS (98.34 vs 57.02 pg/ml; $P = 0.00074$). Phenotype D showed the most significant difference in the kisspeptin levels (130.22 pg/ml; $P = 0.00066$). A negative correlation was observed between kisspeptin and testosterone ($r=-0.230$, $P < 0.05$). The AUC in PCOS was 0.6, with sensitivity and specificity between 62-65%. Phenotype D showed an AUC of 0.728. Serum melatonin levels were quantified in 110 PCOS and 54 controls. Melatonin concentrations were higher in the PCOS (106.08 ± 50.47 vs 50.32 ± 46.34 pg/ml; $P < 0.05$). The hyperandrogenic PCOS showed the most significant differences in melatonin ($P < 0.00001$). A positive correlation was observed between melatonin and LH in the phenotype D ($r = .961$, $P = 0.0001$). The AUC value for hyperandrogenic PCOS was >0.8. None of the

markers are strongly associated with PCOS as a whole. However, melatonin seems a good (AUC >0.8) marker for hyperandrogenic PCOS and kisspeptin for non-hyperandrogenic PCOS, underscoring the significance of our work.

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P220

Study on the effects of 5-alpha reductase inhibitor on hormones and semen parameters in men

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Introduction
5-ARi is a drug used to improve urinary symptoms in men. Recently, it has been widely used in low doses to prevent and improve hair loss in men. This medication is known to affect sexual function, including decreased libido. However, it is still controversial whether it has a direct effect on trying to get pregnant. The purpose of this study was to evaluate whether this drug affects hormonal and semen parameters in men.
Method
The subjects were men who visited our hospital and underwent prenatal testing between September 1, 2023, and August 31, 2024. FSH, estradiol, testosterone, and semen parameters (semen volume, sperm concentration, motility, progressive motility and strict morphology) were compared between patients who had taken 5-ARi for more than 3 months (group I, $n = 107$) and those who had not taken 5-ARi before the test (group II, $n = 107$). Patients with diseases such as azoospermia, chromosomal abnormalities, and varicocele were excluded. Additionally, cases of taking drugs other than 5-ARi were also excluded.
Result
There was no difference between the two groups in age ($P = 0.645$). It was confirmed that there was no difference in the concentrations of FSH, estradiol, and testosterone between the two groups ($P = 0.364$, 0.278, 0.353). Additionally, there were no significant differences in semen volume, sperm concentration, motility, progressive motility and strict morphology between the two groups ($P = 0.494$, 0.383, 0.184, 0.349, 0.825).
Conclusion
There was no difference in sperm production-related hormones and male hormones between the group that used 5-ARi and the group that did not. And it was confirmed that there was no significant difference in semen parameters. Although large-scale studies will need to be conducted in the future, in this study, the administration of 5-ARi is thought to have no effect on attempts to conceive in men of childbearing age.

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P221

Virilization post menopause: the impact of testosterone secreting fibrothecoma

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Background
Ovarian fibrothecomas are rare, typically benign tumours that can cause postmenopausal virilization, such as hair loss. Most are hormonally inactive, with functioning tumours representing less than 0.1% of ovarian neoplasms.
Case presentation
A 78-year-old postmenopausal woman with a background of chronic kidney disease, hypertension, and hyperlipidaemia was referred to the endocrinology clinic for male pattern androgenic alopecia and spontaneous bruising over six months. Her initial blood tests showed significantly elevated free testosterone at 279 (1-20 pmol/l) and total testosterone 14.3 (0.101-1.42nmol/l). Her observations showed BP 172/73 mmHg, HR 79 bpm, height 159 cm and weight of 60 kg. Clinical examination found signs of androgenic pattern hair loss and revealed a noticeably deep voice. Further biochemical investigations showed LH 52.4 (2.4-12.6iu/l), FSH 76.3 (3.5-12.5iu/l), 17b-oestradiol 119 (114-332 pmol/l), prolactin 520 (102-496miu/l), TSH 2.03 (0.27-4.2mu/l), T4 13.8 (11.1-22 pmol/l), DHEA 0.8 (0.9-2.1umol/l), cortisol 323 (133-527nmol/l), androstenedione 4.8 (2-5.4nmol/l) and urine cortisol 34 (0-486nmol/d). An adrenal CT scan revealed no evidence of adrenal hyperplasia or masses. Due to strong suspicion of an ovarian tumour, a transvaginal ultrasound was performed but failed to detect any pelvic mass. However, an MRI of the pelvis identified a 4.2 cm solid mass in the right adnexal region. The patient underwent laparoscopic bilateral salpingo-oophorectomy, removing a 6 cm tumour from the right. Histology confirmed an ovarian cellular fibroma with luteinized cells, hyaline plaques, and a 2mm nodule of Leydig cell hyperplasia. The left ovary had a smaller fibroma with stromal hyperplasia and hyperthecosis. Following surgery, the patient's virilism symptoms resolved, and her total testosterone levels normalized to <0.1nmol/l.
Conclusion
This rare case of bilateral testosterone-secreting fibrothecomas underscores the need to recognize signs and symptoms of virilization as potential indicators of ovarian pathology in postmenopausal women, even without abnormal bleeding, and highlights the importance of timely diagnosis and intervention.

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P222

ZIP9, a zinc importer and membrane androgen receptor, is essential for female reproduction in zebrafish

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Introduction
Androgens mediate their physiological functions via the classical nuclear receptor, and androgen receptor. However, recent studies have identified a new plasma membrane (and non-genomic) androgen receptor- the Zn(II) channel, ZIP9. Indeed, ZIP9 has been reported to regulate oocyte growth and maturation in the teleost ovary. However, how ZIP9 impacts the reproductive hypothalamic-pituitary-gonadal (HPG) axis remains unknown.
Aim
To utilise CRISPR/Cas9 deletion of ZIP9 to determine how ZIP9 modulates HPG axis gene expression and reproductive function.
Methods
CRISPR/Cas9 was used to generate a global zebrafish *zip9* knock-out line. Key reproductive gene expression in adult *zip9*$^{-/-}$ zebrafish was determined via qPCR with a minimum $n = 3$ in triplicate.
Results & Conclusion
In wild-type (wt) adult male and female zebrafish, *zip9* mRNA expression was detected in the brain (hypothalamus and pituitary), testis, ovary and liver. Interestingly, ZIP9 was highly expressed in the ovary and liver, suggesting potential sexual dimorphism in ZIP9 expression levels in these tissues. In the brain of male *zip9*$^{-/-}$zebrafish, *gnrh3* expression was lower than wt while the expression of *gnrh2* showed no change. In female *zip9*$^{-/-}$, *gnrh3* expression was higher than wt while *gnrh2* was unchanged. *zip9* deletion resulted in lower expression of *ar, esr*, and *lhr* in both the ovary and the testis. Interestingly, *fshr* expression was significantly lower in the ovaries of *zip9*$^{-/-}$females compared to wt, this contrasted with zip9-/- testes where *fshr* expression was significantly increased in comparison to wt. Mating studies demonstrated *zip9*$^{-/-}$ females were infertile while the males remained fertile, suggesting an essential role of Zip9 in female reproduction. Differences in key HPG axis gene expression provide a mechanism underpinning the sexual dimorphic roles of ZIP9 in zebrafish reproduction. This may suggest the role of Zip9 in influencing the physiological processes involved in follicle development and maturation in female zebrafish.

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P223

Characterizing the G-protein activities of the membrane androgen receptor, ZIP9

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Androgens mediate their physiological functions via the classical nuclear receptor, AR. However, recent studies have identified a new plasma membrane (and non-genomic) androgen receptor- Zn(II) channel, termed ZIP9. Androgen activation of ZIP9 has been proposed to activate 'non-classical' testosterone signalling pathways, with ZIP9 coupling to G-proteins. However, how androgens and zinc interplay to modulate G protein activation remains unclear. This study therefore aimed to determine how androgens and zinc regulate ZIP9-dependent G protein coupling. HEK293 cells expressing ZIP9 were utilised to assess ZIP9-dependent cAMP production using a live kinetic cAMP reporter- GloSensor. Cells were pre-treated with 10uM forskolin for 10 minutes, then treated -/+ 100nM testosterone, 20uM zinc or testosterone/zinc co-treatment. cAMP production was monitored for up to 30 minutes. Experiments were conducted with a minimum of $n = 3$ in triplicate measurements. Treatment of HEK293 cells expressing ZIP9 with either testosterone or zinc alone, or in combination had no effect on cAMP production. However, pre-treatment with forskolin modulated the

basal activity and Gi-coupling of ZIP9, with dose-dependent effects observed on the level of inhibitory activity dependent on ZIP9 plasmid concentration transfected. Western blot analysis showed that plasmid concentration correlated with the amount of ZIP9 expressed. At high Zip9 plasmid concentration and expression, treatment with either testosterone, zinc or a combination of both, abrogated cAMP production, suggesting ligand-gated Zip9-Gi-activation. Interestingly, at low plasmid concentration and low expression, a single treatment with zinc or testosterone did not affect basal ZIP9-Gi coupling. However, combined testosterone and zinc treatment enhanced cAMP production, suggesting a potential switch to Gs coupling. These data indicate that ZIP9 displays dual Gs/Gi coupling that is dependent on its expression level and ligand concentrations. This may have important implications in the regulation of reproductive disorders with high androgens including PCOS, with the ovarian roles important next steps to explore.

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P224

Influence of hypothyroidism on erectile dysfunction in patients at a south american hospital

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Introduction
Thyroid gland (TG) disorders play a significant role in increasing the prevalence of sexual dysfunction in men.
Objective
To investigate the incidence of reduced thyroid hormone levels in patients with erectile dysfunction (ED) and assess the impact of hypothyroidism on sexual parameters.
Materials and Methods
The study was conducted at the University Hospital of Los Andes with men aged 18 to 60 presenting ED symptoms. Evaluations included physical exams, rectal examinations, and hormonal blood profiles [total testosterone, sex hormone-binding globulin (SHBG), prolactin (PRL), estradiol (E2), thyroid-stimulating hormone (TSH), and free thyroxine (T4)]. Ultrasound studies of the scrotum and prostate were also performed. Data analysis was conducted using Excel 2013.
Results
Subclinical hypothyroidism was detected in 21% of patients with ED, while overt hypothyroidism was found in 13%. Elevated prolactin levels were observed in 8% of all ED patients and in 14% of those with hypothyroidism. Low total and free testosterone levels were identified in 71% of patients overall and in 34% of those with clinical or subclinical hypothyroidism. SHBG, estradiol, and prostate abnormalities were not implicated in ED.
Discussion
The study reveals that hypothyroidism significantly contributes to hormonal imbalances, especially reduced testosterone and increased prolactin, which are linked to the severity of ED. These findings underscore the importance of thyroid function in maintaining male reproductive health.
Conclusion
Thyroid hormone levels are essential for male sexual health. Hypothyroidism was found to be a key factor in lowering sexual hormone levels and exacerbating ED severity ($r = 1.5$, $P < 0.005$).

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P225

Sexual dysfunction in patients with type 2 diabetes and its variables

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Introduction
Sexual dysfunction is prevalent among patients with type 2 diabetes mellitus (T2DM), though clinical and epidemiological data vary with sample size. This study aims to assess the clinical and epidemiological characteristics of sexual dysfunction in men with T2DM at the Hospital de los Andes in Mérida, Venezuela.
Objective
To evaluate the prevalence and characteristics of sexual dysfunction in men with T2DM.
Materials and Methods
This non-interventional, continuous screening study involved 100 men with T2DM, aged 59 $\pm$ 11 years, conducted from January to December 2022. A sexological survey was administered using the International Index of Erectile Function (IIEF-5), alongside measurements of glycosylated hemoglobin (HbA1c) and total testosterone levels. Pharmacodopplerography of penile vessels was performed for patients with erectile dysfunction (ED). Group comparisons were made using the Mann-Whitney U test, considering $P < 0.05$ as statistically significant.
RESULTS
The prevalence of sexual dysfunction was as follows: decreased libido (81%), erectile dysfunction (ED) (72%), delayed ejaculation (24%), premature ejaculation (35%), retrograde ejaculation (7%), and infertility (9%). A significant difference in total testosterone levels was found between patients with and without decreased libido (6.4 vs. 13.5 nmol/l, $P < 0.001$). Higher HbA1c levels were observed in patients with low libido (9.7 vs. 6.3, $P < 0.001$), and patients with ED also had higher HbA1c levels (10.3 vs. 7.1%, $P < 0.001$). No associations were found between carbohydrate metabolism and premature or retrograde ejaculation. Only 11% of patients actively sought medical consultation for sexual dysfunction.
Conclusion
Men with T2DM show a high prevalence of sexual disorders linked to metabolic decompensation and diabetes duration. Hypogonadism significantly contributes to decreased libido, complicating clinical detection of these disorders, highlighting the need for screening programs for effective management.
Keywords
type 2 diabetes, sexual dysfunction, erectile dysfunction, testosterone, libido, glycosylated hemoglobin.

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P226

Qualitative and quantitative evaluation of semen in patients with type 2 diabetes at a south american hospital

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Introduction
With the increasing need for reproductive planning among aging men, particularly those developing type 2 diabetes mellitus (T2DM), it is essential to study the effects of this condition on ejaculation quality.
Objective
To evaluate the quality of ejaculation in men diagnosed with T2DM.
Materials and Methods
This comparative cross-sectional study included 100 men with T2DM and 50 age-matched controls without T2DM, aged 35 to 45 years, at the Hospital Universitario de los Andes in Mérida, Venezuela, during 2022. Semen parameters were analyzed alongside levels of hemoglobin A1c and total testosterone. Differences between groups were considered statistically significant at $P < 0.05$.
Results
The prevalence of normozoospermia was significantly higher in men without T2DM compared to those with the condition. Men with T2DM exhibited a significantly higher prevalence of oligoasthenoteratozoospermia, bacteriospermia, and anti-sperm antibodies, with a notable trend towards increased leukospermia ($P = 0.0031$). Significant differences were observed between the two groups regarding the sperm count per milliliter of ejaculate, viable sperm percentage, motility (A+B), and normal sperm morphology, all favoring men without T2DM. Total testosterone levels were significantly lower in men with T2DM. Furthermore, when comparing hemoglobin A1c levels in men with T2DM based on their sperm morphology (normozoospermia versus pathozoospermia), those with normal spermatogenesis had significantly lower hemoglobin A1c levels ($P = 0.002$).
Conclusion
T2DM negatively impacts the quality of ejaculation, leading to a decline in quantitative indicators. Ejaculation quality is associated with bacteriospermia and inflammatory processes in the genital area. Additionally, carbohydrate metabolism derangement correlates with poorer ejaculation quality indicators.

Keywords
type 2 diabetes mellitus, ejaculation quality, sperm parameters, hemoglobin A1c, testosterone.

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P227

The effects of weight loss on hypothalamic dysfunction in a woman with polycystic ovary syndrome (PCOS)

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Background
Polycystic ovary syndrome (PCOS) is the commonest endocrinopathy in reproductive-aged women. Hypothalamic neuroendocrine dysfunction contributes to the pathogenesis of PCOS. Specifically, gonadotrophin releasing hormone (GnRH) activity is increased, favouring luteinising hormone (LH) secretion, leading to ovarian hyperandrogenism and oligo/anovulation. Herein, we describe changes in reproductive hormone concentrations, LH pulse frequency, and the response to kisspeptin (used to probe hypothalamic GnRH function) in a woman with PCOS and obesity, before and after weight-loss via bariatric surgery.
Case
A 23-year-old woman with PCOS achieved 30 kg weight-loss (BMI 39 to 25 kg/m^2) following sleeve gastrectomy. Three months after bariatric surgery, she regained spontaneous menstrual cyclicity with improvements in her cycle length (from 139-420 days pre-operatively to 42-84 days post-operatively). Changes in her endocrine profile post progesterone-induced withdrawal bleed are presented in **Table 1**. Intriguingly, her LH pulse frequency, reduced from 1 to 0.5 pulse/hour post-bariatric surgery, aligning more closely to a physiological follicular phase LH pulse frequency. Pre-operative kisspeptin-54 stimulation resulted in a peak LH response of 12.9 IU/l, which was reduced to 6.6 IU/L post-operatively.

Table 1: Pre- and post-operative reproductive hormones

	Pre-bariatric surgery	Post-bariatric surgery	Reference range
Luteinising hormone (IU/l)	9.6	1.9	-
Follicle stimulating hormone (IU/l)	4.5	4.5	0.6-9.0
Testosterone (nmol/l)	1.9	1.0	0.0-2.0
Sex hormone binding globulin (nmol/l)	11	29	30-100
Anti-Müllerian hormone (pmol/l)	64.7	40.7	-

Discussion
PCOS is associated with an abnormal increase in hypothalamic GnRH function. Obesity exacerbates PCOS, but is associated with decreased LH concentrations. In this woman with PCOS and obesity, increased LH pulse frequency normalised with weight loss. Additionally, her increased gonadotrophin response to kisspeptin also normalised, consistent with an obesity-related component of her hypothalamic dysfunction. This case highlights the potential of kisspeptin in evaluating the impact of obesity and neuroendocrine dysfunction in women with PCOS.

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P228

Investigating fertility in a down syndrome mouse model

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Background
Down syndrome (DS) is caused by the triplication of chromosome 21, and it is considered one of the most common chromosomal abnormalities. The genetic overload leads to several endocrine irregularities, including early onset of obesity and diabetes, hypothyroidism, and reduced fertility. While the onset and progression of puberty is similar to that of the general population, fertility, particularly in males, has been reported to be reduced in individuals with DS. Here we aim to investigate possible mechanisms behind the reduced fertility using a mouse model of DS.
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 data from Dy1Tyb colony was obtained from our in-house animal facility management system database and compared to wild-type (C57BL/6J) public data from the Mouse Phenome Database (Jackson Laboratory). Animals were sacrificed at 30 weeks of age. Gonads were weighed, and then stained with hematoxylin and eosin and analysed with QuPath software. Plasma hormones and markers involved in fertility and sexual maturation were analysed by ELISA and RT-qPCR.
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. Interestingly, female mutants showed a trend of producing less litters with smaller litter sizes compared to male mutants. The ovaries of female Dp1Tyb mice were similar in weight to that of wild-type, but showed fewer antral follicles and corpus lutea. In contrast, the testicles from Dp1Tyb males showed significantly reduced weight compared to WT, but similar morphology.
Conclusion
Our data shows that Dy1Tyb animals replicate the phenotype seen in the human population with lower fertility observed in both sexes, suggesting that this would be a good model to investigate mechanisms of infertility in DS.

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P229

Ethnic disparities in clinical outcomes among women undergoing IVF treatment

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Background
Significant disparities exist in maternal health and fertility care among ethnic groups, influenced by both biological factors and the intersectionality of systemic injustices and socioeconomic factors. Notably, Black women experience higher rates of infertility but are underrepresented among those undergoing IVF treatment.
Aim
To investigate differences in pre-treatment prognostic factors and IVF treatment responses among women of White, Asian, Black, Mixed, and Other ethnic backgrounds.
Method
In this retrospective, multicenter cohort study, data from 11,120 women who underwent IVF between 2007 and 2023 across ten centres in the UK and Poland were analysed. Primary outcomes included live birth rate (LBR) after fresh embryo transfer, with multivariable logistic regression adjusting for age, BMI, and primary cause of infertility. Ethical approval: 23/HRA/2849.
Results
The distribution of ethnic groups was as follows: White (72.3%, $n = 8{,}258$), Asian (17.9%, $n = 1{,}995$), and Black (2.6%, $n = 284$). Asian women (34.1 years) were younger at treatment initiation ($P < 0.0001$) compared to White (34.7 years) and Black women (35.1 years). Black women had a higher BMI than White women (26.8 vs. 25.0 kg/m^2; $P < 0.001$). Although Black (15.3) and Asian (16.1) women had a lower antral follicle count before treatment compared to White women (17.6), there was no significant difference in the number of mature oocytes retrieved. Black women were almost 50% less likely than White women

to achieve a live birth (OR 0.54, 95% CI [0.36 to 0.78]) even after adjusting for age, BMI, and primary infertility cause. Biochemical and clinical pregnancy rates were similarly lower for Black women, however miscarriage rates did not significantly differ.

Conclusion

The less favourable pre-treatment prognostic factors observed in Black women did not fully explain the differences in LBR. The impact of ethnicity on IVF outcomes is multifaceted, and further research is essential to understand the causes of these disparities in clinical outcomes.

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P230

Molecular changes in diabetic placentas; a systematic review of high-throughput data

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Diabetes during pregnancy is associated with short- and long-term health complications for both mother and offspring, such as cardiometabolic diseases, that are possibly linked to changes in placental development and function. High-throughput experiments can help uncover disease mechanisms, but there is no consensus on the specific molecular changes that occur in diabetic placentas. We conducted a systematic review of the literature to identify commonalities and thus determine which pathways are most frequently affected by maternal diabetes. A systematic literature search was conducted in PubMed to identify studies that performed high-throughput experiments comparing placental tissue or cells from diabetic and uncomplicated pregnancies. Screens were conducted on all types of high-throughput molecular methodologies, however due to limited published studies in other areas, only studies examining changes in protein and RNA level were included in subsequent analyses. Annotation conversion to gene names was performed in g:Convert to identify commonly dysregulated RNA and protein levels and g:GOST was used for functional profiling of individual study datasets and of RNAs and proteins list with same directional changes. From the 56 studies initially identified, the majority ($n = 41$) investigated protein ($n = 12$) or RNA abundance ($n = 29$) in gestational diabetes mellitus (GDM). A total of 15 common differentially abundant proteins (DAPs) and 414 differentially expressed genes (DEGs) were identified in at least two separate studies, with 8 DAPs and 189 DEGs exhibiting a consistent directional change. Functional profiling of individual studies' list and the list of 189 DEGs, demonstrated that pathways associated with coagulation, MAPK, Wnt, IGFBP, TGFB signalling, and several immune and vascular processes were consistently altered in GDM placentas. This study identified key molecular and cellular changes that occur in GDM placentas. Whilst further research is required, the identified changes could serve as therapeutic targets to improve maternal and fetal outcomes in GDM.

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P231

Infertility in women with hyperprolactinemia: a clinicians' blindspot

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Background

Hyperprolactinemia, characterised by elevated prolactin levels, can disrupt ovulation, and menstrual cycles and lead to infertility in women. Despite its implications for reproductive health, there is a limited exploration of infertility issues among affected patients, as highlighted by current NICE guidelines (CG156).

Objective

This pilot audit aimed to assess the burden of infertility in female patients with hyperprolactinemia and to investigate barriers to exploring infertility within this population.

Methods

A retrospective audit was conducted on 78 women diagnosed with hyperprolactinemia from a total of 613 patients identified through electronic records at The Royal Liverpool Hospitals. Data collected included demographics, prolactin levels, causes of hyperprolactinemia, presenting symptoms, and management options.

Results

The median age of participants was 37 years. Pituitary microadenomas were the most common cause of hyperprolactinemia (36%).21% of women presented with infertility concerns. Many (57%) women with no presenting diagnosis of infertility and incidental hyperprolactinemia, lacked discussion on fertility status during their consultation. Amongst women whose prolactin levels normalised, 20% successfully restored fertility, highlighting the need for better fertility discussions during consultations.

Conclusion

This pilot study reveals significant barriers to exploring infertility in women with hyperprolactinemia, suggesting that clinicians might not be routinely addressing fertility concerns. Effective communication and updated guidelines are necessary to ensure that fertility issues are appropriately identified and managed in this population.

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P232

When supplements mislead: elevated testosterone level in a patient on high dose biotin

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A 39-year-old-lady was referred to the endocrinology clinic after presenting to her GP with lethargy, where routine bloods found raised testosterone 5.5 nmol/l (Ref range 0.3 - 1.2) and free androgen index 7.9% (Ref 0.3 - 4.4), with LH <1.5 IU/L and FSH 2.4 IU/l. Otherwise, SHBG, prolactin, TSH and IGF-1 levels were normal. Her menses were regular and she did not have hirsutism, female pattern hair loss, acne, overt virilisation, Cushingoid features or weight loss. A thorough medication history revealed consumption of high dose biotin (10g/day for the past 3 months), leading to a suspicion of biotin induced immunoassay interference. Biotin was discontinued and testosterone levels normalised (0.8 nmol/l) a month later with normal LH (9.2 IU/l) and FSH (5.7 IU/l). DHEAS, androstenedione and 17-OHP levels were normal upon testing following discontinuation, but not tested prior. Biotin interference on immunoassay is widely reported for thyroid function, parathyroid hormone, troponin, proBNP and progesterone assays, however not as widely reported for testosterone. Interference in competitive immunoassays is found to take place when biotin is taken at supra-physiological dose. Adequate Intake (AI) for biotin in adults is 30 mcg/day, but can be obtained over-the-counter at higher doses as a purported supplement for nail and hair growth. Biotin's half-life is 2 hours, and is fully excreted in 5 half-lives. Biotin should be withheld for at least 1-3 days before testing testosterone as the half-life is dependent on the dose and frequency of intake, especially if it is taken ≥ 5 mg/day. It can be further prolonged in renal impairment as it is renally excreted. This case demonstrates the importance of careful drug history taking in female patients with elevated testosterone prior to proceeding with unnecessary investigations, especially in the absence of clinical features of hyperandrogenism.

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P233

Impact of clinical hyperandrogenism on anxiety and depression in PCOS: results from the DAISy-PCOS study

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Introduction
Polycystic ovary syndrome (PCOS) affects 10% of women and is characterized by hyperandrogenism. Women with PCOS have been reported to have an increased risk of depression and anxiety. We aimed to determine prevalance of anxiety and depression in a large cohort of women with PCOS and the impact of hyperandrogenism on these measures.
Method
We prospectively recruited 726 women with PCOS, diagnosed according to the Rotterdam criteria (2003) from 10 centres in the UK & Ireland. The median age was 30 years (IQR: 26–34), 24.2% (n = 169/699) were non-White, and 76.7% (n = 524/683) were overweight or obese. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression (scores >7 considered abnormal). Logistic regression models were used to identify factors that adversely impact mental health.
Results
Among participants, 69.3% (n = 473/682) had symptoms of anxiety, while 35.9% (n = 245/682) had symptoms of depression. Anxiety was associated with self-reported alopecia (OR: 2.3, 95% CI: 1.6–3.4, $P < 0.001$), clinician-assessed alopecia (OR: 1.8, 95% CI: 1.2–2.8, $P = 0.007$), and self-reported hirsutism (OR: 1.7, 95% CI: 1.1–2.7, $P = 0.021$). Both self-reported (aOR: 2.2, 95% CI: 1.5–3.3, $P < 0.001$) and clinician-assessed alopecia (aOR: 1.8, 95% CI: 1.2–2.8, $P = 0.009$) remained significant, after BMI adjustment. For depression, self-reported alopecia (OR: 1.8, 95% CI: 1.3–2.5, $P < 0.001$), weight-related issues (OR: 2.5, 95% CI: 1.6–3.9, $P < 0.001$), and menstrual irregularities (OR: 1.7, 95% CI: 1.0–2.9, $P = 0.048$) showed significant associations. However, only self-reported alopecia remained significant (aOR: 1.7, 95% CI: 1.2–2.4, $P = 0.002$), following BMI adjustment. Acne and acanthosis nigricans, did not significantly affect anxiety or depression.
Conclusion
These results demonstrate that hyperandrogenism, particularly hirsutism and alopecia, play a significant role in the increased prevalence of anxiety and depression in women with PCOS. This underscores the importance of mental health screening for the care of women with PCOS.

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P234

Low protein diet may alter embryo survival and lipid metabolism in mice

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Background
Low dietary protein content has been linked to causing altered lipid metabolism, as well as affecting developmental trajectory of offspring if fed during the periconceptional period, increasing their risk of developing non-communicable diseases in adulthood. Until now, effects of poor maternal or paternal diet have been investigated individually and not in combination. However, a parental combinatorial assessment would have more clinical relevance as both parents would likely be consuming the same diet prior to conception.
Methods
Male and female 8-week-old C57BL/6 mice were fed either a control normal protein diet (NPD; 18% casein) or an isocaloric LPD (LPD; 9% casein) for a minimum of 8 weeks. Mice were mated in a 2x2 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 on embryonic (E) day 1.5 (E1.5) for the collection and culture of preimplantation embryos in a time-lapse system (Embryoscope). RNA was isolated from parental liver and gonadal adipose. Following reverse transcription to synthesize cDNA, qPCR was carried out to determine the difference in relative gene expression between diets.
Results
Though not statistically significant, a 25% reduction in the numbers of embryos reaching the blastocyst stage was observed in the LL diet group when compared to the NN, NL and LN groups. In paternal tissue, liver Cpt1a, adipose Acacb1 and Fasn expression were significantly upregulated following LPD. In maternal tissue, liver Igf1 expression was significantly downregulated, whereas adipose Fasn was significantly upregulated.
Conclusions
Our data indicates that when both parents consume the same sub-optimal LPD, the impact on embryo development is greater than for either parent alone. Sex-specific changes to expression of genes involved in lipid metabolism were observed in both liver and adipose tissues of parents.

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P235

Prevalence of cardiometabolic risk in polycystic ovary syndrome (PCOS): insights from an interim analysis of the DAISy-PCOS cohort

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Introduction
PCOS affects at least 10% of women and is associated with an increased cardiometabolic risk and higher prevalence of hypertension, hyperlipidaemia, insulin resistance and type 2 diabetes in population-based studies. The metabolic burden of PCOS traverses the lifespan of women with PCOS. We describe the metabolic characteristics of the UK-wide prospective multi-centre DAISy-PCOS dcohort.
Methods
We prospectively recruited 726 treatment-naïve women with PCOS in the UK and Ireland. All fulfilled the Rotterdam criteria for diagnosis; median age was 30 (IQR: 26-34) years, body mass index (BMI) 31.1 (25.1-38.4) kg/m^2, 23.3% had non-white ethnicity]. Participants underwent standardised assessments including body composition analysis, fasting bloods and oral glucose tolerance test (OGTT) with insulin and glucose measurements at 0, 30, 60, 90 and 120 minutes after 75g glucose load. Metabolic syndrome was defined using the Adult Treatment Panel (ATP) III criteria. Dysglycaemia included those with diabetes (fasting glucose ≥ 7.0mmol, 2hOGTT glucose ≥11.1, Hba1c ≥48mmol/mol) or a diagnosis of prediabetes defined by the American Diabetes Association (ADA) criteria. The ADA defines prediabetes as impaired fasting glucose between 5.6 and 7mmol/l and HbA1c > 38mmol/mol.
Results
At least one criteria for dysglycaemia was present in 25% [n=166/654] of participants with available glucose parameters (IFG [n=68/662], impaired glucose tolerance (IFG) [n=67/654], HbA1c >38mmol/mol [n=102/654]). Type 2 diabetes was diagnosed in 2.6% [n=17/654] of participants. A pre-existing diagnosis of hypertension and dyslipidaemia was self-reported by 4.4% [n=32] and 6.9% [n=50] respectively. Following phenotyping 18.4% had blood pressure measurements greater than 130/85mmHg, 45.5% had evidence of dyslipidaemia and 63% of participants had a waist circumference exceeding 88 cm. Overall, the prevalence of metabolic syndrome in this cohort was 16.9%.
Conclusion
Our analysis demonstrates a high prevalence of cardiometabolic risk factors present in this prospectively recruited cohort of young women with PCOS.

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P236

Endothelial-to-mesenchymal transition in primary HUVECs from gestational diabetic pregnancies

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Background
Gestational diabetes mellitus (GDM) affects approximately 14% of pregnancies globally, and is associated with endothelial dysfunction, congenital heart defects

and the risk of long-term cardiometabolic complications in offspring. Endothelial-to-mesenchymal transition (EndMT), the transdifferentiation process of endothelial into mesenchymal cells, occurs in normal cardiac development. We hypothesise that altered EndMT may explain some vascular complications in GDM; therefore, the impact of a GDM environment on EndMT was assessed using human umbilical vein endothelial cells (HUVECs) to model the fetal endothelium.
Methods
Commercial HUVECs were treated with TGF-β1 or TGF-β2 alone (10 ng/mL) or in combination (+) with IL-1β (10 ng/mL) for 6 days (n = 3-6). Primary HUVECs isolated from non-GDM (n = 6) and GDM pregnancies (n = 5) were characterised using flow cytometry and EndMT was induced using TGF-β2 (10 ng/mL) + IL-1β (10 ng/mL) for 6 days. Endothelial and mesenchymal markers were measured using RT-qPCR and immunocytochemistry and EndMT signalling components were assessed using RT-qPCR.
Results
In commercial HUVECs, TGF-β2 + IL-1β were optimal for EndMT induction. Non-GDM and GDM HUVECs co-expressed CD31 and VE-Cadherin (98.57 ± 0.23% and 99.59 ± 0.14%, respectively), confirming their endothelial phenotype. Treatment of primary HUVECs with TGF-β2 + IL-1β induced morphological changes, reduced expression of endothelial genes, *PECAM1*/CD31, *VWF* and *CDH5*/VE-Cadherin ($P < 0.05$), and increased expression of mesenchymal genes, *TAGLN* (Transgelin) and *NT5E* ($P < 0.05$). Similarly, TGF-β2 + IL-1β reduced VE-Cadherin ($P < 0.01$), VWF ($P < 0.01$) and increased Transgelin protein expression ($P < 0.0001$) in primary HUVECs. However, no differences were observed between non-GDM and GDM. Expression of *TGFB2* and the TGF-β receptor-1 (*TGFBR1/ALK5*) were lower in GDM HUVECs treated with TGF-β2 + IL-1β, compared to non-GDM ($P < 0.05$).
Conclusions
EndMT can be induced in non-GDM and GDM HUVECs using TGF-β2 + IL-1β. In GDM HUVECs, although EndMT was not altered, reduced *TGFB2* and *TGFBR1* may be linked to other functions of endothelial TGF-β signalling, such as proliferation/migration, and should be investigated further.

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Thyroid

P237

Unexpected thyrotoxicosis: the ustekinumab connection

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A 34-year-old patient was referred to the endocrinology department after a routine blood test revealed an overactive thyroid. Initially, he received Adalimumab for Crohn's disease, but when this proved ineffective, his treatment was changed to Ustekinumab in December 2023. His past medical history includes Crohn's disease and anxiety. He has no family history of thyroid disease. He reported worsening palpitations, feeling hot with increased breathlessness on exertion. On clinical examination, his observations were: height 182 cm, weight 73.9 kg, BMI 22.1, blood pressure 144/77, heart rate 83 beats per minute. His pulse was regular on examination and there was a mild tremor on outstretched hands. There was no sign of proptosis or ophthalmoplegia and there was no swelling of the neck. His heart sounds were normal and there were no added murmurs. Initial thyroid function tests showed a TSH 0.01 mu/L (0.27-4.2), T4 44.2 pmol/l (11.1-22), thyroid peroxidase antibodies 210 iu/ml (0-34) and positive thyroid receptor antibodies 3.5 iu/L (0-3.3). He was commenced on carbimazole 20 mg and prn propranolol which was then reduced to 10 mg daily following improvement in symptoms and thyroid function tests. Post commencing carbimazole his thyroid function tests have improved to TSH < 0.01 mu/l, T4 level 24.4 pmol/l. He is currently under routine endocrinology follow-up for on-going surveillance. Ustekinumab is a monoclonal antibody targeting interleukin-12/23 used in the treatment of psoriasis and inflammatory bowel disease. Ustekinumab's inhibition of Th1/Th17 pathways may disrupt the Th1/Th2 balance, leading to the production of thyroid autoantibodies. Limited long-term data exist on its thyroid effects, with only two previously reported cases of ustekinumab-associated thyrotoxicosis. In conclusion, this case underscores the importance of early identification and treatment, as well as the need for further research into this association.

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P238

Risk to pets belonging to patients receiving radioactive iodine treatment for thyrotoxicosis: conflicting patient information

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Background
Radioactive iodine (RAI) has been used for the treatment of thyrotoxicosis for over 80 years. In the United Kingdom (UK), over 50% of adults own a pet. Therefore, the number of patients requiring information about RAI exposure risk to animals is likely to be significant and warrants research. Patients report receiving inadequate/conflicting information from internet searches and consultations regarding this issue. This study aimed to assess the information provided in patient information leaflets about RAI treatment for thyrotoxicosis regarding precautions around pets.
Methods
A convenience sample of patient information leaflets concerning the use of RAI for the treatment of thyrotoxicosis was obtained from an internet search using the search term 'radioactive iodine treatment patient information' followed by each National Health Service Trust name. Leaflets were examined for information regarding precautions around pets.
Results
Thirty-five leaflets were found representing thirty-three RAI treatment centres and two national bodies in the UK (England, Scotland, Wales). Only ten (28.6%) leaflets mentioned pets in the text. Six of these leaflets (17.1%) mentioned that patients could have usual contact with pets after receiving RAI, one leaflet (2.9%) mentioned for further discussion, while the other three leaflets (8.6%) mentioned that precautions were required. The precautions mentioned in these three leaflets included avoiding close contact with pets, such as avoiding pets sitting on laps, and washing hands before preparing food for pets for the first few days after receiving a dose of RAI.
Discussion
This study demonstrated that less than a third of published patient information leaflets regarding RAI treatment for thyrotoxicosis mention precautions for pets. Those that do mention pets provide conflicting advice. Clear and consistent information concerning RAI precautions around pets is required to alleviate patient concern and aid informed choice regarding definitive treatment for thyrotoxicosis.

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P239

An interesting case of abnormal thyroid function tests due to THR-beta receptor mutation

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Introduction
Thyroid Hormone Resistance (THR) is a rare autosomal dominant condition of impaired sensitivity to thyroid hormone. We present an interesting case of thyroid receptor beta (THRB) resistance.
Case Report
A 54-year-old lady presented to the endocrinology clinic with abnormal thyroid function tests (TFTs). TFTs were done as part of the assessment for newly diagnosed atrial fibrillation. She was found to have raised Free T3 and T4 with thyroid stimulating hormone (TSH) in the high normal range. She was intentionally trying to lose weight through diet and exercise. She denied any other hyperthyroid symptoms. She has a history of hypertension, osteoarthritis, and Barrett's oesophagus. She reported that her father had thyroid receptor problems. Over the year, her free T3 was between 7.8-11.3 pmol/l (range- 3.5-6.5), free T4 between 29.3- 37.8 pmol/l (range- 11.5-22.7), and TSH between 0.7-3.14 miU/L (range- 0.49-5.23). She had negative thyroid receptors and anti-thyroid peroxidase antibodies. Because of her family history, she was referred for genetic testing. Genetic testing using Sanger sequencing method which analyzed mutation surveyors of axons 7,8,9 and 10 of the THRB showed a heterozygous pathogenic missense variant for the THRB gene. Her TFTs were monitored, however, she was not started on any anti-thyroid medications. Genetic testing for this mutation in the family members was planned.
Discussion
Syndromes of reduced sensitivity to thyroid hormone encompass defects interfering with the biological activity of thyroid hormone. Approximately 170 mutated THRB variants have been reported. Monoallelic THRB variants cause autosomal dominant thyroid hormone resistance. There is a 50% risk of transferring pathogenic variants to children.
Learning Points
1. Obtaining a family history is crucial in diagnosing thyroid hormone resistance, as a positive family history will direct correct investigations and early diagnosis. 2. Correct diagnosis of thyroid hormone resistance prevents unnecessary treatment with antithyroid medications.

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P240

Hyperfunctioning papillary thyroid carcinoma: a case study

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Background
According to American Thyroid Association guidelines, hyperfunctioning thyroid nodules do not require cytology due to the low risk of malignancy [1]. Papillary thyroid carcinomas from the isthmus are rare with an incidence of 1.0-9.2% [2].
Case Report
A 26-year-old male presented with a 9-month history of hyperthyroidism, previously treated with carbimazole 15 mg/day. He had a strong family history of autoimmune thyroid disease; his mother had hypothyroidism and his brother was diagnosed with Graves' thyrotoxicosis. TSH receptor antibody was negative, TPO antibody 95 KIU/L (0-34), FT3 5.3 pmol/l, FT4: 16.0 pmol/l, and TSH: 2.3 mIU/ml while on antithyroid treatment. Initial thyroid ultrasound revealed multiple <5mm hypoechoic foci representing pseudonodules /spongiform nodules in both lobes (U2). On the right side of the isthmus was a bulging, well-defined, hypoechoic, solid 1.6 x 0.9 cm nodule, lobulated margins, trace peripheral vascularity, without microcalcifications (U2). There was no cervical lymphadenopathy. Based on these findings, carbimazole treatment was continued and routine follow-up ultrasound planned. On repeated ultrasound at 1 year, the isthmic nodule's dimensions were unchanged at 1.6 X 0.9 cm but due to interval change of microcalcifications and extrathyroidal extension, the nodule was re-stratified U3. Fine needle aspiration revealed features of papillary carcinoma. Total thyroidectomy was performed; histopathological examination confirmed a papillary thyroid carcinoma of classic type 1.7 x 1.5 cm; the excision margins were free of carcinoma and the specimen negative for lymphovascular or perineural invasion; background appearances were of chronic lymphocytic thyroiditis; no local nodal disease was detected. Post-procedure, thyrotoxicosis resolved and serum thyroglobulin was undetectable.
Conclusion
Papillary thyroid carcinoma is sporadic in the context of hyperthyroidism at presentation. In this case, scintigraphy assessment was impeded due to established carbimazole therapy at a relatively high maintenance dose. Routine ultrasound follow-up and re-evaluation were critical to accurate diagnosis and early treatment.

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P241

The effect of selenium on anti-tpo antibody serum levels in hashimoto's thyroiditis, systematic review and meta analysis

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Background
Selenium forms a significant component of seleno-proteins in the body. Seleno-methionine is integrated into proteins instead of methionine and acts as a storage pool. In proteins, the active form of Selenium is seleno-cysteine.in this review we aim to prevail the results of selenium effect on thyroid status in recent clinical trials. The systemic review aims to find out the correlation between supplementation of Selenium and anti-TPO antibodies and T4 levels in Hashimoto's Thyroiditis. Selenium supplementation decreases the level of anti-TPO antibodies. The supplementation of Selenium increases the level of T4 levels.
Methods
The mean and standard deviation (SD) of all 8 studies was were calculated. One of the researches had all the information in figures, and only the levels of anti-TPO antibodies and FT4 were obtained. Heterogenicity was estimated using I2.
Results
The p-value calculated for Anti-TPO by SPSS of the eight groups had a p-value of 0.142. The p-value calculated for T4 levels by SPSS of the five groups had a p-value of 0.239. The heterogenicity test was zero after the I2 test. The studies that were included in the systematic review were assessed by Prisma diagram and selected among the articles resulted from search keywords selenium and anti tpo and hashimotho thyroiditis on different data sources. All the participants were evaluated by sex, ages, duration of the study and the levels of anti tpo ab and thyroxin (t4) and then using SPSS software to deploy metanalysis in the systematic review.
Conclusion
in 6 of 8 studies it was a relation of selenium and thyroid status, whereas 2 studies were not. As We ran meta analysis on the data we realized that there is not significant desired effect from selenium on thyroid antibodies against previous metanalysis done by other researchers.

Keywords
Selenium, autoimmune thyroiditis, and anti-TPO antibodie
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P242

Failure of pulse methylprednisolone combined with oral steroids as well as thionamides and plasmapheresis to obtain remission in amiodarone-induced thyrotoxicosis

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Background
Amiodarone-Induced Thyrotoxicosis (AIT) is often difficult to treat despite several treatment modalities. We present a case of failure of medical treatment despite an initial improvement.
Case Presentation
A 24-year old man with a history of cyanotic heart disease (translocation of main arteries with failure of full correction of the defect) was admitted for cardiac assessment in view of qualification for possible heart transplant. History revealed about 13 kg weight loss over two months. He had been receiving amiodarone for at least a year. Investigations on admission revealed TSH < 0.005μIU/ml (0.27-4.2), FT4 > 7.7ng/dl (0.93-1.7), FT3 31.66pg/ml (2-4.4), consistent with severe AIT. Titres of all thyroid antibodies were negative, with no focal lesions on thyroid ultrasound. Amiodarone was stopped while thiamazole 20 mg tds and prednisone 40 mg od were started. After 10 days there was a fall of FT3 to 21.66pg/ml, but FT4 remained > 7.7ng/dl. Pulse methylprednisolone 500 mg iv twice a week was added. There was a fall in FT3 to 6.75pg/ml (FT4 7.58ng/ml), followed by a rebound increase in FT3 to 20.28 pg/ml (FT4 > 7.77 ng/ml). A decision was made to proceed to thyroidectomy, but in view of FT4 above upper assay limit, a course of plasmapheresis, combined with intravenous thiamazole (80 mg od) was instigated. Glucocorticoid treatment was continued. Following seven courses of plasmapheresis there was a fall of FT3 to 8.3 pg/ml, but FT4 remained > 7.77 ng/ml. Furthermore, the patient developed high temperature and sepsis (*Klebsiella oxytoca*) one day before planned surgery. He responded to meropenemum and vamcomycin. Successful thyroidectomy was performed seven days later (FT3 18.2 pg/ml, FT4 > 7.77 ng/ml before thyroidectomy). He remains stable on thyroxine 100 ug od.
Conclusion
Thyroidectomy is often the only treatment option in severe AIT and appears reasonably safe even in cases of cyanotic congenital heart disease.

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P243

Navigating the balance: risks of glucagon-like-peptide-1 receptor agonist and levothyroxine co-administration

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Introduction
An intrinsic relationship exists between the thyroid gland and diabetes mellitus, alongside their respective treatments. We report a patient with type 2 diabetes mellitus and hypothyroidism on levothyroxine who developed clinical (and biochemical) hyperthyroidism following the initiation of a subcutaneous semaglutide, requiring a dosage reduction in levothyroxine.
Case Report
A 56-year-old female with type 2 diabetes mellitus and hypothyroidism on 100 micrograms of levothyroxine is seen at the clinic. Her thyroid-stimulating hormone (TSH) level increased on two separate visits (4.80 → 11.30 mIU/l) five months apart, for which levothyroxine is increased to 125 micrograms (TSH 1.020 mIU/L five months later). Subcutaneous semaglutide is introduced to treat her body mass index of 41 kg/m^2 and HbA1c (7.3%). At follow-up, she demonstrated clinical and biochemical hyperthyroidism, with weight loss of 39 pounds, sweating, and palpitations (TSH < 0.005 mIU/l). Following a reduction of her levothyroxine to 100mcg, her symptoms abated and TSH normalised.

Discussion

The dosage of levothyroxine for hypothyroidism is weight-based; as depicted, with weight loss, the need for a potential decrease in the dosage, to prevent untoward hyperthyroidism, should be anticipated. This pathophysiological basis is not entirely understood but is believed to occur via two mechanisms: (1) changes in absorption from delayed gastric emptying; (2) secondary to weight loss imposed by semaglutide.

Date	TSH (mIU/l)	Levothyroxine (micrograms)	Subcutaneous Semaglutide
03/2023	3.7	100	N/A
07/2023	4.8	100	N/A
12/2023	11.8	100 → 125	N/A
05/2024	1.020	125	0.25 mg
10/2024	<0.005	125 → 100	0.5 mg

Conclusion

The relationship between the thyroid and diabetes mellitus is not entirely understood. Moreover, the medications used for either disorder appear to affect (positively/negatively) one another. Due to the scarcity of data, our case is presented to highlight this phenomenon and remind clinicians of the potential for iatrogenic hyperthyroidism in such a cohort.

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P244

East sussex healthcare NHS trust (ESHT) radioactive iodine treatment (RAI) outcome: a QIP review

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Introduction

East Sussex Healthcare NHS Trust started radioactive iodine treatment for benign thyroid disease following national training programme. QIP is to review the outcomes after RAI treatment and potential issues.

Data

128 patient's outcomes, at least completed six months following RAI treatment, were collected. 97 patients completed one year and 45 patients completed two years. Four patients' data are not available, one moved out of area, one was discharged early. 74.2% female, 25.7% were male. 57.8 % had autoimmune thyrotoxicosis, 33.6% of patient had toxic multinodular goitre and 8.6% had toxic adenoma.

Results

One patient became pregnant within four weeks of treatment, despite having discussion avoiding pregnancy and had negative pregnancy test on the day of RAI treatment. However, she decided to have termination of pregnancy on her own. Five patients needed steroid treatment; three patients had pre-planned steroid cover to reduce the risk of flare up of non-active thyroid eye disease. 2 patients needed steroid cover after developing new thyroid eye disease. However, all 5 patients did not have any further problem. One patient had second dose of RAI in ESHT RAI service.

Treated patients

	Treated hypothyroid %	Treated euthyroid %	Persistent thyrotoxicosis %
6 months	56.5	32.3	11.2
12 months	60.8	32	7.2
2yr	80	20	0

Outcomes depending on the cause:

	AIT 1yr	AIT 2yr	Toxic MNG 1yr	Toxic MNG	Toxic adenoma 1yr	Toxic adenoma 2yr
Euthyroid (%)	20	14.8	37	45.5	55.6	50
Hypothyroid (%)	66.7	85.2	63	54.5	44.4	50
Hyperthyroid (%)	13.3	0	0	0	0	0

Conclusion

After 2 years of follow up all patients were treated, hence not to consider repeat second dose of RAI at least for 2years. However, more patients' data would help to conclude that. Most of the patients with AIT would become hypothyroid and only 50-55% of Toxic adenoma/MNG patients became hypothyroid by 2yrs.

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P245

Hypothyroidism-induced reversible acute kidney impairment – A rare cause not to be forgotten

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Ms SV is a 27-year-old woman with a history of attention deficit hyperactivity disorder (ADHD). She was referred to the Endocrine team in October 2023 following an incidental finding of abnormal thyroid function tests. The blood test was done as part of the investigations for her alopecia. Her thyroid stimulating hormone (TSH) was significantly elevated at 241 mU/l, while her Free T4 was low at 1.1 pmol/l. Additionally, she was found to have impaired kidney function with an estimated glomerular filtration rate (eGFR) of 58 ml/min/1.73m^2, compared to her baseline eGFR of >90 ml/min/1.73m^2 from 2020. Due to the severe, yet asymptomatic hypothyroidism, Ms SV was started on levothyroxine 50 micrograms once daily by her general practitioner (GP). The dose was subsequently increased to 100 micrograms once daily. Her thyroid peroxidase antibodies were elevated at 53.9 kU/L (normal range: 0-34 kU/l), and her thyroid receptor antibodies were also raised at 3.8 IU/L (normal range: 0 - 0.9 IU/l), confirming a diagnosis of Hashimoto's thyroiditis. The absence of microalbuminuria suggested that her renal impairment was not due to intrinsic renal disease. As her thyroid function gradually normalised, her kidney function also showed improvement, as demonstrated in the table below. This case report highlights a rare cause of reversible acute kidney injury secondary to severe hypothyroidism, which typically resolves after appropriate treatment of the hypothyroidism. In this case, the full recovery of kidney function can take up to 10 months. By recognising the connection between severe hypothyroidism and acute kidney injury, unnecessary invasive investigations for kidney impairment can be deferred until the hypothyroidism is treated.

Outcomes depending on the cause:

Date	TSH (mU/l) normal range: 0.3-4.2	FT4 (pmol/l) normal range: 10-22	eGFR (ml/min/1.73m^2)
12/10/2023	241	1.1	58
29/01/2024	85	9.6	79
15/07/2024	25	12.2	89
18/09/2024	8.1	14.0	

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P246

Familial polyglandular deficiencies with no AIRE mutation: random occurrence or genetic predisposition yet to be discovered?

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Autoimmune Polyglandular Syndromes (APS) are rare disorders characterised by immune-mediated multi-organ dysfunctions. The three main subtypes, APS-1, APS-2, and APS-3 are distinguished by different patterns of endocrine involvement. Mutations in the autoimmune regulator (AIRE) gene on chromosome 21q22.3 that impair thymic immune tolerance causes APS-1, which is strongly associated with autoimmune hypoparathyroidism (90% of cases), chronic mucocutaneous candidiasis and adrenal insufficiency. It can also involve type 1 diabetes, hypothyroidism, pernicious anaemia, vitiligo, hepatitis, oophoritis and keratitis. Recent evidence suggests that existing diagnostic criteria may be inadequate, as not all patients with APS-1 exhibit classical features. We present a woman (index case) with chronic hypocalcaemia due to hypoparathyroidism since birth, type 1 diabetes from age 10 years and autoimmune hypothyroidism in her forties. Her younger sister also has chronic hypoparathyroidism with hypocalcaemia, and hypothyroidism. There is a family history of thyroid dysfunction in another sister, a brother, and their mother. These findings suggest a potential hereditary polyglandular deficiency pattern that does not fully fit the diagnosis of APS-1. It raises the possibility of either a non-classical/variant form of the syndrome, an unidentified gene mutation or a different type of polyglandular syndrome which is yet to be classified. It underscores the heterogeneity of APS, revealing gaps in our understanding of its genetic and phenotypic spectrum.

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Laboratory results:

	PTH (2.0 - 9.3) pmol/L	Parathyroid Antibodies	Adjusted calcium (2.20 - 2.60) mmol/L*	Urinary calcium Excretion Index (0.013 - 0.037) mmol/L	Vitamin D (50.0 - 125.0) nmol/L	Thyroid Peroxidase Antibody (< 35) IU/mL	Islet Cell Antibody	Anti-GAD antibody (< 5.0) U/mL	AIRE gene mutation
Index case	1.2 -3	Negative	1.86 - 2.19	0.052	79 - 99.6	> 1000	Positive	> 2000	Absent
Sibling case	1.5 - 3.2	Not tested	2.08 - 2.19	0.041	55.6 - 96.9	15 (< 35)	N/A	N/A	Awaited

*Prior to endocrine review. N/A, not applicable

P247

A patient with macroadenoma treated with teprotumumab for thyroid eye disease

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Thyroid eye disease (TED) management and treatment options have expanded recently to include multiple new monoclonal antibody treatments which are proving very effective. Teprotumumab is one such drug and is an anti IGF-1R monoclonal antibody. We report on the case of a 60-year-old female, diagnosed with Graves' Disease (GD) in 2014, for which she underwent a thyroidectomy in 2015 for definitive treatment. She suffered from severe TED. A pituitary macroadenoma was picked up in 2016 incidentally on an MRI of her orbits. The adenoma was non-functioning and serial scans had shown slow growth over 10 years. She was initiated on Teprotumumab in September 2022 for worsening TED. Prior to initiation, her bloods revealed a normal pituitary profile, including a normal IGF-1 of 19nmol/l. Due to growth of her adenoma, headaches, poor vision and unreliable visual field testing due to her TED, she was referred to Neurosurgery for trans-sphenoidal surgery. She was found to have an IGF-1 level of 83nmol/l in February 2023, further increasing to 104nmol/l in October. The elevated IGF-1 levels were assumed to be secondary to Teprotumumab, however the decision was made to further investigate to exclude underlying acromegaly. A growth hormone suppression test, an insulin tolerance test, pituitary profile and serial visual field tests performed were normal. After MDT discussion she had trans-sphenoidal surgery to remove her pituitary tumour in April 2024. Histology revealed a silent corticotroph adenoma. This case highlights the importance of understanding the mechanism of action of newer medication used to treat TED. Teprotumumab is a monoclonal antibody against IGF-1R. This results in high serum IGF-1 levels and can cause confusion in patients who have co-existing pituitary adenomas.

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P248

Apalutamide and refractory hypothyroidism

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Background
Apalutamide is known to cause hypothyroidism in 5-8% of people. Worsening of overt hypothyroidism is reported in 30% patients with pre-existing hypothyroidism. We report a case of worsening pre-existing hypothyroidism in a patient treated with Apalutamide.
Case Report
A 79-year-old male patient was referred to endocrine clinic for refractory hypothyroidism. He was diagnosed with prostate cancer in 2019 and had a long standing history of primary hypothyroidism treated with levothyroxine100micrograms daily. In March 2023, after being detected with metastatic prostate cancer, he was started on lifelong treatment with apalutamide. Preceding March 2023, he was biochemically euthyroid with normal TSH of 4.1 mU/l. However, his TSH elevated to 57 mU/L in April 2023 indicating worsening hypothyroidism. In response, levothyroxine dose was increased to 125 micrograms daily, but TSH remain elevated at 11.8mU/l despite his good compliance. Further increase in levothyroxine to 150 micrograms finally achieved biochemical euthyroidism with TSH level of 3.4mU/L
Conclusions
Apalutamide is non-steroidal, oral antiandrogen drug used in prostate cancer. Patients with pre-existing thyroid disorders are more prone to developing worsening hypothyroidism whilst on this therapy. Apalutamide increases the metabolism of levothyroxine by inducing uridine diphosphate-glucanosyltransferases which enhances the conjugation of levothyroxine with glucuronic acid, thereby promoting biliary excretion of thyroid hormones. This process reduces circulating thyroxine levels, leading to an elevation of TSH through a negative feedback mechanism. Hypothyroid patients on apalutamide may require a significant increase in their levothyroxine dosage to achieve biochemical euthyroidism, with some needing 2- to 3-fold increases. The impact of apalutamide on thyroid function is often underestimated, and regular monitoring of thyroid function tests is essential to adjust levothyroxine doses accordingly to maintain a euthyroid state.
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P249

Graves' disease relapse in mediastinal thyroid remnant, post radioactive iodine treatment

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We present a case of relapsing Graves thyrotoxicosis in a 58yr old lady who initially presented in 2005 with a large multinodular goitre with retrosternal extension. She had evidence of mild thyroid eye disease (TED) at the time. A total thyroidectomy was performed in 2014 due to recurrent relapses of thyrotoxicosis and poor compliance with carbimazole. Two years following thyroidectomy she developed thyrotoxicosis. Her thyroxine was stopped. A Technetium uptake scan showed a mediastinal thyroid remnant. She developed worsening TED with elevated TRAB at 26.4U/l. She was commenced on carbimazole again and referred to ophthalmology. Her TED stabilised and due to persistent thyrotoxicosis and at times non-compliance with carbimazole, decision was made to treat her thyroid remnant with radioactive iodine. She was given 524 MBq of radioiodine (I-131) in April 2024. Due to her previous TED this was covered with a one-week course of Prednisolone. One week following RAI treatment she presented to ED with chest pain. This was thought to be due to thyroiditis post RAI in her remnant, as all other cardiac investigation were negative. Her repeat TFT's showed a normal free T4 of 18 pmol/l, mildly elevated free T3 of 7 pmol/l and a suppressed TSH. She stopped carbimazole post RAI despite advice to continue. In August 2024 she presented again with weight loss and palpitations, free T4 29.8 pmol/l, free T3 9.1 pmol/l and a suppressed TSH. Carbimazole 15 mg was recommenced. This case illustrated challenges in the treatment of Graves in a mediastinal remnant. We are currently considering if she would benefit from a second dose of RAI.

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P250

Thyroid eye disease in primary hypothyroidism- a rare manifestation

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Introduction
Thyroid eye disease occurs in around one quarter of patients with Graves' hyperthyroidism. However, it is rarely associated with primary hypothyroidism. We describe a case of a patient with thyroid eye disease secondary to primary hypothyroidism.

Case report
A 50-year-old female with known primary hypothyroidism was referred to Ophthalmology and Endocrinology in May 2024 with symptoms of thyroid eye disease, which have been present for several months. She was diagnosed with primary hypothyroidism in 2012 and has been on levothyroxine since. She was smoking approximately 20-30 cigarettes daily at the time of referral. We reviewed her and organised thyroid function tests and a thyroid ultrasound. Her TSH came back as suppressed with normal free T4 and free T3 levels. TSH receptor antibodies and thyroid peroxidase antibodies came back as positive at 19.4 IU/L (reference range 0.0-0.9) and 190.6 IU/ml (reference range 0.0-9.0) respectively. Thyroid ultrasound came back as unremarkable. Her levothyroxine dose was reduced due to a suppressed TSH. Ophthalmology also reviewed her as an outpatient and diagnosed mild active thyroid eye disease. On examination, she had mild bilateral mild conjunctival injection, chemosis and mild exophthalmos. Ocular motility was not restricted but was painful. Diplopia was not present and visual acuity was normal. She was initiated on regular hydrocortisone and hyaluronic acid eye drops. Despite this, her thyroid eye disease progressed and she is now currently receiving weekly intravenous methylprednisolone.
Conclusion
As TSH receptor antibodies can also be present in euthyroid and hypothyroid patients, thyroid eye disease should always be considered as a differential. If suspecting possible thyroid eye disease in patients with hypothyroidism, it is advisable to check TSH receptor antibody levels and refer to Ophthalmology.

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P251

Transforming thyroid hormone analysis: a novel LC-MS/MS profiling method

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Thyroid hormones (TH) are vital for many biological processes, including development, growth, and metabolism. Despite the existence of numerous thyroid hormone metabolites (THM) with potential biological significance, research and clinical evaluation has been largely limited to the measurement of pro-hormone thyroxine (T4) and the active hormone triiodothyronine (T3) by immunoassays. These assays are not suitable for detecting multiple THM as their similarity leads to cross-reactivity, therefore more accurate quantification methodologies are required. We developed a novel liquid chromatography tandem-mass spectrometry (LC-MS/MS) method for an extensive panel of twelve THM, enabling investigation into the thyroid hormone metabolic pathway. We determined the quantification range and investigated pooled male serum (Merck) after the addition of a mixture of internal standards (T3, rT3, 3-T1, and T4, all $13C_6$). Extraction was optimised using an Evolute Express AX 30 mg SPE plate, and samples were analysed on a Waters Acquity with Xevo-XS on a Luna Omega 1.6µm Polar C18 column. Complete chromatographic separation of all twelve THM was achieved within a 7-minute method (T0, 3-T1, 3'-T1, 3,5-T2, 3,3'-T2, 3',5'-T2, T3, rT3, T4, TA2, TA3, TA4). Average recovery for nine THM was 101% (range 95.96-107.11%). Further optimisation is needed to improve recovery of thyroacetic acids (TA2, TA3, TA4). We were able to detect nine THM in pooled male serum. Our method provides a novel tool that will significantly advance THM research. Further optimisation and full method validation as well as determination of reference ranges in healthy populations is underway. This method will facilitate the simultaneous measurement of multiple THM to better understand TH metabolism in normal physiology and in thyroid disorders, leading to the potential development of THM signatures to support clinical diagnosis and management.

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P252

A case of thyrotoxicosis and heart failure: the high cost of non-adherence

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History
A 51-year-old man presented to the Emergency Department in February 2023 with shortness of breath, palpitations and tremor. He had a background of atrial fibrillation with rapid ventricular rate, anxiety, depression, asthma, excess alcohol consumption, and known a user of Heroin and Cocaine. He was diagnosed with worsening thyrotoxicosis on a background of known hyperthyroidism. He had been non adherent with his Carbimazole for the previous two weeks. He was discharged with Carbimazole and propranolol and counselled on the importance of adherence. In July 2023, he re-presented to the Emergency Department with breathlessness and was diagnosed with congestive heart failure.
Course of illness
When he re-presented, he stated that he had not been taking his medications for many months. An echocardiogram showed severe LV dysfunction. He was diagnosed with Decompensated HFrEF secondary to Thyrotoxicosis likely because of non-adherence to his medications. He was admitted and managed with diuretics, rate control and anticoagulation. He improved clinically and a follow up in cardiology clinic was arranged however, he did not attend this appointment. Subsequently, attended a nurse led heart failure clinic facilitated from prison. After further discussion, the cardiology team have planned to implant a CRT device for his heart failure. In October 2024, he belatedly attended his endocrine clinic appointment and has taken his Carbimazole regularly for the past 2 months, but the cardiac issues are permanent.
Conclusion and Points for Discussion
In conclusion, this case highlights the complex psychosocial factors contributing to adverse patient outcomes. This patient had a potentially preventable cause of heart failure; however, the treatment delivery was complicated by multiple factors. These include – treatment adherence, illicit drug use, unhealthy alcohol use, lack of social support and mental health diagnoses. When managing such patients it may be worthwhile to address these factors alongside the hyperthyroidism treatment.

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P253

Referrals for thyroid ultrasound from primary care to a tertiary centre: a review of clinical indications, outcomes, and follow-up

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Referrals for thyroid or neck ultrasound from primary care are commonly made for a wide spectrum of clinical presentations, many of which result in the identification of thyroid nodule pathology which is often incidental, and unrelated to patient symptomatology. A structured guideline with clear clinical indications for thyroid ultrasound from primary care is lacking. We aimed to assess the clinical indications, relevant ultrasound findings, and subsequent referrals for specialty review or follow-up investigations from thyroid ultrasound referrals to our centre from primary care. Preliminary analysis for referrals made from January to December 2022 revealed 224 thyroid ultrasounds performed; female $n = 196$ (87.5%); mean age 48 years (standard deviation 15.6). Average time from referral to imaging was 2.7 months. Referrals deemed appropriate for imaging as per local policy included a palpable nodule ($n = 28$, 12.5%), thyroid nodule on alternative imaging ($n = 16$, 7.1%), surveillance of known thyroid malignancy ($n = 4$, 1.5%). Referrals which were not indicated included hypothyroidism ($n = 30$, 13.4%), hyperthyroidism ($n = 13$, 5.8%), non-specific local symptoms ($n = 131$, 58.5%), previous history of thyroid benign nodules not requiring follow-up ($n = 41$, 18.3%), euthyroidism with TPO positive antibodies ($n = 14$, 6.3%). Ultrasound findings were normal in 33 patients (13.7%), with 44 (19.6%) showing a >/=1 cm U2 and 73 (32.6%) showing a U3 nodule. There were no U4 or U5 nodules identified. One patient (0.45%) had an 8mm U3 nodule and a subsequent diagnosis of medullary thyroid cancer with a known family history of MEN2. Repeat ultrasound was performed in 29 patients (12.9%), fine-need aspiration (FNA) in 27 (12.1%), referral to subspecialty services in 83 (endocrinology $n = 49$ (21.9%); ENT $n = 34$ (15.2%)). Preliminary data suggest a large proportion of referrals from primary care for thyroid ultrasound are not clinically indicated, with an impact on subspecialty services. Clear guidelines for practitioners outlining clinical indications for ultrasound are warranted.

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P254

Carbimazole induced myositis in a patient with graves' disease: a case presentation

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Antithyroid drugs (ATD) therapy is a common first-line treatment for Graves' disease (GD). Patients are routinely counseled about rare side effects including agranulocytosis and pancreatitis. We report a rare case of myositis in association with ATD treatment in a patient with GD. A 37-year-old male with an acute presentation of symptomatic GD was commenced on carbimazole 30 mg daily in late November (TSH receptor antibody 9.2 Int Unit/l). He re-presented in January with progressively worsening muscle cramps, pain, and generalized weakness. Investigations showed deranged liver function tests, severely elevated creatinine kinase (CK) 15,920 Int Unit/l, and TFTs with a low FT4 at 6.0 pmol/l, TSH < 0.01munit/ L, FT3, 4.3 pmol/l. Renal function and urinalysis were within normal limits. There were no clinical features of other systemic illness or inflammatory myopathy, and no obvious contributing medication including statins. The patient was treated with intravenous (IV) fluids, and carbimazole was discontinued. CK levels normalized after treatment with IV fluid and cessation of carbimazole. Following a period of observation, the free T3 rose, so a trial of low-dose Propylthiouracil was started to try and prevent full recurrence of the thyrotoxicosis. This was also associated with recurrence in muscle cramps and a moderate CK (2239) rise, so it was stopped. This patient underwent definitive treatment with a total thyroidectomy. There are a few case reports of carbimazole-associated myositis in the literature, but these document no similar symptoms when switching to alternative ATDs. Our case illustrates that caution is needed on trialing alternative ATDs in case of recurrence of myositis. We also reiterate the importance of considering an alternate diagnosis including inflammatory myositis, thyrotoxic myopathy, and thyrotoxic periodic paralysis. Finally, we highlight myositis and rhabdomyolysis as a rare complication of ATD therapy to increase clinician awareness and for early consideration of alternative definitive treatment in GD.

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Association between socioeconomic position and the risk of thyroid cancer diagnosis: a 10-year follow-up cohort study in china

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Background
The incidence of thyroid cancer has been increasing rapidly in China, which is mainly contributed by overdiagnosis. Among the main drivers of overdiagnosis is the increased access to healthcare system, especially for the advantaged populations. We aimed to explore the association between socioeconomic position (SEP) and thyroid cancer diagnosis in China.
Methods
The China Kadoorie Biobank recruited over 500,000 adults from 10 geographic regions during 2004-2008. SEP-related factors (education attainment, household income, and occupational prestige) and covariates were collected through questionnaires. We assessed the overall SEP levels by point-based scoring method and latent class analysis (LCA), and evaluated their consistency by the Kappa test. Multivariate Cox models were used to estimate the hazard ratios (HRs) of SEP on the risk of being diagnosed with thyroid cancer.
Results
After a median follow-up of 10 years, 520 thyroid cancer cases were diagnosed among 504,456 participants. The point-based scoring method classified 212,345, 145,166, and 146,945 participants into low, medium, and high SEP groups, respectively, and the LCA classified 243,723, 196,460, and 64,273 participants into low, medium, and high SEP groups, respectively (Kappa coefficient 0.36, $P < 0.001$). The HRs (95%CI) of SEP on thyroid cancer diagnosis are shown in the Table below.

Variable (referent: low)	Medium	High	*P* for trend
Education	1.57 (1.29, 1.91)	3.83 (2.89, 5.07)	<0.001
Household income	1.59 (1.20, 2.13)	3.09 (2.40, 3.98)	<0.001
Occupation prestige	0.66 (0.41, 1.07)	1.50 (0.91, 2.46)	<0.001
SEP level (point-based scoring method)	1.55 (1.22, 1.97)	2.17 (1.70, 2.77)	<0.001
SEP level (LCA)	1.14 (0.91, 1.42)	1.89 (1.45, 2.46)	<0.001

Conclusions
Higher SEP is associated with an increased risk of thyroid cancer diagnosis in China. Targeted public health strategies, particularly focusing on wealthier and more developed regions, are needed to enhance awareness of thyroid cancer overdiagnosis.

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P256

Immune checkpoint inhibitor (ICPi) induced thyroiditis

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Immune checkpoint inhibitors have revolutionised the treatment of aggressive cancers by improving survival. However, immune-mediated endocrinopathies can occur and could be life-threatening if undiagnosed. Among hypophysitis, adrenalitis, thyroiditis and diabetes mellitus, thyroid dysfunction is the most common event. Among anti-PD-1/PD-L1 and anti-CTL4, the former carries a greater risk. Here, we present two cases of thyroiditis following the commencement of Pembrolizumab (ICPi) for carcinoma of breast. The first patient was a known case of hypothyroidism on levothyroxine and was euthyroid before starting Pembrolizumab (PD-1 inhibitors). Following 2 cycles, TFTs showed hyperthyroidism (TSH-0.01 mIU/l, FT4- 31.9 pmol/l). TSH receptor antibodies (0.31) and early morning cortisol levels were normal. TFTs were monitored regularly as she was at risk of hypothyroidism. She developed hypothyroidism within 3 weeks, was restarted on levothyroxine and the dose was titrated over the next few weeks. However, she required a higher dose of levothyroxine compared to her previous dose. Her thyroid function improved over 2 months and became normalised. She has completed her immunotherapy, and her thyroid functions were monitored 6-weekly. The second patient was euthyroid as well before starting immunotherapy. After receiving 3 cycles of pembrolizumab, she developed generalised body swelling. She had subclinical hyperthyroidism transiently which later progressed to severe hypothyroidism (TSH > 100 mIU/l, FT4 < 1.3 pmol/l) and myxoedema. She was started on high dose levothyroxine, swelling improved and her FT4 has gradually increased. These cases reinforce the importance of monitoring thyroid function tests frequently (2 to 3 weekly) rather than 6 to 8 weekly during treatment with ICPis. Initial transient hyperthyroidism is often underreported and is followed by hypothyroidism which can be permanent and needs regular follow-up. Thyroxine should not be initiated without excluding adrenal insufficiency. Close monitoring for other endocrine organ dysfunctions such as hypoadrenalism, hypophysitis, and diabetes is also recommended.

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P257

Navigating thyroid FNAC's-overcoming diagnostic challenges and inadequacies

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Introduction
Ultrasound guidance is now standard for improving diagnostic accuracy in thyroid FNACs. Its success depends on operator skill, emphasizing the need for trained personnel to enhance sample quality. Although generally safe and minimally invasive, it requires technical expertise and awareness of limitations.

Factors such as lesion characteristics, needle localization, sampling methods, and the number of samples can significantly affect outcomes.
Aims of the Study
High Thy 1 rates (insufficient samples) lead to increased patient visits, anxiety, repeat procedures, and strain on healthcare systems. Audits conducted from January to June 2023 assessed aspirator performance at South Tees Trust, identifying those with FNAC specimen rates above 15% for further training, following RCP 2021 guidance.
Results
Of the 234 Thyroid aspirates, 91 were Thy 1. 8.79 % underwent two FNAC 's in same setting. D, an advanced practitioner, performed under the supervision of Aspirator C. Nearly 60% of cases were right-sided. Larger nodules had higher inadequacy rates, while smaller nodules had the lowest. Nearly 70% required repeat FNAC, with over 50% returning a Thy 1, and 10% underwent surgery, revealing two malignancies. Continuity of care was a concern, as 8% lacked follow-up and only 10% were referred to multidisciplinary teams.

ASPIRATOR	Thy 1	%
A	47	20.08
B	5	2.136
C	17	8.54
D	20	0.85
OUTCOMES		
USG Surveillance	15%	
Repeat FNAC	67.34%	
Diagnostic Hemithyroidectomy	6.37%	
Total Thyroidectomy	4.55%	

Conclusion
Assessing inadequacy rates in FNAC procedures is essential for improving diagnostic accuracy. Findings stress the need for standardized clinician training and auditing to enhance sample adequacy, address healthcare resource strains, and improve patient care. Further analysis of inadequacy rates is ongoing, identifying critical areas for improvement in FNAC methodology.
Limitations
Reliance on a single individual for many FNACs may introduce bias due to skill variability, higher case volume, workload fatigue, and lack of cross-validation.
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P258

Gene expression dynamics in endometriosis and hashimoto disease: insights into potential overlaps
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Objective
To investigate the relationship between endometriosis and Hashimoto's thyroiditis and analyze their potential molecular mechanisms.
Methods
1. Mendelian Randomization Analysis: Utilized GWAS data to assess the causal relationship between endometriosis and Hashimoto's thyroiditis. 2. mRNA Expression Analysis: Analyzed mRNA expression patterns in endometriosis and Hashimoto's thyroiditis tissues from the GEO database, including differential gene expression analysis, functional enrichment analysis, and pathway analysis. 3. Gene Regulatory Network Analysis: Constructed regulatory networks involving transcription factors (TFs), microRNAs (miRNAs), and target genes associated with highly expressed genes.
Results
1. Mendelian Randomization Analysis: No direct causal relationship was found between endometriosis and Hashimoto's thyroiditis. 2. mRNA Expression Analysis: Common upregulated and downregulated genes were identified in both diseases. Functional enrichment analysis showed that downregulated genes were associated with regulation of cell structure and function, while upregulated genes were associated with phosphorylation and deamination. Pathway analysis revealed significant enrichment of the NOTCH signaling pathway in both diseases. Friend analysis identified TNFRSF21 and MBNL3 as highly expressed genes in both diseases. 3. Gene Regulatory Network Analysis: Identified TFs and miRNAs that may regulate highly expressed genes. Constructed regulatory networks involving TFs, miRNAs, and target genes.
Conclusion
Despite the lack of a direct causal relationship established by Mendelian Randomization, significant overlap in mRNA expression patterns, cell signaling pathways, and immune regulation between endometriosis and Hashimoto's thyroiditis suggests potential shared molecular mechanisms. Future research can further explore shared therapeutic targets for developing targeted treatment approaches.
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P259

Neutropenia in thyrotoxicosis is not always due to drug treatment: the importance of chronology
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Introduction
Antithyroid drugs-induced neutropenia can occur in up to 0.5% of patients with Grave's disease receiving ATDs. However, thyrotoxicosis-associated neutropenia has been seldomly reported. We describe a case of severe neutropenia (neutrophils <0.5) induced by florid thyrotoxicosis.
Case history
A 33-year-old lady was reviewed in endocrinology clinic following a year of palpitations, dizziness and diarrhoea. TSH <0.05mIU/L and FT4 was 92 pmol/l. WCC was 2.4 and neutrophils 1.08 with platelets of 73. Anti-TPO antibodies were positive. Carbimazole 40 mg was commenced and as FT4 reduced to 13 pmol/l, WCC improved to 5.8, neutrophils 3.4 and platelets 140 after 4 weeks. Carbimazole dose was reduced to 20 mg/day. Three weeks later, she developed cough. She was thyrotoxic (FT4 = 47 pmol/l, TSH <0.05mIU/l) with evidence of bone marrow suppression (WCC 3.1, neutrophils 1.1 and platelets 106). Carbimazole was stopped following haematology advice. Two weeks later, she was admitted to hospital with severe thyrotoxicosis (FT4 = 132 pmol/l, TSH $<$ 0.05mIU/l). WCC was 1.5 and neutrophil 0.2 with platelets of 66. She developed Moraxella in sputum and treated with antibiotics. Carbimazole was restarted at 60 mg/day. Over the following 2 weeks, bone marrow suppression completely resolved. She was not keen on surgery and had a young child, and therefore, continued on Carbimazole.
Discussion
Thyrotoxicosis-associated neutropenia has been reported in about 10% of cases. Excessive thyroid hormones levels can reduce the proliferation of haematopoietic cells. Additionally, autoimmunity might shorten the survival of neutrophils via anti-TRab mediated effect on neutrophil TSH receptors. This case highlights the importance of recognising thyrotoxicosis-associated neutropenia and considering definitive treatment of thyrotoxicosis.
Learning points
Neutropenia can be a sign of new onset hyperthyroidism and is not always due to treatment. Neutropenia should not be regarded as contraindication to starting ATDs. WBC count should be assessed prior to starting ATDs.
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P260

Evaluating the link between both thyroid stimulating hormone (TSH) and free thyroxine (FT4) both extensively measured mainly in primary care to diagnose, rule out and treat hypothyroidism, using thyroid function test (TFT) results taken from the greater manchester care record 2010-2023
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Introduction
Over 10 million thyroid function tests (TFT) are undertaken in England annually. To reduce test numbers laboratories often measure TSH and then only reflex measure FT4 if result fall outside TSH reference range (TSH-RR). The relationship between FT4 and TSH results was considered for patients both on and off thyroid medication.
Methods
Simultaneous TSH and FT4 results from 47,869 diagnosed hypothyroid including dose and 393,101 untreated/euthyroid individuals who had been tested once or twice were included.
Results
Of 452,463 results untreated/euthyroid population, 90%(406,700) were within TSH-RR and 99%(448,171) within FT4-RR. As 3,319(83%) of 3,992 with FT4 $<$

9 and 175(58%) of 300 with FT4 > 25 had TSH within TSH-RR, both these groups might not receive a reflex FT4 result. In 407,075 results in the treated population, 176,833(43.4%) were in TSH-RR; this relatively low proportion would then avoid FT4 reflex testing. The discrepancy between TSH and FT4 could be missed including 1,368(15.1%) of the 9,068(2.2%) with low FT4 < 9 that had had low/normal range TSH < 4.0 and the 3,065(21.7%) of the 14,123(3.5%) with high FT4 > 25 with TSH in RR. These effects were more prevalent in people taking lower dose levothyroxine. Treated individuals were almost 40-times more likely to have a high FT4 despite a normal TSH than untreated individuals.

TSH (mu/l): FT4 (pmol/l)	FT4 < 9	FT4-RR:9-25	FT4 > 25
UNTREATED:TSH < 0.4	48	13,146	115
UNTREATED:TSH-RR 0.4-4	3,319	403,206	175
UNTREATED:TSH > 4	625	31,819	10
TREATED:TSH < 0.4	201	92,574	10,195
TREATED:TSH-RR 0.4-4	1,368	172,400	3,065
TREATED:TSH > 4	7,499	118,910	863

Conclusion

Given risks associated with prolonged exposure to high and low FT4 levels and importance of dose adjustment, it's clear that both FT4 and TSH should both be measured, especially for those treated with levothyroxine. This difference in TSH–T4 relationship by treatment status needs urgent attention.

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P261

Unraveling the contribution of the thyroid-gut axis in colorectal cancer pathogenesis: a literature review

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Background

There is bidirectionality in the relationship between the thyroid and the gut. Based on recent studies, dysfunctional thyroids could predispose to colorectal cancer by affecting gut health. More specifically, it has been identified that hyperthyroidism, also known as the overproduction of thyroid hormones, can result in microbiome imbalances in the gut, which create an inflammatory state that may promote cancer.

Objective

The issue is that despite growing data supporting that hyperthyroidism alters gut microbiota composition, there is a lack of research demonstrating its role as a risk factor in colorectal cancer. This review thus attempts to answer the question of whether hyperthyroidism-induced gut dysbiosis constitutes a risk factor for colorectal cancer and whether this risk can be diminished through microbiome-directed therapies.

Methods

We performed a systematic literature search on multiple databases including PubMed and Web of Science, focusing on studies (2000-2024) about the thyroid-gut axis and colorectal cancer (CRC).

Results

This unbiased review revealed that hyperthyroidism-induced dysbiosis may contribute to precancerous conditions by increasing harmful bacterial phyla like '*Clostridium* and *Enterococcus*' while decreasing beneficial species such as '*Faecalibacterium* and *Flavobacteria.*' In addition, an imbalance between *Bacillus* and *Actinobacteria* species is observed. Another revelation is that thyroid patients have low diversity of gut microorganisms, leading to poor absorption of iodine, selenium, and zinc, which are important for thyroid function. These changes result in a pro-inflammatory state.

Conclusion

This review highlights that the management of hyperthyroidism and prevention of cancer could be potential targets of therapy if we understand the bidirectional thyroid-gut axis. Future studies should examine these approaches and evaluate the impact on the microbiome and the risk factors associated with the thyroid.

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P262

Autoimmune thyroid disease screening in patients with type1 diabetes in sligo university hospital

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People with type 1 diabetes are at increased risks of developing other autoimmune conditions. These include Hashimoto's thyroiditis and Graves' disease. There is a prevalence of 4 to 18% of autoimmune hypothyroidism in patients with type 1 diabetes; 8% more than the general population. Only 17% of autoimmune thyroid antibodies are detected during initial diagnosis of type 1 diabetes therefore it is recommended by the American Diabetes Association (ADA) that thyroid function should be checked every 1 to 2 years post diagnosis. The aim of this audit was to determine if patients with type 1 diabetes were screened for autoimmune thyroid disease every 1 to 2 years after diagnosis as per the ADA guidelines. This retrospective study occurred in September 2023. All patients with type 1 diabetes attending Sligo University Hospital were included in the study. Data including demographics, duration of diabetes and date of last thyroid function screening were obtained from the Prowellness diabetes database. Thyroid function screening comprised of thyroid stimulating hormone (TSH) and thyroxine measurements. A total of 584 patients data were analysed. Demographics included 44% female and 56% males with an average age of 28. 92% (n = 538) had thyroid function screening performed with majority (78%, n = 418) occurring within one year and 22% (n = 120) within two years. Of the patients screened, 6.5% (n = 35) were hypothyroid and 2.4% (n = 13) were hyperthyroid. Autoimmune thyroid disease has a high prevalence in type 1 diabetes due to the sharing of HLA antigens. It is important that we screen and detect asymptomatic thyroid dysfunction in order to prevent overt hypothyroidism and associated complications. Whilst this audit highlights excellent screening rates for thyroid autoimmune disease (92%) in Sligo University Hospital, actions can be implemented to increase rates to 100%.

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P263

Propylthiouracil induced antithyroid arthritis syndrome and successful pregnancy

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Antithyroid Arthritis Syndrome (AAS) is a rare but serious side effect of antithyroid drugs (ATDs) which can present symptoms that severely impact quality of life, such as severe myalgia and arthralgia, shortly after starting the culprit medication. It can be difficult to differentiate from other arthritis causes, and its immune-mediated pathophysiology is not fully understood. This report discusses a patient who developed AAS following antithyroid therapy and was difficult to manage due to patient very keen to have children.

Case Presentation

31 years old Japanese women was previously diagnosed with thyrotoxicosis and confirmed Graves' disease in Japan and started on Carbimazole 20 mg daily. The patient visited our endocrine clinic as she was eager to conceive. She was advised to switch to Propylthiouracil. Shortly after starting Propylthiouracil, she reported symmetrical joint pain and swelling particularly of her hands, with minimal lower limb involvement, particularly the knees. AAS was diagnosed due to the timing of arthritis onset after Propylthiouracil initiation and exclusion of other causes. Anti-neutrophil cytoplasmic antibody (ANCA) negativity is needed to differentiate from antithyroid agent-induced ANCA-associated vasculitis, which shows arthritis similar to AAS

Management and Outcome

Propylthiouracil was disco¬ntinued, Carbimazole restarted and alternative treatment options, including surgery and radioactive iodine, were discussed. The patient's joint pain and swelling significantly improved after stopping the culprit medication. However, due to patient wish for pregnancy, Propylthiouracil was restarted and she was complained again of joint pain. Patient struggled during first trimester but then as soon as was safe – was changed back to Carbimazole.

Conclusion

This case highlights the need to recognize AAS. High vigilance required in patients of Japanese origin who complain of polyarthritis on ATDs. Early identification and cessation of the drug is essential for complete resolution of symptoms.

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P264

Outcomes of the use of radioactive iodine therapy for benign thyroid disease

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Introduction
Radioactive iodine -131 (RAI) has been used to treat hyperthyroidism for the past eight decades.[1] Despite this, controversy remains regarding radiation dosage.[2] The National Institute for Health and Care Excellence (NICE) recommends fixed dose regime with varying doses depending on underlying thyroid condition.[3] The European Journal of Nuclear Medicine and Molecular Imaging (EANM) offers similar guidance.[4] We offered all our patients single dose of 400MBq rather than variable doses irrespective of underlying thyroid condition causing hyperthyroidism. This audit aims to assess the outcomes for patients with benign thyroid disease after receiving a single dose (400MBq) of RAI at a single secondary care centre.
Method
Patients who underwent RAI at Sunderland Royal Hospital were identified retrospectively by electronic clinic notes over a 15-month period. In addition to patient demographics, details extracted included the indication for RAI, thyroid state, dose received, and the clinical outcome of RAI. If applicable, the length of remission and whether any further doses of RAI were required were also recorded.
Results
102 patients underwent RAI between June 2022 and September 2023. 53 (51.9%) patients had a multinodular goitre (MNG), 48 (47%) had Graves' Disease and 1 (0.9%) had a toxic adenoma. 92 patients (90.2%) went into remission, just greater than half of which were subsequently euthyroid. The remaining were hypothyroid following their RAI. 10 patients (9.8%) failed to go into remission, 8 of which had Graves' disease and 2 had a MNG.
Discussion
This audit has highlighted the large percentage of patients went into remission after receiving a fixed dose of RAI (400MBq) irrespective of underlying cause of hyperthyroidism. In turn, the small proportion of patients who failed to achieve remission has reinforced the efficacy of a single dose of RAI in the treatment of benign thyroid disease. Following on from this, reauditing outcomes at multiple centres aims to gain a greater understanding of RAI outcomes in the context of benign thyroid disease.
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P265

An audit into the endocrine specialist nurse role in managing thyroid disorders in pregnancy

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Background
With increasing numbers of patients accessing endocrine antenatal services, a pilot was undertaken for Endocrine Specialist Nurse (ESN) management of thyroid disorders in pregnancy. An audit was completed to review the impact and efficacy.
Audit Methods
1. Identified pregnant patients with thyroid disorders in the Endocrine antenatal clinic, seen by the ESN from May -Dec 2023. 2. TFT results during pregnancy reviewed to:
1. Assess whether TSH pregnancy targets were achieved and maintained throughout pregnancy.
2. Ensure appropriate TRAb surveillance completed for those with Graves' disease
3. Were GP management plans provided for those with hypothyroidism
4. Were there follow-up appointments for those with hyperthyroidism postpartum
Results
Total of 37 patients reviewed by the ESN. Primary Hypothyroidism 22, secondary Hypothyroidism 7, Hyperthyroidism 8. Hyperthyroidism (Grave's disease)
Thyroid receptor antibodies:
- 6 patients negative
- 2 positive
- 4 patients relapsed

100% of patients with hypothyroidism had a GP management plan and had their 6 week postpartum blood test. 100% patients with hyperthyroidism received postpartum follow-up clinic appointments with ESN. 43% had recurrence of hyperthyroidism requiring thionamides restarting up to 24 weeks postpartum.

Table 1: TSH targets at the beginning of Pregnancy

Thyroid diagnosis	TSH target achieved	TSH target not acheived
Hypothyroidism	36%	64%
Secondary hypothyroidism	67%	33%
Hyperthryoidism	100%	0%

Table 2: TSH targets achieved by the end of pregnancy

Hypothyroidism	Secondary Hypothyroidism	Hyperthyroidism
TSH Average nadir 1.69	TSH Average nadir 1.04	TSH Average nadir 0.67

Conclusion
The ESN role in managing thyroid disorders during pregnancy is effective and releases consultant time for complex patients. Postnatal follow-up pathway of Hyperthyroidism is required due to high relapse rate a prenatal thyroid ESN led clinic due to significant percentage of patients with above target TSH on referral.
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P266

Liothyronine and a sudden unexplained death: cause or coincidence? – a deep-dive into the evidence

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Introduction
Levothyroxine is the standard treatment for hypothyroidism- safe, inexpensive and effective. However, guidelines now suggest a trial of Liothyronine in some cases, to improve persistent symptoms. There is less safety data available for this. Here we report a case of sudden death in a patient using Liothyronine and present a thorough literature review on its safety profile.
Case Summary
A 42-year-old woman, previously fit and well, was found dead in her house, unexpectedly. She was reportedly using Liothyronine, bought off the internet, unprescribed. Post-mortem examination showed no cardiac abnormalities, but did show bilateral pulmonary oedema, focal hepatic necrosis without inflammation, and an atrophic thyroid gland. Serum toxicology was unremarkable. The medical examiner reported the cause of death as 'Sudden Unexpected Death in the setting of (chronic) liothyronine use'.
Literature Review
To set the coroner's conclusion in context, we assessed national statistics for mortality in Wales from 2013-2022, which showed that while deaths 'due to unknown causes' are rare ($n = 681$, 0.185% of all deaths), deaths attributed to thyroid disease (excluding cancer) or thyroid medications, are even rarer ($n = 101$, 0.029% of all deaths). Also, the number of adverse events (AEs) including deaths due to Liothyronine and Levothyroxine in reports published by MHRA showed 23 deaths associated with Levothyroxine with no reported deaths associated with Liothyronine. Disproportionality analysis of the FDA database also showed no signal for death associated with Liothyronine. Finally, a systematic literature review including cohort studies and case-reports also showed that most Liothyronine AEs are mild-moderate symptoms of thyroid excess, with occasional serious AEs occurring only on significantly excessive doses than recommended.
Conclusion
While this case report highlights the common misconception of Liothyronine being harmful, overall, the evidence in literature confirms that the safety profile of Liothyronine isn't much different than any other drug, especially in a monitored environment.
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P267

Two cases of recurrent thyrotoxicosis secondary to graves' disease post-total thyroidectomy

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Graves' disease is an autoimmune disease with thyroid stimulating immunoglobulins (TSI) causing hyperthyroidism. Anti-thyroid drugs are used for disease control pending spontaneous remission and radioiodine or thyroidectomy are definitive treatment resulting in the need for lifelong levothyroxine treatment. We present two cases where total thyroidectomy was not curative due to the presence of ectopic thyroid tissue not identified at time of surgery. Case 1, aged 32, female. Thyrotoxic with fT4 45.2 pmol/l, fT3 19.6 pmol/l, TSH <0.02 mU/L and TSI 11.6 IU/l. Mild/moderate thyroid eye disease present. Following treatment with carbimazole 40 mg od for two weeks – fT4 23.1 pmol/l, fT3 7.4 pmol/l and TSH <0.02 mU/L but a rise in transaminase suggested hepatotoxicity. Radioiodine ablation declined, therefore total thyroidectomy undertaken. Case 2, aged 52, female. Thyrotoxic with fT4 >76.2 pmol/l, fT3 >46.1 pmol/l, TSH <0.02 mU/L and TSH receptor antibodies 28.5 U/l. Mild/moderate thyroid eye disease present. Treatment with a block replacement regime of carbimazole 40 mg plus levothyroxine 100 mg od resulted in euthyroidism but with relapses four and nine years after stopping treatment. Total thyroidectomy undertaken. In both cases there was a decrease in requirement for post-operative levothyroxine replacement progressing to total withdrawal. Hyperthyroidism then returned. Tc-99m pertechnetate scan demonstrated a solitary foci in case 1 and 2 foci of uptake in case 2. Case 1 opted for further medical treatment and case 2 further surgical intervention which was successful. Following subtotal thyroidectomy if Graves' disease remains active there is a risk of recurrence of hyperthyroidism. Post-total thyroidectomy recurrence of hyperthyroidism is rare even in active Graves' disease but can occur in the presence of ectopic thyroid tissue. Pre-operative isotope scanning is not justified on cost grounds due to the rarity of this phenomenon.

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P268

DOTATATE avid metastatic follicular thyroid carcinoma with elevated plasma normetadrenalines

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A 71 year old man with history of left hemithyroidectomy in 2021 for a large goitre was found to have widely invasive PT3a follicular carcinoma. MDT recommended completion thyroidectomy and radioiodine ablation. Patient delayed his treatment and eventually had imaging in 2023 to restage the disease. CT and ultrasound neck did not identify progression of thyroid cancer. CT chest, abdomen and pelvis showed multiple lung lesions, 6.4 cm necrotic left adrenal mass and L3-4 destructive bone lesion invading right psoas muscles with pathological fracture of left four pedicle and possible encroachment of the spinal canal. He had elevated plasma normetadrenalines of 1354 pmol/l, normal metadrenalines of 341 pmol/l and high thyroglobulin levels of 12,816 µg/l. G68DOTATATE PETCT showed multiple subcentimeter pulmonary nodules, DOTATATE avid left adrenal mass, mild prominent tracer accumulation at pancreatic tail and lytic DOTATATE avid mass L3/L4 disc space. The right thyroid was unremarkable. He was treated with alpha and betablocker. Biopsies of spinal and adrenal lesion were consistent with well differentiated follicular thyroid carcinoma. He had completion thyroidectomy and histology showed follicular variant multifocal papillary thyroid microcarcinomas with no adverse features. He received two doses of post operative radioactive iodine therapy and palliative radiotherapy to spinal metastasis. The expression of somatostatin receptors by non-medullary thyroid carcinomas are poorly studied. There are several reports on expression of SSTRs in thyroid tumours. There is evidence to suggest that follicular and anaplastic thyroid carcinoma also express somatostatin receptors. All types of SSTRs are expressed in human non medullary thyroid carcinoma tissue but the SST2 and SST3 are most abundantly expressed. This opens a new area of research where targeting somatostatin receptors could be a treatment modality in patients with DOTATATE avid non medullary thyroid carcinomas. Elevated catecholamine concentrations in this case could be related to haemorrhage/infarction of the left adrenal gland.

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P269

Paralysed by hyperthyroidism: a rare case of graves' thyrotoxicosis and thyrotoxic periodic paralysis

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Background
Thyrotoxic periodic paralysis (TPP), a rare but serious complication of untreated or poorly managed hyperthyroidism, characterized by hypokalaemia and muscular weakness
Case history
A 25 year-old male of mixed White-Asian background presented with 8-10hr history of limb weakness and chest discomfort. His profound limb weakness made him unable to mobilise out of bed. He had a 4-year history of autoimmune thyrotoxicosis, treated with Carbimazole 20 mg OD and Propranolol 40 mg BD. He had stopped treatment 3 weeks prior due to personal stress. On examination, he had fine tremors, irregular pulse, normal JVP without oedema or cardiac murmurs. Neurologically, GCS was 15, with intact cranial nerves, reduced upper limb power (3/5 bilaterally), lower limb power (2/5 bilaterally), exaggerated reflexes, and inability to complete the finger-nose test due to weakness. ECG showed Mobitz type II conduction block and ST depression in lateral leads. He had severe hypokalaemia; K+ 1.8 mmol/l, with sodium 142 mmol/l, magnesium 0.84 mmol/L and glucose 7.4 mmol/l, TSH <0.01 mU/l, freeT4 48.9 pmol/l, and freeT3 15.0 pmol/l. Cardiac markers were normal (troponin 11 ng/l, NT-proBN*P* $<$ 50 pg/mL). His TSH-RAb and anti-TPO antibodies were elevated at 2.45U/L and 574U/mL respectively. His K+ improved to 2.9 after 40mmol of IV potassium. Further 40mmol of IV made is K+ 4.77, the muscle weakness improved and ECG reverted to normal-sinus-rhythm. Muscle power regained completely within 18-24 hours. His Carbimazole and Propranolol were re-instated.
Discussion
Early recognition and treatment of TPP is critical to prevent cardiac complications. Acute management includes oral or IV potassium with close monitoring of blood levels due to rebound hyperkalaemia risk. Non-compliance is a significant risk factor for the recurrence of thyrotoxicosis and its complications. Long-term management should focus on achieving euthyroidism to prevent recurrence, with discussion of definitive treatments.

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P270

The advantage of combined thyrotropin and free thyroxine measurement for monitoring patients with primary hypothyroidism receiving levothyroxine

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Background
Since serum free thyroxine levels raise after levothyroxine ingestion and take several hours before returning to baseline, thyrotropin is recommended as a laboratory test for monitoring the adequacy of levothyroxine replacement in primary hypothyroidism patients. However, immunoglobulin-bound thyrotropin causing falsely high thyrotropin levels is commonly found and leads to unnecessary increase in levothyroxine dosage. Polyethylene glycol (PEG) precipitation is an accepted method for correcting this interference.
Objective
To use serum thyrotropin in combination with free thyroxine levels obtained before levothyroxine dosing in order to reduce unnecessary adjustment of levothyroxine dosage due to immunoglobulin-bound thyrotropin in patients with primary hypothyroidism receiving levothyroxine.
Methods
This is a cross-sectional study using blood specimens obtained before levothyroxine dosing from the patients with primary hypothyroidism receiving levothyroxine. Thyrotropin and free thyroxine were measured by electrochemiluminescence immunoassay. A 25% PEG-6000 solution was used to precipitate immunoglobulin-bound thyrotropin, and thyrotropin levels after PEG precipitation were used as the reference range.
Results
In 125 patients, 60 patients had normal thyrotropin levels (0.27-4.2 uIU/mL) and 65 patients had elevated thyrotropin levels (>4.2 uIU/mL). In patients with normal thyrotropin levels, 51 (85%) had free thyroxine levels ≥ 1.2 ng/dL, and all had thyrotropin levels after PEG precipitation within normal range. In those with

elevated thyrotropin levels, 51 (78.5%) had free thyroxin <1.2 ng/dL and 14 (21.5%) had free thyroxine ≥ 1.2 ng/dl. In patients with free thyroxin <1.2 ng/dL, 37 (72.5%) still had elevated thyrotropin levels after PEG precipitation, while the rest had normal levels. In patients with free thyroxin ≥ 1.2 ng/dL, all but 1 (93%) had normal thyrotropin levels after PEG precipitation.

Conclusion

It is unnecessary to increase levothyroxine dosage in patients with primary hypothyroidism who have elevated thyrotropin levels if free thyroxine levels before levothyroxine dosing are 1.2 ng/dL or more.

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P271

The rarest cause of thyroid eye disease

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We present the case history of a 73-year-old woman who presented to ophthalmology reporting 'eyelids opening too much' with orbital grittiness, watering and a staring gaze for 9 months. The patient had unequal palpebral apertures with bilateral upper lid retraction, worse on the left. Her clinical activity score was 4/7 with gaze evoked orbital pain, active swelling of the lids, conjunctival redness and caruncle inflammation. Visual acuity was normal (6/6 right eye, 6/12 left eye) and no evidence of impaired colour vision on Ishihara testing. The left eye was proptosed (21mm) with firm retropulsion. The patient had been diagnosed in 2010 with follicular thyroid carcinoma (FTC) with pelvic, spine and rib metastatic disease. Her treatment for thyroid cancer comprised of total thyroidectomy in 2010 and three doses of radioactive-iodine (RAI) between 2010 and 2012 (total dose 17GBq). Thyroid metastases remained stable between 2010 and 2018 until there was progression at the iliac crest which was treated with external beam radiotherapy in 2018 and 2020. She had further RAI in 2019, 2022 and 2023 (total dose 16.5GBq). In 2023 an increased rate of progression was noted and following failed lenvatinib treatment, the decision was made for best supportive care. At joint endocrine/ophthalmology review, previous investigations were noted showing suppressed TSH with normal FT4 and FT3 levels until 2023 when FT3 levels became raised, despite taking only levothyroxine 100 mg daily. TRAb levels were elevated at 39.4 IU/l. We concluded that the patient developed Graves' orbitopathy following total cumulative RAI dose of 33.5GBq with elevated TRAb levels contributing to progression of malignancy with mild T3 toxicosis originating from metastatic FTC. This is a rare case highlighting the importance of measuring TRAb levels in cases of thyroid cancer if disease progression suddenly increases particularly for patients treated with multiple doses of RAI.

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P272

Unmasking myxoedema coma: a case report of severe hypothyroidism initially diagnosed as depression

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Myxoedema coma is a rare, fatal manifestation of severe hypothyroidism characterized by altered mental status and multisystem dysfunction. It often occurs in the setting of long-term untreated hypothyroidism, triggered by infection and hypothermia. This case explores a patient presenting with myxoedema coma as the initial presentation of autoimmune hypothyroidism which was initially misdiagnosed as depression. A previously healthy 46-year-old woman was admitted to the emergency department with a sacral fracture following a fall. Her examination showed cognitive slowing, non-pitting oedema and proximal myopathy. Despite a history of recurrent falls, she avoided seeking medical attention due to negative past experiences. Following the death of her mother for whom she had been a caregiver, she experienced severe self-neglect, social isolation and significant weight loss. She was diagnosed with depression in the community a few weeks prior to hospital admission and prescribed antidepressants. On admission to hospital, investigations confirmed profound hypothyroidism with positive thyroid antibodies. Her condition was complicated by severe electrolyte imbalances, acute kidney injury, ischemic liver injury secondary to persistent hypotension, pleural effusion, clotting abnormalities, malnourishment and inpatient falls. Her clinical presentation combined with biochemical abnormalities was indicative of myxoedema coma with multiorgan dysfunction. Treatment was initiated with high dose thyroxine and supportive measures. This case illustrates the importance of considering organic causes of psychiatric symptoms such as depression, particularly when accompanied by physical signs like proximal muscle weakness and recurrent falls. The patient's delayed presentation, compounded by social isolation and caregiving responsibilities allowed her condition to progress without timely intervention. Initial misdiagnosis in the community led to delayed initiation of treatment and subsequently multiorgan dysfunction. Early recognition, prompt thyroid replacement combined with a multidisciplinary approach were key to her recovery. This case also highlights the importance of considering psychosocial factors in the management of chronic conditions.

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P273

Autoimmune overlap: a case study on coexisting systemic lupus erythematosus and hashimoto's thyroiditis in southwestern nigeria

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Background

Systemic lupus erythematosus (SLE) is an autoimmune disorder with a predilection for women of reproductive age and is characterized by multi-organ involvement. Hashimoto thyroiditis, an autoimmune thyroid disease mediated by thyroid-specific antibodies, anti-thyroid peroxidase (TPO-Ab), often presents with hypothyroidism and goiter. Although autoimmune thyroid diseases are known to coexist with other autoimmune disorders, association of Hashimoto thyroiditis with SLE is rare, particularly in Sub-Saharan Africa. Here, we present a case of coexistent Hashimoto thyroiditis and SLE in a young lady.

Case Summary

A 23-year-old Nigerian lady presented with a 10-month history of goiter and symptoms including lethargy, cold intolerance, weight gain, and menorrhagia. Physical examination revealed a diffusely enlarged, warm goiter (17 x 12 cm). Laboratory results indicated hypothyroidism with elevated TSH (74.29 uIU/mL), low fT4 (3.46 pmol/l), and normal fT3 (3.74 pmol/l). Anti-TPO antibodies were >2000 IU/mL Thyroid ultrasound showed diffusely enlarged lobes with heterogeneous echo-pattern and thyroid inferno on Doppler. She was diagnosed with Hashimoto thyroiditis and commenced on levothyroxine. Subsequently, the patient developed joint pain, frothy urine and facial edema, leading to further investigations. Notably, ANA was 1:2560 (speckled pattern), anti-dsDNA and anti-Sm antibodies were both elevated >200 U/mL, fulfilling the 2012 SLICC criteria for SLE. The hemogram showed anemia, leukopenia, and raised ESR. Urinalysis showed nephrotic-range proteinuria and hematuria while lipid profile was deranged. Renal biopsy was indicative of Class V lupus nephritis. She was started on prednisolone, hydroxychloroquine, mycophenolate mofetil, atorvastatin, and supportive therapies. Her symptoms and laboratory features improved within two months of treatment and remained clinically stable.

Conclusion

This case underscores the potential for coexistence of SLE and Hashimoto thyroiditis, possibly due to shared autoimmune and demographic features. We suggest thyroid assessment in SLE patients, as early diagnosis and treatment of thyroid involvement may improve clinical outcomes.

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P274

Utilization of 11C-Methionine PET-CT and somatisation analogues to detect pituitary microthyrotropinoma that is not evident on conventional pituitary MRI

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TSH-secreting pituitary adenomas are rare, comprising under 1% of hyperthyroidism cases and 0.5-3% of functioning pituitary tumors. Ultrasensitive immunometric assays, now routine in thyroid testing, have improved diagnostic accuracy. Gadolinium-enhanced MRI is the main imaging method, as most adenomas ($>90\%$) are macroadenomas. Early diagnosis and treatment help prevent complications. A 47-year-old female presented with dysfunctional uterine bleeding, dysmenorrhoea and irregular periods along with headache, lethargy and

palpitations. Thyroid function tests since 2016 revealed persistently raised FT4 with normal TSH. Initial and repeated Pituitary MRI showed no focal mass with incidental possible meningioma in the upper left cavernous sinus. Her pituitary profile was normal. Tests for interference confirmed persistent FT4 elevation with normal TSH, negative thyroid antibodies, SHBG at 183 nmol/l (24.6-122) and a normal alpha subunit. A TRH stimulation test showed TSH remained under 5 mU/l. 11C-Methionine PET-CT showed tracer uptake on the gland's left-side suggestive of a small microthyrotropinoma but it was difficult to discern a discrete lesion in absence of anatomical correlate from MRI. She was commenced on lanreotide 90 mg as a therapeutic and diagnostic manoeuvre (suppression imaging), resulting in FT4 normalisation and TSH suppression. Following four SSAs injections, repeated 11C-Methioine-PET-CT and MRI showed post SSAs therapy change in T2 signal characteristics in the same area of tracer uptake. This anatomical correlate confirmed a thyrotroph tumour. Lanreotide was stopped due to side effects and a trail of Cabergoline was poorly tolerated. The case is due for re-discussion in the Pit MDT regarding surgical intervention. In conclusion, 11C-Methionine-PET-CT scan with the help of SSAs can be useful tool in localizing microthyrotropinoma when conventional MRI pituitary hasn't been successful.

	FT4 (12-22) pmol/L	TSH (0.3- 4.2)mu/L	FT3(3.1- 6.8) pmol/L
24/05/2016	**31.4**	**1.78**	
10/04/2019	**38.2**	**1.57**	
05/02/2020	**28.0**	**1.80**	**7.2**
14/05/2021	**37.5**	**2.14**	**9.2**
09/06/2023	**36.2**	**1.80**	

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P275

A case of hypokalaemic periodic paralysis worsened by thyrotoxicosis affecting a caucasian lady

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Thyrotoxic Periodic Paralysis (TPP) is a rare channelopathy associated with hyperthyrodism causing potentially fatal complications of hypokalemia due to a massive intracellular potassium shift and severe muscle paralysis. TPP is rare in non-Asians, however with population migration increasingly seen in Western countries. The diagnosis is often delayed due to the subtleness of underlying thyrotoxicosis and the similarities of the paralysis with familial hypokalaemic periodic paralysis (FHPP). The channelopathy is of genetic/acquired in nature affecting sodium and potassium ion channels across cell membranes including KCNJ family and L-type calcium channel. A 24-year old, White European lady presented with tetraparesis and profound hypokalemic. These paralytic episodes were recurrent for previous 6 years, occuring once/twice per year. Only few weeks prior, she was diagnosised with Graves' thyrotoxicosis (free thyroxine (FT4) 43.7 (12-22 pmol/l), free triiodothyronine (FT3) 24.6 (2.0-7.0 pmol/l), thyroid stimulating hormone (TSH) <0.02 mIU/L (0.4-4.5 mIU/l)), positive thyrotropin receptor antibodies) and commenced on carbimazole. Her father had hypokalemic periodic paralysis, but the details were unknown. Biochemstry at presentation revealed, low potassium 1.6mmol/l, raised FT4 27.1 pmol/l and FT3 11.6 pmol/l, and supprsed TSH of <0.02 mIU/l. She was treated with IV potassium and higher doses of carbimazole with full recovery from the episode. Her genetic analysis are awaited. TPP can be confused with FHPP. TPP is a sporadic disease seen mainly in Asian males, and the familial trait is rare while the FHPP is an autosomal dominant condition mainly affecting Caucasians. Additionally, there may be an overlap of genetic predisposition between FHPP and TPP. Although, our patient had paralytic episodes prior to Graves' thyrotoxicosis, this episode was severe; her underlying diagnosis of TPP vs. FHPP is unclear pending gentics analysis. We highlight a rare case of hypokalemic periodic paralysis and complexities incurred in its diagnosis and management.

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P276

A case of gestational thyrotoxicosis

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It can be challenging to differentiate between gestational thyrotoxicosis and intrinsic hyperthyroidism; the former being the commonest cause of thyrotoxicosis in pregnancy and usually requiring supportive care only. A 34 year-old lady, gravida 4 and para 2 was admitted at 11weeks of gestational age with an initial diagnosis of hyperemesis gravidarum. She was referred to the endocrinology due to severe symptoms and tachycardia, palpitations, excessive sweats, $>5\%$weight loss with deranged thyroid function tests. She had hyperemesis gravidarum with gestational thyrotoxicosis in previous two pregnancies with resolution of symptoms after first trimester. Examination showed fine tremors, a diffuse, non-tender goitre without bruit and no evidence of eye disease, acropachy or pretibial myexedema. Biochemistry revealed significantly elevated beta-HCG level of 62700 IU, free thyroxine (FT4) 26.9 (12-22 pmol/l), free triiodothyronine (FT3) 8.86 (2.0-7.0 pmol/l) thyroid stimulating hormone (TSH) <0.02 mIU/L (0.4-4.5 mIU/l), and negative thyroid peroxidase (TPO) and thyrotropin receptor antibodies (TRAB). A diagnosis of gestational thyrotoxicosis was made and she was managed conservatively leading to its spontaneous resolution in second trimester.

Discussion

Gestational thyrotoxicosis occurs from the stimulatory action of HCG on the TSH receptor, as they share structural homology resulting in an increased production of T4 and T3 and a low TSH levels. Differentiation of Graves' disease from GTT can be supported by the presence of clinical evidence of autoimmunity, a typical goiter, and presence of TRAb. Our patient presented with severe symptoms including weight loss posing challanges in diagnosis and management. In the context of hyperemesis, previous gestational thyrotoxicosis, and the absence of TRAB, a diagnosis of severe gestational thyrotoxicosis was made and treated with close monotand treated with close monoting and supportive care.

Conclusion

Severe gestaional thyrotoxicosis can pose a clinical challenge, adopting a careful approach based on clinical and biochemical features enables accuarte diagnosis and appropriate treatment.

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P277

Thyroid clinic audit of patients on non-standard thyroid hormone replacement: review of practice at the university hospital of wales (UHW)

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Introduction

Levothyroxine is the drug of choice for treating patients with hypothyroidism. However, a certain subset of individuals continue to experience symptoms despite biochemical normalization of their thyroid function.

Objectives

To evaluate our clinical practice of individuals on non-standard treatment modalities for hypothyroidism.

Methods

Retrospective analysis of the Thyroid clinic electronic database of all patients on non-standard treatment for hypothyroidism between 2010-2024 at UHW.

Results

Data of 176 patients (158 women and 18 men) was available for analysis. Median age was 55 years, range was 22 to 91 years. 54% ($n = 95$) patients had previously trialed non-standard treatment before their first clinic appointment (either on their own or via private clinic consultation). Patients were screened for complications through clinical monitoring for atrial fibrillation (AF) and a DEXA bone density scan. 25% patients ($n = 44$) underwent day curves and 22.7% ($n = 40$) had answered a quality of life questionnaire. On their last clinic letter, 87.5% of them remained on non-standard treatment for hypothyroidism (T3 only $= 29$, Armour (dessicated thyroid) only $= 39$, T3 + T4 $= 82$, Armour + T4 $= 4$) whereas 12% continued on T4 alone and 1 patient (0.5%) was not on any treatment due to intolerance to all forms of medication. Four patients were discharged from the clinic towards the end of the study period.

Table 1 Clinical response to treatment as perceived by patients:

TOTAL	176
Complete response	70.5% ($n = 124$)
Partial response	17% ($n = 30$)
No response	12.5% ($n = 22$)

Conclusion

In our cohort of 176 patients on non-standard thyroid hormone replacement we report high levels of satisfaction. Substantial adverse complications were not observed. However, a significant proportion remained on dessicated thyroid extract and T3 monotherapy. More work is needed to assess complications and formally assess quality of life.

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Innovation in Teaching and Assessment

P278

The role of simulation training for prospective diabetes and endocrine trainees

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Background
Simulation is an important part of medical training and allows for the training of doctors in a safe environment without the risk to patients. These 'high-risk' scenarios provide an opportunity for doctors to increase their confidence in managing clinical cases without detriment to patient safety while allowing them to make mistakes and gain clinical competence.
Aims
Simulation can also provide useful in diabetes and endocrinology (D&E) training. Many clinicians will encounter patients with diabetes but exposure to endocrinology scenarios may be variable. This means that trainees may not consider this as a career, due to lack of exposure. We aim to target resident doctors early in their training and to give them more opportunity to learn about D&E by simulation training. This may in turn promote more resident doctors to apply to this specialty.
Methods
A training day was held at Derriford Hospital, a teaching hospital in the Southwest of England. Small group teaching was directed at trainees considering a career in D&E who opted in for the training day. The day was then split up into simulation and actor training with micro-teach sessions, common referrals and clinic simulation. Feedback was then obtained from participants before and after the training day.
Results
Feedback included ratings of individual scenarios, confidence pre and post course and likelihood of applying to D&E. Overall feedback was positive throughout, with educational benefit rated as excellent for all scenarios. Confidence in managing these conditions increased from 3.2 to 4.6 and the likelihood of applying to this specialty increased from 4 to 4.4.
Conclusion
Simulation training is used across many areas of medicine. This is no different for diabetes and endocrinology and can increase confidence in managing these conditions as well as encourage trainees to pursue a career in this field.

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P279

Society for endocrinology competency framework for adult endocrine nursing – 3rd edition

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The second edition of the Society for Endocrinology (SfE) Competency Framework for Adult Endocrine Nurse was published in 2015, utilising Benners competency model from competent to expert level. Modifications for the 3rd edition were shaped by feedback from the SfE membership, the changing NHS workforce and professional practice guidance, e.g., the multi-professional framework for advanced clinical practice.
Method
A working group of expert nurses was formed to review the framework. The 2nd edition competencies were updated and a clinical practice template was utilised to provide consistency for the 3rd edition. Prioritisation of new competencies was agreed, based on safety, nurse led services and clinical need. Leadership/Management, Research and Education were included to ensure alignment with the four pillars of advanced clinical practice. A guide to evidencing competency was developed with an evidence log template.
Outcomes
Key improvements included:
- Novice and Advanced Beginner levels for nursing support workers
- Incorporation of the four pillars of Advanced Clinical Practice
- Changes to competency names to fit with current practice
- Inclusion of an evidence guide, evidence log and resources
- Nine additional competencies
- Categorisation of core competencies (Safety, Clinical Practice, Nurse Led Service)
- Access to competency framework and resources via the Online Learning Platform BES 2025 will mark the launch of the 3rd edition framework in hardcopy. In future, changes to the framework will be digital via the SfE Online Learning Platform, available globally to SfE nurse and nursing support worker members.

Conclusion
The 3rd edition of the SfE Competency Framework for Adult Endocrine offers a robust, structured and inclusive tool in supporting endocrine nurses and nursing support workers in their professional development. SfE membership provides nurses and nursing support workers with access to the SfE Online Learning Platform, whereby competencies and resources are reviewed and added in a more timely, efficient and cost-effective manner.

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P280

Growth and development of the society for endocrinology patient support group network

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Background
The Patient Support Group Network Group (PSGNG), established in 2021, is comprised of representatives from the Society for Endocrinology (SfE) affiliated Patient Support Groups (PSG), Clinical and Nurse Committees.
Aim:
The main aim of the PSGNG is to encourage and support collaboration between the SfE and affiliated PSG whilst highlighting the valuable work of the PSG in supporting clinicians and patients.
Outcomes:
Main developments in 23/24
- Utilisation of MIMS to share learning across a wider platform, active engagement in MIMS live events, e.g. British Thyroid Foundation webinars
- Raising awareness – MIMS, PSG page in *The Endocrinologist,* PSG Linktree: https://linktr.ee/PSGs
- Highlighting nonaligned endocrinology resources
- Joint PSG collaboration enabling shared expertise and wider audience
- New affiliated SfE PSG, Verity and TEDct

PSG Network Group Accomplishments over the past 3 years
- Improved collaboration, sharing expertise and communication via PSG network meetings/email, Facebook page and PSG Linktree
- Formal SfE affiliation process for PSG
- Endorsement of PSG webinars via Clinical Committee and wider reach via MIMS
- PSG resources linked via SfE Clinical Resource Hub and Events Page
- Working group for GP collaborations established
- Engagement with NICE and NIHR representatives, e.g., NICE Public Involvement Programme
- SfE publications, e.g., *The Endocrinologist*
- Active participation in SfE activities, e.g., Data Registries, BES
- PSG collaboration to create joint resources for Health Care Professional (HCP) conferences, e.g. MIMS Learning Live
- Regular updates between PSG Network, Clinical and Nurse Committee
- Developing tools for clinical use to mutually benefit HCP and Patient, e.g., PSG QR codes poster

Conclusion
The SfE PSGNG is a symbiotic forum. It allows direct engagement between the SfE and PSG enabling and developing education on disease-specific areas for both endocrinology and non-specialist HCP, improved patient centred quality of care and highlighting the value of PSG to the Endocrine community.

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Late Breaking

P281

Cushing's due to mixed corticomedullary tumour (MCMT) of the adrenal gland

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52 male presented with a 2 year history of easy bruising, hypertension, sleep apnoea, and poorly controlled type 2 diabetes (HbA1c of 125mmol/L). He had a cushingoid appearance, with central obesity, striae, proximal myopathy, and easy bruising. BMI of 29.7kg/m2 and blood pressure 163/107mmHg.

Results and treatment

Biochemical testing showed raised cortisol which does not suppress with dexamethasone. Low but detectable ACTH and plasma metanephrine raised > x4 ULN. Urine steroid profile did not demonstrate any common markers of adrenocortical carcinoma. CT adrenal - left sided 41mm adrenal lesion. 41HU pre-contrast with an absolute washout of 52%, atypical for adrenal adenoma FDG PET - increased metabolic activity in left adrenal mass (SUV_{max} 5.8) Pre-operative low dose metyrapone (250mg qds) was commenced which led to a pronounced response, cortisol reduced to mean 73nmol/l. Laparoscopic adrenalectomy was performed without complication and he was commenced on oral hydrocortisone. Post-operative biochemistry showed normal plasma metadrenaline and full suppression of cortisol on ONDST. Post operatively his HbA1c improved to 41 and he is no longer on insulin. Histology demonstrated a well-circumscribed nodule (36mm), comprising haphazardly arranged, adrenal-cortical elements (positive for synaptophysin Melan A and calretinin) and medullary elements (positive for chromogranin and Gata 3). This is diagnostic of a mixed corticomedullary tumour (MCMT) of the adrenal gland

	Result	Reference range
Random cortisols	606 and 428nmol/l	n/a
ONDST	735nmol/l	<50nmol/L
Low dose dexamethasone suppression test	551nmol/l	n/a
ACTH	11ng/L and 9ng/L	0-30ng/L
Plasma metanephrine	2398	0-509pmol/L
Plasma normetanephrine	1739	0-1179pmol/L
3-methoxytyramine	<157	0-179pmol/L
DHEA-S	4.6μmol/L	2.2 - 15.2μmol/L

Discussion

This case illustrates clinical Cushing's syndrome, with some paradoxical biochemical findings, caused by a mixed corticomedullary tumour, composed of separate populations of cortical and medullary cells that simultaneously produce adrenocortical hormones and catecholamines. These tumours are extremely rare, and to date approximately 30 cases have been reported.

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P282

Atypical presentation of primary hyperaldosteronism- a case report. hypokalaemia induced rhabdomyolysis encountered as an initial presentation of conn's syndrome, in a young lady presenting with debilitating myalgia and quadriparesis

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Primary hyperaldosteronism, is a well-documented cause of secondary hypertension characterized with resistant hypertension, hypokalaemia and metabolic alkalosis, However, its initial presentation as Hypokalaemia induced rhabdomyolysis with hormal blood pressure is rare. We report a case of Hypokalaemia induced rhabdomyolysis encountered as an initial presentation of Conns syndrome in a 38-year-old lady presented with severe myalgia, cramps, quadriparesis and fatigability. Her Serum potassium was found to be 1.68 mmol/L (reference ranges of 3.3–5.5). Her neurological assessment showed power of 3/5 in all limb with generalised hyporeflexia with intact sensory and cerebellar modality, MRI brain study was reported Normal. She was commenced on IV Fluids and potassium replacement following which CK and myoglobin levels gradually improved, but the serum potassium recovery was poor. Further evaluations strongly suggested Primary aldosteronism by an aldosterone-producing adenoma as the cause of her findings.

Discussion

Hypokalemia-induced rhabdomyolysis is a rare and potentially life-threatening condition that can arise from a variety of underlying disorders. Through this report, we aim to highlight the need for clinicians to remain vigilant in identifying rare but serious conditions like Conns syndrome, which, although rare, should not be dismissed when faced with appropriate clinical presentations. This case serves as an important teaching point that early detection and intervention are crucial for favorable outcomes.

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P283

Metrics that matter: evaluation of cambridge university hospital (CUH) adrenal incidentaloma service

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Background

Adrenal Incidentalomas (AI) are identified during 4–7% of cross-sectional imaging studies of the abdomen. The European Society of Endocrinology guidelines (ESE, 2023) set out key recommendations for AI assessment, including the use of non-contrast CT to determine if typical features of a lipid-rich adenoma are present. We reviewed our local AI service, with specific evaluation against current ESE AI guidelines.

Methods

All external and internal referrals to CUH over a 6-month period (Aug23 to Jan24) were analysed. In addition to demographic details, initial radiological characterisation and endocrine laboratory assessments were noted, along with the findings of subsequent investigations that were required to enable clinical decision-making. Reasons for referral were compared with ESE guidelines.

Results

Of 155 referrals, 70% were internal and 30% were external referrals (female 56%; male 44%). Dedicated adrenal imaging was available in 65% of cases at the time of referral, in the remainder, additional imaging was recommended to permit characterisation or guide further investigations or intervention. 56% of cases had undergone some form of hormonal evaluation prior to referral, with 31% showing biochemical evidence of autonomous hormone secretion, including 22% showing mild autonomous cortisol secretion. After radiological work up, 54% were deemed benign, 12% indeterminate, 6% suspicious for a primary adrenal malignancy, 3% suspicious for metastases, 4% myelolipomas, 5% adrenal hemorrhages, and 2% as other conditions (e.g., hemangiomas, hyperplastic adrenal glands); 6% of cases remained uncharacterized, and 8% were deemed not to have an AI.

Conclusion

Our findings confirm that referrals to the CUH AI service largely adhere to ESE guidelines. An important observation was that 35% of cases could not be adequately assessed radiologically at the point of referral due to non-dedicated adrenal imaging. To streamline the review, a formal referral proforma has been introduced, which standardizes the collection of clinical, biochemical, and imaging data.

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P284

Urine steroid metabolomics and timed urine steroid profiling for the diagnosis and differential diagnosis of cushing's syndrome

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Introduction
Twenty-four-hour urinary free cortisol is used to diagnose Cushing's syndrome (CS); amongst its limitations is failure to differentiate ACTH-dependent CS (AD-CS) from ACTH-independent CS (AI-CS). We tested the performance of urine steroid metabolomics (USM), the computational analysis of 24-hour urine steroid metabolome data by machine learning, for the diagnosis and differential diagnosis of CS. Given the physiological diurnal rhythm of cortisol secretion and its loss in CS, we also hypothesised that the difference in glucocorticoid excretion between CS and controls should be higher during nighttime, thereby facilitating more sensitive detection of CS.
Methods
264 subjects completed a 24-hour urine collection (40 AD-CS, 103 AI-CS due to adrenocortical adenoma or hyperplasia, 121 healthy subjects). A subset of 52 subjects (13 CS, 39 healthy) provided a nighttime urine collection and a daytime urine collection. Mass spectrometry-based multi-steroid profiling was used to quantify the urinary excretion of 27 steroid metabolites. Data were analysed by generalised matrix learning vector quantisation, a prototype-based supervised machine learning approach.
Results
Twenty-four-hour USM demonstrated very high accuracy in differentiating CS from healthy subjects (area under the receiver-operating characteristics curve [AUC-ROC] 0.99), reflected by higher urinary excretion of glucocorticoid and glucocorticoid precursor metabolites in CS. USM yielded high accuracy in differentiating AD-CS from AI-CS (AUC-ROC 0.88), with androgen metabolites being the most discriminatory. Timed steroid excretion in healthy subjects reflected the diurnal pattern of adrenal steroid secretion, with lower nighttime than daytime excretion of glucocorticoid metabolites. Nighttime glucocorticoid metabolite excretion (AUC-ROC 0.97) performed better than daytime (AUC-ROC 0.85) and 24-hour excretion (AUC-ROC 0.92) in separating CS cases from healthy subjects.
Conclusions
USM is a non-invasive, one-step candidate test for the accurate diagnosis and differential diagnosis of CS. Timed nighttime urine collection leverages cortisol circadian rhythmicity and improves the diagnostic accuracy of the current reference standard 24-hour collection.

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P285

Diagnostic performance of morning serum cortisol in glucocorticoid weaning in children and adults

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Introduction
Glucocorticoid-induced suppression is the commonest cause of adrenal insufficiency (AI). The morning serum cortisol levels recommended by recent NICE guidelines to confirm or exclude adrenal insufficiency (AI) are not derived from studies in patients with AI due to glucocorticoids. The aim of this study was to identify the morning serum cortisol that predicts a normal 30-minute post-synacthen cortisol in children and adults with suspected glucocorticoid-induced AI.
Materials and Methods
A retrospective cohort study of paediatric and adult patients on long-term glucocorticoids with suspected tertiary AI undergoing a short synacthen test (SST). Main outcome: morning serum cortisol cut-offs with 95% and 99% specificity and sensitivity determined via receiver operating characteristic (ROC) curve analysis. A pass for the SST was defined as a post-synacthen 30-minute cortisol of $\geq$430 nmol/L using immunoassays, Vitros 5600 (Ortho Clinical Diagnostics) in paediatric cohort, and Elecsys II (*Roche)* in the adult cohort.
Results
173 and 443 SSTs were included in the paediatric and adult cohorts, respectively, of which 32% and 36% were normal. The ROC curve analysis demonstrated that basal morning cortisol performed well in both cohorts with area under curve (AUC) of 0.77 (95%CI 0.70,0.85) and 0.89 (95%CI 0.85,0.92), respectively. Morning serum cortisol cut offs to predict a normal SST in children and adults were 280 and 285 nmol/L at 95% sensitivity, and 316 and 349 nmol/L at 99% sensitivity, respectively. In a longitudinal analysis carried out in adults, using the 95% cut off, 54 of 57 patients with morning serum cortisol values $\geq$285 nmol/L were weaned from glucocorticoids within three months.
Conclusion
A morning serum cortisol of $\geq$285 nmol/L means that most patients can be weaned from glucocorticoids without the need for synacthen testing.

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P286

A retrospective analysis of the 9am cortisol predictive value of adrenal insufficiency

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Aim
To establish 9am cortisol predictive value of adrenal insufficiency with normal/abnormal short synacthen tests (SSTs) and whether test indication influences this.
Methodology
- SSTs completed from 01/01/2023 - 30/09/2024
- Beckman assay for cortisol analysis
- Electronic patient records used to identify: SST results, pre-test 9am cortisol levels, test indication

• SST's categorised into normal (peak cortisol >450) and abnormal (peak cortisol <450)
• 9am cortisol cutoff for completing SSTs <300, although from January - November 2023 it was <350
• Two patients discounted from analysis due to questions about steroids taken pre-SST

Results

• 450 SSTs identified. 32 discounted as lacked pre-test 9am cortisol
• 418 results analysed: 355 normal, 63 abnormal
• 42 patients with normal SSTs had 9am cortisol <150, 17 of which <100
• 9 patients with 9am cortisol 151-300 had abnormal SSTs
• No patients with 9am cortisol >300 had abnormal SSTs

Table 1. Breakdown of sensitivity and specificity of 9am cortisol values

9am cortisol	<100	<150	<200	<300
Sensitivity	0.556	0.825	0.921	0.969
Specificity	0.952	0.882	0.696	0.135

The most common indications for SSTs were: GP referrals (39%), pituitary disorders (22%), long-term steroid usage (13%), immunotherapy (5%).

Table 2. Sensitivity/specificity for common test indications, 9am cutoff <150

	GP referrals	Pituitary disorders	Long-term steroid usage	Immunotherapy
Sensitivity	0.75	0.7	0.824	0.76
Specificity	0.93	0.82	0.667	0.75

Conclusion

9am cortisol <150 is a good predictor of abnormal SSTs, however testing is still required to prevent unnecessary overtreating as 45% of SSTs were normal. Equally, 3% of 9am cortisol >151 and <300 were abnormal, so testing for any 9am cortisol <300 remains necessary to prevent missed diagnosis. Categorising SST indications does not demonstrate marked improvement in sensitivity and specificity except predicting normal SST results for GP referred patients.

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P287

Statins drive sex-specific effects on macrophages and white adipose tissue

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Cardiovascular disease (CVD) is the leading cause of death worldwide, affecting both men and women. This has led to the widespread prescription of statins, with over 145 million people taking them globally. However, recent clinical data has identified sex-specific variations in statin efficacy and statin-induced type 2 diabetes (T2D). Women have historically been underrepresented in basic research and clinical trials for statins, resulting in the mechanisms underlying sex disparities in statin responses being poorly understood. Macrophages and white adipose tissue play critical roles in the pathophysiology of both CVD and T2D. Using the well-established hypercholesterolemic *Ldlr*$^{-/-}$ mouse model, this study investigated sex-specific *in vivo* responses to atorvastatin treatment over 6 months. Female mice exhibited significantly greater weight gain and larger gonadal fat depots relative to controls, whereas males showed slightly reduced weight gain without notable changes in gonadal fat deposition. Atorvastatin significantly increased insulin sensitivity, with this effect being more pronounced in female mice. RNA-seq analysis showed male bone marrow-derived macrophages exhibited more extensive transcriptomic changes compared to females (541 differentially expressed genes (DEGs) in males vs 69 in females), with statin treatment affecting genes related to motility, morphology, and viral defence responses. Conversely, atorvastatin treatment had a greater impact on gene expression in female gonadal white adipose tissue (15 DEGs in males vs 124 in females), influencing pathways associated with B cells, immunoglobulins and antiviral defence mechanisms. Protein validation of novel targets identified through RNA-seq is ongoing to further characterise the sex-specific responses to prolonged atorvastatin treatment. Overall, these findings demonstrate that sex significantly influences cellular and tissue-specific responses to statin treatment, highlighting the importance of integrating sex-specific considerations into the development and optimisation of CVD therapies for improved disease management across the whole population.

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P288

Evaluation of the overnight dexamethasone suppression test in a large cohort of patients with incidentally discovered adrenal nodules

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Introduction

Incidentally discovered adrenal nodules (AN) are detected in 1–7% of abdominal imaging studies. The 2023 ESE guidelines recommend the 1-mg overnight dexamethasone suppression test (ODST) for screening autonomous cortisol secretion (ACS). Previous studies suggest 20-50% of AN patients will fail an ODST which, in the absence of clinical evidence of Cushing's syndrome (CS), is termed mild autonomous cortisol secretion (MACS). Herein, we report findings from a large cohort of patients with AN.

Methods

512 patients (239 males, 273 females) referred between 2019 and 2023 were included. Patients with a positive ODST (cortisol ≥50 nmol/l) had dexamethasone level measured on the same sample to rule out false positives (defined as dexamethasone ≤3.7nmol/l). Patients with abnormal ODST and dexamethasone levels >3.7nmol/l were investigated for additional evidence of ACS defined as at least two of the following: elevated 24-hour urinary free cortisol, elevated late-night salivary cortisol, 9AM plasma ACTH <10pg/mL, suppressed DHEAS level.

Results

Of the 512 patients, 57 were excluded due to incomplete data, leaving 455. ODST was normal in 292 (64%) and abnormal in 163 (36%). Among the latter, 149 had adequate dexamethasone levels; 53/149 were not recommended for further investigations by the specialist adrenal MDT. Of the remaining 96 patients: 73/96 had no other clinical or biochemical evidence of ACS; 23/96 findings suggest ACS, including 3 with overt CS. Median cortisol was 88nmol/L in patients with additional positive biochemistry versus 78nmol/L in the abnormal ODST-only group ($P=0.18$).

Conclusion

Failed ODST occurred in 163 patients, with 14 false positives identified through dexamethasone measurement. Persistent biochemical evidence of ACS was identified in 23/96 patients, including 3 with overt CS. This study highlights the need to consider new biomarkers to identify MACS detection and stratify those at highest cardiovascular risk, while considering the economic and clinical burden of MACS screening.

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P289

Insights into the health status of adults with CAH in the UK and Ireland - CaHASE2

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Congenital adrenal hyperplasia (CAH) is one of the commonest forms of primary adrenal insufficiency with an incidence of about 1 in 15,000. The first CaHASE study highlighted the suboptimal health status and care provision in adults with CAH. This was associated with significant co-morbidities in relatively young adults. In 2023, we implemented CaHASE2 (https://www.endocrinology.org/clinical-practice/research-projects/cahase-2/) to develop a strategy for prospective collection of longitudinal data. After agreeing a minimal dataset for the collection of real-world data, participating centres collect the longitudinal data using the international CAH registry (I-CAH; https://sdmregistries.org/). A total of 351 adults with CAH (213 females, 138 males) have been recruited until now and 1213 clinic visits were available for analysis. In the current dataset, there is a preponderance of younger to middle-aged adults in the patient cohort that has been currently recruited. Preliminary data collection and analysis suggests that there might be a temporal change in used glucocorticoids over time with an increased use of hydrocortisone and a decreased use of prednisolone. Based on available 17OHP concentrations a significant proportion of patients appear to be overtreated. A significant proportion of patients with CAH who have been recruited are overweight or obese. Currently 18 centres are actively recruiting and 5 are awaiting local approval to use the I-CAH registry. The data will be analysed in 12-month cycles, to assess the current level of care provision and inform the development of national CAH standards. Once longitudinal data are collected, we

will be able to investigate differences in health care provision and potential differences in health status and outcomes.

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P290

Diagnosis and management of mild autonomous cortisol secretion (MACS) suppressible to dexamethasone in patients with incidentally discovered bilateral adrenal masses

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Background
MACS is defined as hypercortisolism not suppressed by dexamethasone in patients without overt Cushing's syndrome (CS) features. In patients with bilateral macronodular adrenal disease (BMAD), excess cortisol production is frequently due to aberrant cortisol responses leading to perturbed cortisol rhythmicity, yet in some patients cortisolemia is suppressed by dexamethasone.
Aim
To describe the clinical characteristics and management of patients with BMAD and dexamethasone-suppressible cortisolemia.
Results
10 patients (8F/2M) out of 104 patients evaluated between 2015-2024 for incidentally-discovered bilateral adrenal masses were identified. Median age at diagnosis was 62 yrs (range 42-74). Prevalence of overweight/obesity was 70%, diabetes mellitus 50%, arterial hypertension 90%, osteoporosis 20%, obstructive sleep apnoea 20%. Cortisolemia was <50 nmol/L after 1mg DST or LDDST at the initial evaluation. UFC was elevated only in one patient (M, 42yo). Midnight serum cortisol was elevated in 8/9 patients (90.5-344 nmol/L). Morning ACTH was <10 pg/mL in 50% of patients (range 5.02-24.66). All patients tested (7) demonstrated aberrant cortisol responses: to food (all), GnRH agonist (2/7) and orthostatism (1/7); 2 patients showing multiple responses. 4 patients had increased ARR, 2 with confirmed primary hyperaldosteronism. Median follow-up was 33 months (range 0-108). No patient manifested cyclical CS. Progression of hypercortisolism was discrete: baseline ACTH decreased and dexamethasone suppression was lost in 2 patients. One patient (M, 42yo) underwent unilateral adrenalectomy, with improvement of diabetes and hypertension control and remission of concomitant hyperaldosteronism. The remaining patients were monitored for comorbidities attributable to hypercortisolism, without intervention.
Conclusion
Patients with dexamethasone-suppressible BMAD have a high morbidity burden. Demonstration of autonomous cortisol production requires additional tests (midnight cortisolemia/screening for aberrant adrenal receptors). Management remains predominantly conservative, in line with current guideline, although these patients are candidates for treatment with inhibitors of steroidogenesis (chronotherapy/block and replace).

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P291

Early-Onset Hajdu-Cheney Syndrome: Case Report of Severe Phenotype and Response to Zoledronic Acid Therapy

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Background
Hajdu-Cheney syndrome (HCS) is a rare genetic skeletal disorder characterized by diverse phenotypic features, leading to delayed diagnosis. The syndrome involves significant skeletal abnormalities, including acro-osteolysis and severe osteoporosis. No definitive pharmacological treatment exists for HCS, and bisphosphonate efficacy remains uncertain due to limited studies. Here, we present a case of early-onset HCS in a preschool-aged female with severe features and her response to zoledronic acid.
Case Presentation
The patient, born to healthy parents, presented with facial deformities, micrognathia, and cranial defects at birth. During the first year, she also developed hearing impairment, congenital cardiac anomalies, and developmental delay. At one year, she underwent surgery for patent ductus arteriosus (PDA) and ventricular septal defect (VSD), during which skull radiographs revealed wormian bones, initially overlooked. By age seven, the patient showed worsening skeletal deformities, including acro-osteolysis, osteoporosis, fractures, and short stature. Radiographic assessments confirmed reduced bone mineral density, while elevated serum alkaline phosphatase indicated increased bone turnover. Genetic analysis identified a de novo pathogenic duplication in exon 34 of the NOTCH2 gene (c.6426dupT, p.E2143X), confirming HCS. The patient began treatment with calcium carbonate, cholecalciferol, and annual zoledronic acid infusions. Over 4.5 years, bone mineral density (BMD) improved significantly, especially in the whole body (excluding the cranium), with a 33.7% increase. Alkaline phosphatase levels normalized within the first year, and no new fractures occurred.
Conclusion
This case is the second documented occurrence of HCS linked to the c.6426dupT mutation in the NOTCH2 gene, demonstrating early onset and severe phenotype. Early recognition of HCS is essential for effective management. Zoledronic acid treatment was associated with significant BMD improvements and may help reduce osteoporosis progression and prevent fractures. Further studies are needed to confirm the long-term efficacy and safety of this approach.

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P292

An insidious cause of bilateral hip pain in pregnancy

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Tumour-induced osteomalacia (TIO) is a paraneoplastic syndrome caused by the overproduction of fibroblast growth factor (FGF23) from a tumour. It is characterised by renal phosphate-wasting, resulting in hypophosphatemia, osteomalacia and fragility fractures. Clinical manifestations are non-specific, often leading to misdiagnosis or delayed diagnosis. A thirty-five-year-old female presented to her GP with bilateral hip/groin discomfort at seven months gestation and was diagnosed with Symphysis Pubis Dysfunction. She experienced worsening bony pain in her ribs and back, particularly after childbirth. She was breastfeeding. An MRI of her hips revealed multiple pelvic ring insufficiency fractures and bilateral femoral neck stress fractures. DEXA scan showed low BMD at the spine and hips (Z-scores: -2.8 and -3.1, respectively). She was referred to the Endocrine Bone clinic, where Pregnancy-Lactation-induced osteoporosis was initially suspected. Blood tests showed ALP bone isoenzyme 73(5-16 units/L), calcium 2.33(2.20-2.60 mmol/L), vitamin D 99.3(50-150 nmol/L), low phosphate 0.45(0.80-1.50 mmol/L). Tubular maximum re-absorption of phosphate to GFR ratio was significantly reduced at 0.32(0.84-1.23 mmol/L), demonstrating a renal phosphate leak. FGF23 level was inappropriately raised at 313(<100 RU/mL) with low 1,25 Vitamin D. Oral phosphate replacement and alfacalcidol were started with some biochemical improvement but continued symptoms. A Gallium DOTATE PET identified a DOTATE avid lesion within the flexor compartment of the upper right thigh. She successfully underwent surgery to remove the lesion with histology in keeping with a phosphaturic mesenchymal tumour. By day 5 post-operatively, her phosphate level had normalised off supplements. Despite presenting with debilitating symptoms and multiple fractures, our patient's diagnosis was delayed in primary care. Overlapping symptoms led to an early misdiagnosis of SPD and suspicion of PLO. It is vital to raise awareness of TIO so that appropriate and timely investigations and potentially curative surgery are performed.

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P293

Systems-level analysis of [^{18}F]FDG PET to study bone metabolism in healthy and osteomyelitis pigs

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Introduction
Our understanding of complex tissue interactions at a systems level remains rudimentary, limiting our ability to dissect mechanisms underlying diseases and develop novel therapeutics. Skeletal research has focused on the pathogenicity of obesity and diabetes mellitus on the skeleton; however, it has been recently revealed that the skeleton is not merely an endocrine target but also a secretory organ, modulating systemic energy homeostasis. We have recently discovered that different bones within the murine skeleton have a unique glucose metabolism and form a complex metabolic network. Pigs are remarkably like humans in terms of their physiology and are the biomedical model of choice for bone anatomy and physiology studies, yet the endocrine role of bone in the pig is yet to be investigated.
Hypothesis
Different bones within the porcine skeleton have unique molecular signatures and form a distinct metabolic network, which is altered by osteomyelitis.
Methods
Pigs (healthy n = 5/*S. aureus* n = 3) underwent static [^{18}F]FDG PET/CT and were analysed to measure bone and bone marrow adipose tissue (BMAT) glucose metabolism. Bone and BM volumes of interest were segmented in CT images using Hounsfield Unit (HU) > 300 (bone) and -200 to 115 (BMAT). Standardised uptake values were used to perform network analysis (Graphia).
Results
Similarly to what has previously been observed in the mouse and human, there was an increased incorporation of [^{18}F]FDG in the axial skeleton compared to the appendicular skeleton in both healthy and osteomyelitis pigs. Osteomyelitis pigs had a lower bone density, increased BMAT volume, and increased incorporation of [^{18}F]FDG into the bone and BMAT compared to healthy controls. Network analysis indicated a shift in bone metabolic profiles between healthy and osteomyelitis pigs.
Conclusion
Different bones within the porcine skeleton have a unique glucose metabolism and form complex metabolic networks, which are altered by osteomyelitis.

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P294

Urinary calcium measurements in patients with hypercalcaemia; results from united kingdom national survey of endocrinologists and endocrine surgeons

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Introduction
In patients with hypercalcaemia, assessment of urinary calcium excretion helps differentiate primary hyperparathyroidism (PHPT) from familial hypocalciuric hypercalcaemia (FHH). International guidelines recommend 24-hour calcium to creatinine clearance ration (CCCR) as the preferred test for this purpose, but other tests like random (or spot) CCCR test, 24-hour urine calcium excretion (UCE), and calcium to creatinine ratio (CR) are frequently used. The aim of this survey is to evaluate the current practice among UK endocrinologists and endocrine surgeons.
Methods
A web-based anonymous cross-sectional survey, consisting of 8 multiple-choice questions was developed using Survey Monkey®. The survey was disseminated to members of Society for Endocrinology (SfE) and British Association of Endocrine and Thyroid Surgeons (BAETS) between 20/11/2025 and 12/12/2025.
Results
248 responses from 192 endocrinologists (83.9% consultants) and 56 surgeons (98.2% consultants) were received. Respondents worked in both university/tertiary hospitals (n = 128; 51.6%) and district general hospitals (n = 114; 46%). Although the most commonly performed urinary calcium excretion test in hypercalcaemic patients is 24-hour UCE (60.1%), for differentiation between PHPT and FHH, the most preferred test was 24-hour CCCR (43.1%), followed by random CCCR (24.6%), 24-hour UCE (14.5%), and CR (8.5%). Of the respondents who had experience or knowledge with using CCCR, most (59.5%) used a cut-off of > 0.01 to rule out FHH, while > 0.02 cut off was used by 27.7% respondents. Most clinicians (75.9%) used albumin-adjusted calcium for CCCR calculation, and 71.8% respondents considered vitamin D levels on ≥ 50 nmol/L to be adequate for any type of urinary calcium measurement. Simultaneous urinary sodium measurement is never or rarely performed by most respondents (71.4%).
Conclusion
The survey provides valuable insight into current UK practice. 24-hour and random CCCR are the most commonly used tests to exclude FHH, but overall, the practice varies widely.

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P295

Bisphosphonates: are they always useful in hypercalcaemia of known malignancy?

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Hypercalcaemia due to malignancy can be treated with intravenous (IV) bisphosphonates. However, not all should receive bisphosphonates. It is important to establish the hypercalcaemia's causes to guide treatments. A 71-year-old female initially presented to GP with back pains, lumbar spine magnetic resonance imaging showed widespread abnormal bone marrow signal, suspicious of metastasis. Bloods found hypercalcaemia (3.23mmol/L), raised parathyroid hormone (14.7pmol/L) and low 25-OH vitamin D (32nmol/L). She was admitted via the Emergency Department, given IV fluids, bisphosphonates (pamidronate), and Vitamin D replacement; treated for hypercalcaemia secondary to malignancy of unknown primary and referred to the Endocrinology team. When her calcium levels improved, she was discharged with plans for calcium monitoring at the Ambulatory unit. Further investigations were also done to locate the primary. A week later, her calcium levels were again, raised. She was given further IV fluids and bisphosphonates. Despite good initial responses to treatments, including zoledronic acid, her calcium levels kept creeping back up a week later, necessitating weekly attendances to the unit. Due to the imaging findings, and primary hyperparathyroidism, atypical presentation of osteitis fibrosa cystica was initially suspected. Following further investigations, It was later discovered she had metastatic breast cancer, and parathyroid adenoma (the culprit for treatment resistance). The adenoma was eventually removed surgically and her calcium has improved since. Using bisphosphonates to decrease calcium levels could trigger parathyroid adenomas to release more parathyroid hormone, causing rebound hypercalcaemia. Surgical removal of adenoma is more useful. Denosumab could also be considered because it is can lower parathyroid hormone-induced bone turnover. Nevertheless, further studies are required because there are limited data available on the use of denosumab in resistant hypercalcaemia secondary to primary hyperparathyroidism. In summary, patients with possible or known malignancy with hypercalcaemia could also have concurrent primary hyperparathyroidism. Giving them bisphosphonates might not solve their problems.

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P296

Hypercalcemia with abnormal pathology

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Introduction
Primary hyperparathyroidism (HPTH) and familial hypocalciuric hypercalcemia (FHH) are two important differential diagnoses for high calcium with non-suppressed parathyroid hormone (PTH). In this case report, we would like to present an unusual cause of hypercalcemia.
Clinical case
A 68-year-old lady was seen in endocrine clinic for hypercalcemia with normal PTH. She reported fatigue, depression, and abdominal pain intermittently but denied polyuria, polydipsia, or thyroid disease. She was diagnosed with FHH in her thirties. She denied taking Vitamin D, calcium supplements or family history of FHH.
Investigations
The adjusted calcium ranges from 2.86 to 3.06 mmol/L (2.2 - 2.6) with non-suppressed PTH. Her initial urine calcium creatinine clearance ratio (UCCCR) was 0.0056. Her vitamin D was 66nmol/L. The ultrasound of the urinary tract was unremarkable. Her bone density showed osteopenia at the femoral neck. The Sestamibi scan and the ultrasound parathyroid failed to localize an adenoma.
Management
She attended ambulatory care twice for hypercalcemia of more than 3mmol/L that required treatment. She was discussed in a multidisciplinary team (MDT) meeting, which recommended the low UCCCR was suggestive of FHH whereas the calcium of 3.01mmol/L was more in favour of HPTH. The plan was to repeat UCCCR, replete vitamin D, to send genetic testing for FHH and perform a 4D CT neck. Vitamin D was replaced. The genetic testing confirmed CASR gene-related FHH. The CT neck revealed a 6mm nodule that is highly suggestive of a left inferior parathyroid adenoma and a 3mm possible right parathyroid adenoma. She was discussed again in the MDT meeting and was referred to a tertiary centre for further management given dual pathology.
Conclusion
This rare case highlighted that one needs to be vigilant of the possibility of concurring FHH and primary hyperparathyroidism when calcium level is disproportionate to UCCCR.

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P297

From sunshine to setbacks: the untold stories of vitamin D toxicity

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Vitamin D, vital for overall health beyond its traditional role in bone metabolism, has seen a significant increase in use in recent years, particularly during the COVID-19 pandemic, due to its cited immune-boosting properties. An Irish Longitudinal Study on Aging (TILDA) reported a significant rise in vitamin D supplementation during pandemic, particularly among women (17.3%) compared to men (11.1%). However, this surge in consumption has been accompanied by a rise in cases of vitamin D toxicity. This increase is linked to misuse of over-the-counter supplements or erroneous prescriptions. Vitamin D toxicity leads to hypercalcemia, with symptoms ranging from fatigue to confusion and kidney injury in severe cases. Among cases of toxicity, vitamin D levels > 375 nmol/L have been observed. Hypercalcemia in this context can persist for up to 18 months. Diagnosis requires clinical history, laboratory testing and exclusion of alternative causes of hypercalcemia. We report two cases of hypercalcemia secondary to vitamin D toxicity. The first case involves a 74-year-old male who presented with constipation, polydipsia, fatigue, weight loss and renal impairment. He had been self-administering high-dose vitamin D (10,000IU daily) since the COVID-19 pandemic, leading to confirmed vitamin D toxicity with levels > 375 nmol/L. The second case involves a 73-year-old female who presented with confusion, weight loss, and decreased appetite. Tests revealed vitamin D levels > 375 nmol/L. Both patients had been using excessive over-the-counter vitamin D and calcium supplements, with other causes of hypercalcemia excluded. In the wake of the COVID-19 pandemic, the widespread use of vitamin D supplements increased due to broad recommendations. With high-dose supplements readily available online without prescription, there has been a significant increment in vitamin D toxicity incidence. This observed rise in cases represents a need for education and awareness about potentially dangerous consequences among healthcare providers and the general population.

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P298

Navigating the rare intersection: parathyroid adenoma in a patient with pseudohypoparathyroidism

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Introduction
We present a rare case of a 59 year old female patient with Albright's Hereditary Osteodystrophy (AHO), a phenotype of pseudohypoparathyroidism (PHP), who developed a parathyroid adenoma. We aim to highlight the diagnostic and therapeutic considerations in managing the development of hypercalcaemia in the context of AHO/PHP.
Case
The patient was diagnosed with pseudohypoparathyroidism at age 33 after presenting with symptoms of hypocalcaemia. She exhibited phenotypic features of AHO, including an elevated BMI (34.5kg/m^2) and short metacarpals, but genetic tests were negative. She was treated with alfacalcidol and cholecalciferol to maintain calcium at a target of 2.40mmol/L. DEXA scans indicated normal bone density and she did not develop nephrolithiasis. At age 51 she joined our service, and her albumin adjusted calcium (aaCa) level whilst on alfacalcidol ranged between 2.55 - 2.76 mmol/L. At age 58, the patient's PTH level had risen to 26.8 pmol/L with an aaCa level of 2.67 mmol/L. Alfacalcidol was discontinued, but hypercalcemia persisted prompting further investigation. A whole-body SPECT CT scan showed no brown tumours. A parathyroid ultrasound localised a left inferior nodule, further corroborated on sestamibi scan, measuring 9x6x6 mm. There was a possible second, right inferior nodule that was equivocal. The multidisciplinary team concluded that the patient had developed a parathyroid adenoma, possibly due to tertiary hyperparathyroidism (THPT) in the context of PHP. She has since been managed with cholecalciferol alone and referred for consideration of parathyroid surgery.
Discussion
In more than 20% cases of THPT the underlying pathology has been observed to be a result of single or double parathyroid adenomas. Although PTH resistance is characteristic of PHP, hypercalcemia can occur due to partial resistance, potentially leading to THPT. In the context of PHP, elevated calcium levels should lead clinicians to consider the possibility of parathyroid adenoma development.

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P299

Hidden in time: delayed-onset hypoparathyroidism diagnosed decades post-thyroidectomy

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Hypoparathyroidism is a rare complication that may occur as a result of thyroid surgery, this typically occurs in the immediate postoperative period. While resolution of hypoparathyroidism usually occurs on an average of two months postoperatively, approximately 1.9% become permanent. The delayed appearance of hypoparathyroidism decades after surgery is exceptionally rare, with no previously documented cases of hypocalcaemia manifesting more than 40 years postoperatively. We present a case of an 82-year-old patient whom was referred for an incidentally detected low calcium level (1.93 mmol/L). She had undergone a total thyroidectomy 40 years earlier for a compressive goitre. Postoperatively, no calcium levels were documented, and the patient had remained largely asymptomatic throughout her life. Laboratory tests had revealed a parathyroid hormone (PTH) level of 3.0 pmol/L (inappropriately low), elevated phosphate (1.75 mmol/L), and adequate vitamin D levels. Although no histology results were available to confirm parathyroid preservation during surgery, the patient's findings were consistent with a diagnosis of late-onset partial hypoparathyroidism. She was thereafter started on low dose of alfacalcidol to help regulate her calcium levels. This case highlights a rare presentation of delayed protracted post thyroidectomy hypoparathyroidism (> 40 years post operatively), that to our knowledge has never been reported before. There are currently no available guidance for long term monitoring for post thyroidectomy patients and periodic surveillance of calcium levels may be necessary considering hypoparathyroidism may occur even after protracted periods of time as described as the case above.

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P300

Dual hypercalcaemic pathologies: familial hypocalciuric hypercalcaemia (FHH) and primary hyperparathyroidism

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Introduction
It is rare for someone with FHH to have co-existing primary hyperparathyroidism. We describe a case of a 50-year-old woman who was assumed to have FHH due to her strong family history of hypercalcaemia. However, her recurrent admissions with hypercalcaemia prompted further investigations that suggested primary hyperparathyroidism.
Clinical History
Patient was known to have hypercalcaemia since age of 12 years. Father had parathyroidectomy, her sister, children and grandchildren were also known to have hypercalcaemia. However, none had any diagnostic genetic testing. Since 2019 she attended emergency department 5 times due to symptoms of palpitations, nausea and headache. Three of these visits occurred in the past 12 months.
Diagnostics
Initial tests in primary care in 2018 showed PTH 7.8 pmol/L, adjusted calcium 3.15mmol and phosphate of 0.59mmol/L. In 2019 her PTH was 11.8pmol/L and recently it was 16.9pmol/L. Her adjusted calcium remained above 3.10 mmol since 2018. 24hr Urine Calcium was 2.19mmol/24hr (low) in 2019 and 4.00 mmol/24hr (normal) in 2022. Her DXA and renal ultrasound were normal. MIBI/SPECT CT in 2020 revealed no abnormality. However, Ultrasound of Neck in 2023 showed 8mm nodule close to trachea and a repeat MIBI/SPECT CT revealed a 7mm nodule in the tracheo-oesophageal groove. Genetic testing in 2024 was positive for heterozygous variant in CASR causing FHH Type 1.
Management
Her symptoms during admissions were managed with intravenous fluids and bisphosphonates. In late 2023 she was prescribed Cinacalcet 30mg twice daily which was later increased to 90mg three times daily. Currently she is awaiting surgery
Conclusion
This case elucidates that progressive rise in PTH and recurrent admissions with symptomatic hypercalcaemia despite high doses of cinacalcet were important cues for an additional cause of hypercalcaemia.

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P301

Low bone mass in a young female: a case report

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Introduction
Low bone mass in young patients is often poorly managed. There is little guidance/consensus in investigating and managing this condition among specialists. There are numerous causes of low bone mass including genetic, hormonal disturbances, nutritional disorders, chronic diseases of childhood or adolescence, medications, etc. Coeliac disease is one of many secondary causes of osteopenia and osteoporosis. It is under-diagnosed and often not diagnosed until adulthood.
Case
A 41-year-old female with a history of non-osteoporotic fracture and low bone mass was referred for specialist review. She was on bisphosphonate therapy for 1 year before the specialist consultation. Her diet predominantly consisted of salads. Most foods caused her abdominal discomfort and bloating.
Investigations
Bone mineral density (BMD) revealed a normal bone profile with Vitamin D of 49.3 nmol/L. Her BMD revealed a Z-score of -2.1 in the lumbar spine, -2.1 in the left femoral neck and -1.8 in the left total hip. She had a coeliac screen which was positive with normal IgA levels. Subsequent duodenal biopsy demonstrated villous atrophy.
Discussion
The patient had confirmed coeliac disease. Her vitamin D deficiency was treated. She was advised about a gluten-free diet. Following her diagnosis, her children were also diagnosed with vitamin D deficiency and coeliac disease. The diagnosis had a life-changing impact on the patient and her family. This case highlights the importance of good history-taking and the importance of considering secondary causes in young patients presenting with low vitamin D and low bone mass. Vitamin D is the most common vitamin deficiency in the developed world. Currently, there is no guidance on the treatment of vitamin D insufficiency/deficiency in adults and children without CKD. Establishing national/international guidance is suggested.

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P302

Benign adrenal adenoma transforming to adrenocortical carcinoma – the challenge in consultation with patient and family in this rare occurrence

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Introduction
The transformation of benign adrenocortical adenoma (ACA) to adrenocortical carcinomas (ACC) are extremely rare (<1%). In this situation, it is often very challenging in breaking the bad news to patients and families. We present a case of 69-year old female investigated for an incidental ACA with stable radiological appearance over 3 years but unfortunately transformed into ACC in just over 12 months.
Case Presentation
A 69-year old non-smoker lady with background of bronchiectasis, single agent- and well-controlled type 2 diabetes and hypertension, was found to have an incidental well-defined right sided adrenal nodule (26x17x36mm) on CT chest for bronchiectasis investigation. The lesion did not meet the signal dropout criteria for a benign lesion, but over 3 years of follow up, the radiological appearance remained stable. Clinically, she did not exhibit features suggestive of hormonal hypersecretion. Her biochemistry suggested possible mild autonomous cortisol secretion (MACS) but otherwise unremarkable renin, aldosterone, 24-hour urinary catecholamines, DHEAS, testosterone, and 24-hour urinary steroid profile (USP). After adrenal MDT discussion and with patient, we agreed to discharge her with community monitoring of metabolic markers in view of MACS. Unfortunately, she represented with severe hyperglycaemia in a years' time. Her CT imaging showed significant increase in size of the previous ACA (100x45x60mm). Repeat adrenal biochemistry showed clear-cut hypercortisolism and significant difference in the 24-hour USP, suggesting steroid excess and possible ACC. Full radiological screening including PET-CT confirmed a solitary adrenal mass. Breaking the bad news to an understandably upset patient and family was extremely challenging in view of the rare occurrence and previous reassurance of the benignity. She underwent a right adrenalectomy when stable.
Learning Point
Although rare, it's crucial to highlight the small risk of ACA transforming to ACC. However, the balance of doing this with risk of 'over-worrying' the patient needs to be achieved.

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P303

Immune checkpoint inhibitors in patients with pre-existing graves' disease

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Background
Immune checkpoint inhibitors (ICIs) have transformed cancer treatment by boosting the immune system to target and destroy cancer cells. However, they are associated with immune-related adverse events, including endocrine toxicities. Thyroid dysfunction, especially hypothyroidism following transient thyrotoxicosis, is a common side effect, with a reported incidence of 2.5-15%. The effects of ICIs on patients with pre-existing autoimmune thyroid disease, particularly Graves' disease (GD), are not well-documented, and the concern would be risk of precipitating recurrent hyperthyroidism and thyroid eye disease (TED); we report three recent cases with a history of GD treated with ICIs.
Cases presentation
Case 1:57-year-old male with melanoma and past history of GD complicated by TED requiring IV methylprednisolone. After receiving two cycles of ipilimumab and nivolumab, followed by nivolumab alone, he developed transient thyrotoxicosis characteristic of ICI thyroiditis, which later progressed to hypothyroidism without exacerbation of his TED. He required levothyroxine treatment and had complete response to immunotherapy. Case 2: 56-year-old female with melanoma who received pembrolizumab. She had a history of GD treated with carbimazole, and after starting ICIs, she developed thyroiditis, followed by hypothyroidism requiring treatment with levothyroxine. Case 3: 76-year-old female with inoperable oesophageal SCC and newly diagnosed GD with thyroid eye disease. After starting chemotherapy and pembrolizumab, her thyroid function remained stable, with ongoing tapering down in carbimazole dosage and no worsening of mild TED.
Conclusion
No patient developed flare of GD/TED. Patients with past GD do need careful warning of theoretical risk of recrudescence and TED symptoms flagged. Vigilant monitoring for thyroid abnormalities is essential. Potential adverse outcome data are limited, and benefits of ICIs in treating cancer in patients with Graves' disease outweigh the theoretical risk.

Keywords
immune checkpoint inhibitors, Graves' disease, thyroid dysfunction, hypothyroidism, cancer treatment, endocrinopathies

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P304

Oestradiol: immunoassay measurement can be inaccurate in patients taking fulvestrant

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Introduction
Fulvestrant, a selective oestrogen receptor regulator and Exemestane, a steroidal aromatase inhibitor therapy, are used in the treatment of oestrogen receptor positive breast cancer. Most manufacturers of oestradiol (E2) immunoassays state that Fulvestrant interferes in their assay, some also state that aromatase inhibitors may interfere.
Method
Sample pools (n = 3) were prepared from off-the-clot human serum obtained from female donors: Sample A – the base serum with no added analytes, Sample B – the base pool with Fulvestrant (25ng/mL) added, and Sample C – the base pool with Exemestane (150pg/mL) added. The samples were distributed to all participants measuring E2 in the UK NEQAS for Steroid Hormones EQA Scheme (Distribution 523). The cross-reactivity of each method was calculated for both drugs, comparing the results obtained from the base pool with those from the spiked samples. Participants were asked to answer some web Q&A's on how requests are processed for patients on Fulvestrant and Exemestane.
Results
No significant changes in E2 concentrations were observed in samples containing Exemestane when compared to the base pool. However, in samples containing Fulvestrant a positive bias was observed for several methods including the Siemens ADVIA Centaur and Atellica, and Abbott Alinity and Architect methods. Negligible cross-reactivity was observed in other manufacturers' methods and the LC-MS/MS group. Of the Q&A respondents, 85% do not vet

oestradiol requests on the basis of clinical details, only 27% of respondents refer E2 requests for analysis by LC-MS/MS at the request of the clinician or after reviewing clinical details.
Conclusion
Fulvestrant significantly interferes in some E2 immunoassays and may lead to over-estimation of oestradiol concentrations in patients receiving therapy. While most manufacturers state that Fulvestrant interferes in oestradiol immunoassays, many laboratories do not act on this information. This could lead to inappropriate management of patients being treated with Fulvestrant.

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P305

A rare case of adrenocortical carcinoma in a young male with familial cancer susceptibly

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Background
Adrenocortical carcinoma (ACC) is a rare malignancy with varied clinical presentations. While sporadic cases are common, familial predisposition plays a significant role in some cases, particularly in younger patients. We present a case of aggressive ACC in a young adult with strong familial cancer susceptibility.
Case Presentation
A 29-year-old male presented with a 4-month history of pleuritic chest pain, dyspnea, right upper quadrant abdominal mass, and 15kg weight loss without any features of hormonal excess. Initial imaging revealed a 17x14.3cm mass between the right kidney and liver, with extensive pulmonary and hepatic metastases. Ultrasound-guided biopsy confirmed adrenocortical neoplasm with oncocytic features, necrosis, and high mitotic activity. Immunohistochemistry showed diffuse positivity for Melan A and Synaptophysin, consistent with ACC. Family history revealed familial predisposition to cancer including adrenocortical, breast, and uterine cancers.
Management
Adrenal MDT commented that tumor was inoperable, and palliative chemotherapy was recommended. However, the patient developed complications including sepsis and acute kidney injury. Repeat CT abdomen showed portal empyema and renal & IVC thrombosis. An overnight dexamethasone suppression test done during initial response to antibiotics revealed hypercortisolemia. Despite initial response to antibiotics, the patient's condition deteriorated rapidly and scummed before cortisol-lowering therapy could be initiated.
Discussion
This case highlights the aggressive nature of ACC in young adults and the importance of considering genetic predisposition. ACC runs in families 50% of the time. Genetic testing is recommended for all close relatives of people with ACC.
Conclusion
This case emphasizes the importance of early recognition of ACC, particularly in young patients with family history of cancer. Diagnosis in this rare case was delayed due to nonspecific presentation. The aggressive course and rapid deterioration highlight the need for prompt diagnosis and treatment.

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P306

A case of multiple endocrine neoplasia type 1 presenting with dopamine agonist-resistant aggressive macroprolactinoma and PTH-driven hypercalcemia

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Background
Multiple Endocrine Neoplasia type 1 (MEN1) is a rare hereditary endocrine cancer syndrome characterized by tumors predominantly affecting the parathyroid glands (95%), gastroenteropancreatic tract (30-80%), and anterior pituitary (15-90%)(1). We present a case of MEN1 initially manifesting with headaches and visual symptoms due to an aggressive macroprolactinoma.
Case Presentation
A 39-year-old male presented in 2018 with headache and visual disturbances. MRI revealed a 33x31x24mm pituitary lesion with optic chiasmal compression, suprasellar and left parasellar extension, encasing bilateral internal carotid arteries. Initial investigations showed markedly elevated prolactin (28,267 mIU/L) and hypogonadotropic hypogonadism. Though Concurrent hypercalcemia with inappropriately normal parathyroid hormone levels was initially overlooked but later led to diagnosis of Primary Hyperparathyroidism. PHPT diagnosis was supported by elevated 24-hour urinary calcium. The patient reported multiple renal stones since youth. DEXA scan excluded osteoporosis.
Management
One year of dopamine agonist therapy showed poor response (prolactin 9,055 mIU/L), necessitating transsphenoidal resection. Histopathology confirmed a lactotroph adenoma. Post-operatively, despite continued cabergoline, prolactin remained elevated (3,000-4,000 mIU/L). Testosterone replacement was initiated for hypogonadism. The combination of resistant macroprolactinoma and primary hyperparathyroidism prompted MEN1 genetic testing. Further investigations revealed mildly elevated gastrin (48 pmol/L) and an incidental non-functional 1.6cm adrenal adenoma. Despite negative parathyroid localization, the patient underwent successful parathyroid exploration in May 2024.
Discussion and Conclusion
This case highlights the importance of systematic endocrine screening in patients with pituitary tumors, particularly when accompanied by hyperparathyroidism. Early recognition of MEN1 syndrome specially in young patients with resistant macroprolactinomas is crucial for appropriate surveillance and management of concurrent endocrine neoplasms.
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P307

Impact of diabetes and plasmodium berghei NK65 infection on immune and metabolic parameters in BALB/C Mice

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Diabetes mellitus, a chronic metabolic disorder, adversely affects organs such as the heart, liver, and kidneys over time. Malaria, caused by *Plasmodium* species transmitted by infected mosquitoes, is a life-threatening disease and has been reported to be more prevalent in diabetic individuals in Nigeria. This study investigated the biochemical and immune alterations in mice subjected to co-morbid diabetes and *Plasmodium berghei* NK65 infection. Fifty-four male BALB/c mice were divided into eight groups: Group 1 (Normal Control), Group 2 (Malaria only), Group 3 (Diabetes only), Group 4 (Diabetes + Malaria), Group 5 (Malaria + Artemether-Lumefantrine [AL]), Group 6 (Diabetes + Metformin [MTF]), Group 7 (Diabetes + Malaria + MTF), and Group 8 (Diabetes + Malaria + MTF + AL). Diabetes was induced using streptozotocin (40 mg/kg for five consecutive days), and malaria was established by inoculating mice with *P. berghei*. Treatments included metformin (200 mg/kg body weight) for diabetes and artemether-lumefantrine (1.14/6.86 mg/kg) for malaria. The results indicated a significant reduction in body weights of infected groups compared to treated groups. Fasting blood glucose and parasitemia levels were significantly elevated ($P<0.05$) in co-morbid mice (Group 4) compared to single-condition groups (Groups 2 and 3). Creatinine levels significantly decreased in treated groups compared to untreated controls, while no significant differences were observed in urea concentrations or median TNF-α levels across groups. However, interleukin-6 (IL-6) levels were significantly elevated ($P=0.046$) in co-morbid mice compared to the Normal Control. This study highlights the increased susceptibility of diabetic mice to *P. berghei* infection and reveals that metformin lacks prophylactic efficacy against malaria. These findings emphasize the need for targeted therapeutic strategies in managing diabetes-malaria co-morbidities.

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P308

Evaluating #diabetesmanagement content on tiktok: accuracy, influence, and patient guidance

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Introduction
The popular social media platform TikTok has emerged as a significant influencer on healthcare information. It enables the sharing of medical advice, personal experiences, and community building. However, concerns about the accuracy of health-related content persist. This study evaluates the reliability of diabetes

management information on TikTok and examines the accuracy of the guidance provided.
Methodology
We conducted a qualitative content analysis of the 50 most-viewed TikTok videos tagged with #diabetesmanagement over a 30-day period. Videos were analysed based on creator affiliation, content accuracy, format (educational, narrative, or promotional), and the use of evidence-based references.
Results
Only 26% of the videos were produced by healthcare professionals. Content accuracy varied considerably, with 46% of posts being accurate, 28% partially accurate, and 26% inaccurate. Educational content comprised 68% of the posts, while 24% focused on personal experiences and 8% on promotional content. Notably, only 14% of posts cited references, with the remaining 86% lacking credible supporting evidence.
Discussion
TikTok offers opportunities and challenges for patient education. While the platform enables engaging health content, the prevalence of misinformation remains a concern. Numerous studies, including ours, highlight the rapid spread of inaccurate information on social media. TikTok's viral nature often amplifies unverified claims. Our findings show a tendency for posts to prioritise quick fixes over addressing the chronic, multifactorial nature of diabetes and its complications. We emphasise the need for healthcare professionals to recognise social media's influence on patient perceptions and engagement with diabetes management. By doing so, we can work collaboratively with patients to improve their understanding, guide them toward evidence-based resources and provide tailored support. Ultimately, this aims to improve engagement with ongoing care and empowers patients to make informed health decisions.

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P309

Mass spectrometry imaging reveals spatial lipidomic profiles of human liver in metabolic dysfunction-associated steatotic liver disease

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Metabolic dysfunction-associated steatotic liver disease (MASLD) results from excessive fat accumulation in the liver while metabolic dysfunction-associated steatohepatitis (MASH) is the progressive, inflammatory form that can lead to fibrosis, cirrhosis, and liver cancer. Patient heterogeneity, variable disease progression and diagnostic challenges complicate early MASLD detection. Novel biomarkers of disease may be revealed by spatial disease-specific lipidomic profiles through matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI). Human liver biopsy samples (n = 30, 32-83y) from the HepaT1ca study (ClinicalTrials.gov NCT03213314) were categorized by %fat content (low < 5%, medium 5-33%, high > 33%) based on histology, with 5 samples/sex/group. MALDI-MSI was applied for untargeted lipid profiling at 75-micron resolution on a SYNAPT G2-Si qToF-MS (Waters Corp.). LipidMaps database was used for lipid identification while data were processed using MassLynx™ and Lipostar MSI™ software. Statistical analyses, including sum normalization and Pareto scaling, were performed in MetaboAnalyst. Lipid markers distinguishing groups and sex were identified using partial least squares discriminant analysis (PLS-DA), orthogonal PLS-DA and variable importance for projection (VIP) scores. PLS-DA showed clear separation between the %fat groups, with components 1 and 2 explaining 12% and 16.8% variance, respectively. The high-fat group had a distinct lipid profile, while the mid and low-fat groups overlapped. Sex differences in lipid profiles were observed within each %fat group. Key lipid markers distinguishing high- from low-fat groups across sexes included triglycerides (e.g., TG 54:10, VIP score = 1.75), diacylglycerols (e.g., DG 36:2, 1.74), and phosphatidylcholines (e.g., PC 32:0, 1.13). In the high-fat group, males had higher levels of phosphatidylcholines (e.g., PC 36:1, 2.2) and lysophosphatidylcholine (e.g., LPC 18:1, 1.8) while females had more phosphatidylcholines (e.g., PC 34:2, 1.0 and PC 38:5, 1.1). Thus, MSI can identify sex-specific biomarkers of liver pathology which may aid early MASH diagnosis or treatment if further explored as imaging tools, blood-based biomarkers, or therapeutic targets.

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P310

The unseen hypoglycemia: leveraging freestyle libre for diagnosing endocrine disorders

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Background
Late dumping syndrome (LDS) is characterized by episodes of hypoglycaemia occurring 1 to 3 hours after carbohydrate ingestion due to excessive insulin secretion (hyperinsulinemia), commonly seen in individuals post-gastric surgery1. Hypoglycaemia diagnosis typically follows Whipple's triad2 but can be challenging in patients with hypoglycaemia unawareness, who lack classic symptoms. In such cases, continuous glucose monitoring (CGM) technology, like Freestyle Libre, offers valuable insights into glycaemic trends.
Case Presentation
We report a 75-year-old male who underwent oesophagostomy 15 years ago for cancer. After an uneventful recovery, he presented with severe hypoglycaemia (1.5 mmol/L) and no awareness of symptoms, detected by emergency responders after a collapse. To evaluate recurrent hypoglycaemia, Freestyle Libre was employed to monitor glucose levels over 14 days. Despite not being validated for reactive hypoglycaemia, CGM identified consistent postprandial hypoglycaemia occurring 3 hours after meals, consistent with LDS. Investigations, including fasting glucose, insulin, C-peptide, cortisol, thyroid function, and IGF2, were normal, ruling out other causes. The lack of hypoglycaemia awareness in patients following upper gastrointestinal surgery remains a not understood area3. A prolonged oral glucose tolerance test4 confirmed the diagnosis. Dietary modifications were recommended, and follow-up CGM revealed improved glycaemic control, suggesting successful intervention.
Conclusion
This case highlights the utility of CGM technology in diagnosing hypoglycaemia unawareness in complex scenarios, especially when conventional methods fall short. The uniqueness of this case lies in the onset of late dumping syndrome and hypoglycaemia unawareness 15 years after oesophagostomy, an uncommon occurrence. CGM played a critical role in confirming the diagnosis and guiding management, underscoring its potential in addressing similar cases presenting with late-onset, atypical symptoms.
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P311

Glucagon-like peptide-1 analogs reduce alcohol intake

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Background
Alcohol use disorder (AUD) is a chronic, relapsing condition contributing to 4.7% of global deaths. It involves neurobiological and psychosocial factors affecting mesolimbic dopamine pathways. Currently approved treatments (disulfiram, naltrexone, acamprosate) show high relapse rates (~70% in the first year). Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) like liraglutide and semaglutide reduce alcohol intake in animal models by modulating reward circuitry and decreasing dopamine release. We aimed to assess changes in alcohol intake in patients treated for obesity with GLP-1 RAs.
Methodology
We collected data from routine clinical care over 15 months (January 2023–March 2024). Adult patients (n = 262) with BMI $\geq$27 kg/m^2 initiated on liraglutide or semaglutide were included. Alcohol intake was categorized as non-drinkers, rare drinkers, or regular drinkers. Quantifiable weekly units were recorded. Changes in alcohol intake and body weight were assessed at baseline and ~3–6 months post-initiation. The Mann-Whitney U test was used for analysis. Approval was obtained from St Vincent's Healthcare Group (2024/4161).
Results
Of 262 patients (79% female, mean age 46 years), 179 (68.3%) were regular drinkers at baseline. After initiating GLP-1 RA, 188 (71.8%) had follow-up, mean interval 112 days. Post-intervention, alcohol intake data were available for 117 patients (44.7%). No patient reported increased intake. Mean alcohol intake declined from 11.8 $\pm$ 1.0 to 4.3 $\pm$ 0.5 units/week ($P < 0.001$). High consumers ($\geq$11 units/week) decreased from 23.2 $\pm$ 1.8 to 7.8 $\pm$ 0.9 units/week ($P < 0.001$). Low consumers (<11 units/week) decreased from 5.5 $\pm$ 0.3 to 2.5 $\pm$ 0.3 units/week ($P < 0.001$). Weight loss averaged 7.7 $\pm$ 0.3kg over four months. A weak positive correlation was observed between alcohol reduction and weight loss (r = 0.24, n = 72).

Conclusion
In a real-world setting, patients treated with GLP-1 RAs reduced alcohol intake significantly alongside weight loss. This suggests GLP-1 RAs may influence both energy balance and alcohol-related behaviors.

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P312

Biomechanical regulation of cell fate: the role of stiffness in adipogenic differentiation of human adipogenic precursors

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Introduction
Ectopic accumulation of fat in highly metabolic tissues is a hallmark in ageing, metabolic and neuromuscular diseases. The effects of ectopic accumulation of lipids in muscle include, glucose intolerance, switch of fibre types, reduced tolerance to exercise, etc. Less is known about what are the changes in the muscle niche driving this maladaptive remodelling. Here, we set to explore the role biomechanical changes (stiffness) on driving the cell-fate of human adipogenic precursors into adipocytes.
Methods
Human fibro/adipogenic progenitors (FAPs) and human pre-adipocytes (SGBS) were seeded in different stiffness (0.2 - 10^6 kPa). We use FAPs control and from muscles with Duchenne Muscular Dystrophy/DMD (impaired remodelling). Differentiation into fibroblast was evaluated after treatment with TGF-ß1 (3d) and differentiation into adipocytes was evaluated after treatment with adipogenic media (3, 5, 10d). Collagen I, Fibronectin, a-SMA and FABP4 and PPARG (adipogenesis) were evaluated by western blot, as key differentiation markers. Further, targeted proteomic assay was done in FAPs after adding adipogenic media (1d) to assess involvement of protein kinases regulating the process of differentiation.
Results
We identified decreased cell survival in cells (SGBS and FAPs) at soft surfaces, this effect was greater in FAPs DMD. Increased levels of adipogenic markers (FABP4 and PPARG), were observed in SGBS and FAPs at stiffer surfaces. The effect of differentiation was less clear in fibrosis. Results from the proteomic analysis identified WNK1 and PRAS40 as relevant kinases involved in adipogenic differentiation.
Conclusions
Our results suggest higher tissue stiffness (muscle and adipose tissue), common in ageing, metabolic and neuromuscular diseases, could promote ectopic accumulation of fat by increasing the adipogenic commitment on FAPs and pre-adipocytes. The identification of targets such as, WNK1 and PRAS40 will allow us to further dissect these pathways and work on strategies to tackle adipogenesis in muscle.

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P313

Targeting AMPK to attenuate lipid accumulation in Huh7 human hepatocytes exposed to physiological and pathophysiological concentrations of lipids

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Introduction
Metabolic dysfunction-associated steatohepatitis (MASH) affects approximately two billion people worldwide, which if untreated, can progress to hepatocellular carcinoma and increase the risk of early mortality. Targeting 5' AMP-activated protein kinase (AMPK) pharmacologically could attenuate lipid accumulation in hepatocytes and reduce the risk of liver disease progression. Therefore, computational modelling and *in vitro* experiments in the human hepatocytes model of MASH sought to establish the effects of the AMPK agonist, BI-9774, on triglyceride accumulation and cell respiration.
Methods
Computational modelling was used to establish BI-9774 binding mode to AMPK and its positive allosteric mechanism to increase AMPK activity. *In vitro*, experiments using Huh7 human hepatocytes were exposed to BI-9774 (1μM) for two days with increasing concentrations (0-800μM) of lipids. Immunofluorescence imaging with BODIPY was employed to detect the presence of neutral lipids. In addition, cell respiration analysis assessed the impact of BI-9774 on oxygen consumption rate (OCR) and extracellular acidification rate (ECAR).
Results
Computational modelling showed that the phosphorylation of AMPK Ser^{108} and BI-9774 binding have similar and cumulable effects on the dynamics of the β-subunit, suggesting an allosteric mechanism triggered by its proximity to the α-subunit. *In vitro* experiments showed that the total intensity of BODIPY was attenuated following BI-9774 treatment compared to control hepatocytes cultured with lipids ($P < 0.01$). There was an effect of BI-9774 on maximal OCR ($P < 0.01$). In hepatocytes exposed to 800μM of lipids, BI-9774 resulted in lower basal and maximal ECAR ($P < 0.01$).
Conclusions
These experiments show how BI-9774 binds and affects AMPK regulation and in an *in vitro* model exposed to pathophysiological concentrations of lipids, can attenuate triglyceride accumulation, and increase maximal OCR while lowering ECAR. Further analysis is required to determine the transcriptional and protein responses that underpin the effects of BI-9774 on HuH7 hepatocytes exposed to pathophysiological concentrations of lipids.

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P314

Dalbavancin reduces healing times and hospital inpatient stay for patients with diabetic foot osteomyelitis

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Diabetic foot osteomyelitis (DFO) poses great clinical challenges due to prolonged treatment with antimicrobial therapy. Dalbavancin is a new lipoglycopeptide antimicrobial that has shown great potential in treatment of osteomyelitis. With a two-dosing regimen on day 1 and day 8, dalbavancin cortical bone concentration lasts 8 weeks demonstrating great bone exposure. This single centre, retrospective, observational analysis aimed to assess resolution of infection and healing outcomes in patients with DFO and soft tissue infection. Patients who received two doses of intravenous dalbavancin as an outpatient were compared to a similar cohort who received a prolonged inpatient course of alternative antibiotics (intravenous or oral) prior to dalbavancin availability. Adult patients (60-95 years) presenting with DFO susceptible to Staphylococcus Aureus in Sligo University Hospital from 2016 were eligible for enrolment in the control group. The control group consisted of those who received a prolonged course of inpatient antibiotic therapy prior to dalbavancin's availability. They were compared to those who received two doses of intravenous dalbavancin as an outpatient. In total 82 patients were identified for inclusion. (58 patients treated with dalbavancin and 24 patients treated with alternative intravenous antibiotics). After exclusion, 44 patients were deemed eligible for analysis in the primary group and 20 patients were deemed eligible in the control group. Healing was achieved between the two groups with no significant difference ($P = 0.293$). Of those who achieved healing, there was a significant difference in healing times between patients receiving two courses of intravenous dalbavancin versus a prolonged course of alternative intravenous antibiotics ($P = 0.038$). Healing occurred within 97 $\pm$113.7 days in the primary group compared to172 $\pm$ 119.8 days in the control group. Results of this research suggests that dalbavancin use in DFO reduces healing times when compared to alternative intravenous antibiotics resulting in reduction of inpatient length of stay.

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P315

The effect of probiotics, prebiotics and synbiotics on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis

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Hypothesis
Some trials has been done on the use of probiotics, prebiotics and synbiotcs for better glycaemic control in type 1 diabetes mellitus, but their findings are conflicting. A previous systematic review conducted on this topic did not include adult patients or more recently published trials; this review aims to address this research gap.

Methods
After searching MEDLINE, EMBASE and COCHRANE databases, seven trials were included in the trial. A meta-analysis was conducted on HbA1c differences at three and six months respectively. Data on other measures of glycaemic control are presented narratively.
Results
Probiotic use resulted in a non-significant decrease in HbA1c at three months (-1.23; 95% CI -4.28, 1.81) and at six months. (-0.18; 95% CI -1.12;0.75).
Conclusion
Currently, the results do not suggest that probiotics, prebiotics and synbiotics should be used as an adjuvant treatment for glycaemic control in T1DM. More into probiotic strains, doses and intervention length are necessary before further suggestions can be made.

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P316

Pembrolizumab-induced diabetes mellitus presenting as diabetic ketoacidosis: a case report

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Pembrolizumab, a programmed cell death protein-1 (PD-1) immune checkpoint inhibitor, has transformed cancer therapy but can lead to immune-related adverse events (IRAEs), including insulin-dependent diabetes mellitus. This report details a case of pembrolizumab-induced diabetes mellitus (PIDM) presenting acutely with diabetic ketoacidosis (DKA). A 42-year-old woman with Stage IIIC melanoma, receiving adjuvant pembrolizumab, presented to the emergency department, with a five-day history of polydipsia, abdominal pain, and breathlessness, three weeks after her last treatment. She was diagnosed with DKA, confirmed by an arterial pH of 7.10, serum ketones of 6 mmol/L, bicarbonate of 9 mmol/L, and blood glucose of 26.2 mmol/L. She had no prior history of diabetes, with an HbA1c increasing from 39 mmol/mol four weeks earlier, to 69 mmol/mol at admission. Investigations showed an undetectable C-peptide level (<7 pmol/L), consistent with beta-cell dysfunction, and negative diabetes-associated autoantibodies. Pembrolizumab was identified as the likely cause. This case highlights the importance of recognizing pembrolizumab-induced diabetes mellitus (PIDM) as a potential cause of acute DKA in patients on immune checkpoint inhibitors. Early diagnosis and management, alongside coordinated care between oncology and endocrinology teams, are essential to optimize outcomes.

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A rare cause of rhabdomyolysis in a patient with type 1 diabetes mellitus

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Carnitine palmitoyl transferase II (CPT II) deficiency is a rare inherited metabolic disorder affecting the mitochondrial beta-oxidation of long-chain fatty acids, which may manifest as recurrent episodes of muscle pain, weakness, and myoglobinuria, often triggered by prolonged exercise, fasting, or illness. Diagnosis is typically confirmed through enzyme assays, genetic testing with muscle biopsy and elevated creatine kinase (CK) levels supporting the diagnosis during acute episodes. Management focuses on preventing episodes through dietary modifications, such as a high-carbohydrate, low-fat diet, and avoiding known triggers. Early recognition and treatment are essential to improving patient outcomes and preventing complications such as rhabdomyolysis and acute kidney injury. We present the case of a 34-year-old female with a background of poorly controlled type 1 diabetes mellitus (T1DM) who was admitted with severe muscle aches following a short walk, along with dark urine and significantly elevated creatine kinase (CK) levels. Her family history was notable for CPT II deficiency. Subsequent investigations revealed a new deficiency in carnitine palmitoyl transferase II (CPT II). She made a rapid recovery with Glucose infusions and oral Glucose polymers. This novel case highlights the need to consider a broad differential diagnosis including metabolic myopathies in the evaluation of severe Rhabdomyolysis. The potential challenges of managing CPTII deficiency in a patient with T1DM would also be discussed.

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GSDME deficiency sensitizes mice to high-fat diet induced obesity by suppressing lipolysis

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Background
Obesity, as a worldwide healthcare problem, has been attracting more and more attention. Chronic low-grade inflammation is regarded as an inducer of adipocyte cell death. Pyroptosis, a kind of inflammatory cell death, is involved in various inflammatory diseases. Gasdermin E (GSDME) is a mediator of pyroptosis via the cleavage of caspase-3. However, whether GSDME is involved in the regulation of adipose tissue function remains unknown. In the present study, we aim to investigate the role of GSDME in the development of obesity.
Methods and results
To investigate the role of adipose GSDME, we generate GSDME knockout ($GSDME^{-/-}$) mice. As compared with control mice, GSDME-/- mice show obesity when induced with a high-fat diet (HFD), along with hepatic steatosis, insulin resistance, glucose intolerance, and hypercholesterolemia. The effect of GSDME ablation on basic metabolic activity was also evaluated. Under the HFD condition, $GSDME^{-/-}$ mice showed significantly increased respiratory exchange rate (RER) and reduced oxygen consumption as compared with the controls. Gene array assay of control and GSDME-deficient adipose tissue revealed that lipolysis-associated genes including ATGL were significantly decreased with GSDME ablation in adipose tissues. Furthermore, the epiWAT from HFD-fed control and $GSDME^{-/-}$ mice was isolated and treated with isoproterenol (ISO). ISO-stimulated glycerol and FFA release were decreased in $GSDME^{-/-}$ explants. In vivo, the serum FFA and glycerol levels were measured after stimulated lipolysis by CL316243. Serum FFA as well as glycerol levels were significantly lower in $GSDME^{-/-}$ than control mice 15min after CL316243 stimulation.
Conclusions
This study reveals that GSDME functions as a positive regulator of lipolysis by the ATGL expression regulation. Deletion of GSDME promoted HFD-induced obesity, impaired adipose function and deteriorated glucose intolerance and insulin resistance. GSDME may be a potential therapeutic target for ameliorating obesity and obesity related metabolic disorders.

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P320

A rare case of heterozygous APOE variant associated hypertriglyceridemia with lipaemia splenomegaly

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Introduction
Hypertriglyceridemia is a common lipid disorder linked to cardiovascular risks. While lifestyle factors are often implicated, genetic mutations can also play a role. This case presents a rare instance of hypertriglyceridemia associated with lipemic splenomegaly due to a heterozygous variant in the apolipoprotein E (*APOE*) gene.
Case Presentation
A 32-year-old man, who never smoked and drinks occasionally, presented to the Same Day Emergency Care (SDEC) with atypical chest pain. Routine blood tests revealed isolated hypertriglyceridemia (20.1 mmol/L), hypothyroidism, and thrombocytopenia (initial samples were lipaemic). Physical examination showed

no xanthelasma, corneal arcus, or xanthomas. An abdominal ultrasound revealed significant splenomegaly, measuring approximately 232mm. His father and twin brother both have similar conditions, including hypothyroidism, elevated triglycerides, and splenomegaly. Genetic testing confirmed a heterozygous *APOE* variant associated with hypertriglyceridemia.
Management
The patient was initially treated with Fenofibrate for hypertriglyceridemia and Levothyroxine for hypothyroidism. Due to persistent high triglyceride levels, low-dose Atorvastatin was added. Haematology recommended no active intervention for the mild thrombocytopenia. The patient's hypertriglyceridemia is now well-controlled without complications, and he is under regular follow-up in the endocrine clinic.
Discussion
The *APOE* gene is vital for lipid metabolism, and its variants can alter lipoprotein profiles. While the exact mechanism of lipemic splenomegaly in this patient is unclear, it is hypothesized that the genetic mutation may disrupt lipid clearance, leading to lipid accumulation in the spleen.
Conclusion
b> This case underscores the importance of considering genetic factors in the assessment of hypertriglyceridemia. The presence of lipemic splenomegaly highlights the need for genetic testing to determine the underlying cause. Follow-up is essential not only for the patient but also for close relatives. Further research is needed to better understand the relationship between the *APOE* mutation and splenomegaly, with the goal of developing targeted therapeutic strategies.

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P321

Challenges in the diagnosis and management of type 1 diabetes in older adults: a comparative study between older and younger populations

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Aim
Diagnosing type 1 diabetes(T1DM) in older adults is often challenging due to atypical presentation and co-morbidities. This study aims to compare glycaemic control, microvascular complications, and diabetic emergencies between younger (<50) and older (≥ 50) adults in the first few years following diagnosis to better understand the challenges in older populations.
Method
Retrospective-cohort study was conducted on individuals diagnosed with T1DM between 2018 and 2024. Data were collected from SCI Diabetes and Clinical Portal at diagnosis, first and second year, and the most recent follow-up. Information gathered included demographics, HbA1c levels, use of blood glucose monitoring technology, biochemical parameters, and complication rates.
Results
Study included 219 patients: 148 under 50 years (mean -31) and 71 aged 50+ (mean-59). In the younger cohort, the mean HbA1c at diagnosis was 115 mmol/mol, dropping to 69 mmol/mol at follow-up. In the older cohort, it decreased from 114 to 66 mmol/mol. Continuous glucose monitoring (CGM) use was higher in younger groups (92.57%) than older group (86%), while insulin pump usage was similar between two (11.49% in the younger vs. 9.86% in the older). Retinopathy (17%) and diabetic ketoacidosis (29%) were more common in the younger cohort, whereas foot disease (9%) and severe hypoglycaemia (4%) were more frequent in the older. In the younger cohort 0.68% deceased and 2.03% moved out of area whereas 4.22% died in the older cohort. DKA at diagnosis was notably higher during the 2020-COVID year.
Conclusion
Older adults with T1DM face unique challenges, such as higher rates of foot disease and hypoglycemia, while younger adults are more prone to retinopathy and diabetic ketoacidosis. Early integration of technologies like CGM and insulin-pumps, when used effectively, can enhance diabetes care. Personalized, age-specific care strategies are essential for addressing unique needs of each age group and achieving optimal outcomes.

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Enteropancreatic neuroendocrine tumours (EP- NETS): current concept and controversies; a systematic review

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Enteropancreatic neuroendocrine (EP-NET) tumours consist of a wide range of malignancies initially thought to be rare. The incidence of this disease has increased dramatically in the last three decades, possibly due to advancements in imaging techniques and a better understanding of the tumour's natural history. Based on clinical trial results, various therapeutic options have emerged, including somatostatin analogue, molecular targeted therapy, cytotoxic agents, and surgery. This systematic review studied EP-NETS's evolution and natural history, explored current diagnostic and treatment modalities with a special focus on morbidity and mortality, and critically appraised available evidence to recommend future research. A qualitative systematic review was conducted using MEDLINE and Google Scholar studies, and the results were presented in a narrative format using tables and figures. The review critically explores the issues that must be elucidated and highlights existing controversies regarding the currently established therapeutic approach. It also explores potential treatment areas for these tumours to improve overall survival in the near future. Currently, the ENETS and other neuroendocrine expert bodies recommend monotherapy with somatostatin analogue with a switch to molecular therapy (Peptide receptor radionuclide therapy) if there is disease progression; it is suggested that a more aggressive combination systemic therapy should be explored to achieve a better outcome (for instance, combination with everolimus, which has superiority for advanced NETs). There is no data exploring the role of adjuvant chemotherapy in individuals who had curative surgery and are at high risk of relapse. The last decade has witnessed a rapid improvement in the therapeutic options available for patients with EP-NETs; however, the criteria for defining these treatment modalities with regard to timing, sequence, and priority of use are largely debated. More RCTs comparing active agents rather than placebo, and consequently, additional data on the appropriate sequencing of treatments, will lead to better patient outcomes.

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P324

Does hypophysectomy cause oxytocin deficiency in cats?

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Humans with hypopituitarism post-pituitary surgery can develop altered emotional behaviour and hyperphagia, consistent with reduced oxytocin levels. Almost all cats diagnosed with acromegaly have concurrent diabetes mellitus (DM). Hypophysectomy provides the most favourable quality of life and endocrine outcomes. However, approximately 66% experience persistent diabetes insipidus and require long-term DDAVP supplementation, and experience a median weight gain of 1.2kg by 12 months post-hypophysectomy. The effects of hypophysectomy on serum oxytocin concentrations have not been described. The current study evaluated the effect of hypophysectomy on serum oxytocin concentration in cats treated for acromegaly. Paired serum samples from cats with acromegaly and DM pre- and post-hypophysectomy were analysed using a commercial ELISA validated for the measurement of feline oxytocin. Patient descriptive and outcome data were recorded, including serum IGF1 concentration and remission of DM. Serum oxytocin concentration pre- and post-hypophysectomy was compared using Wilcoxon matched pairs signed-rank test. Relationships between oxytocin and DDAVP requirement, and oxytocin and percent bodyweight change were analysed using Mann-Whitney U test and Spearman's correlation respectively. Twelve paired samples were included with 11/12 cats achieving normalisation of serum IGF1 concentration and resolution of DM following hypophysectomy. There was no difference between pre- and post-hypophysectomy oxytocin concentrations (pre-hypophysectomy median 16 pg/mL, range 0 - 61 and post-hypophysectomy median 22 pg/mL, range 0 – 42, $P=.65$), no relationship between post-hypophysectomy oxytocin concentration and requirement for long-term DDAVP supplementation ($P=0.81$), and no correlation between post-hypophysectomy oxytocin concentration and percentage change in bodyweight at 3 to 6 months ($P=0.70$). This study suggests that cats continue to produce and secrete oxytocin following hypophysectomy, and oxytocin deficiency is not a contributor to post-operative weight gain.

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P325

Isoechoic insulinoma: a rare case with diagnostic challenges

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Introduction
Insulinomas are rare neuroendocrine tumours that cause excessive insulin secretion and lead to hypoglycemia. Diagnosing these tumours can be challenging, with around 20% of patients initially misdiagnosed with neurological or psychiatric disorders. Moreover, locating the tumour is often difficult. This report discusses a 33-year-old man who experienced neuroglycopenic episodes for a year before being diagnosed with an insulinoma, highlighting the localization challenges faced in his case.
Case Report
A 33-year-old male with no significant medical history was referred for evaluation of non-diabetic hypoglycaemia on April 12, 2024, due to symptoms of light-headedness, confusion upon waking, fatigue, irritability, and difficulty concentrating that began in July 2023. Observations indicated that his symptoms improved with food intake, prompting the couple to purchase a glucose monitor, which recorded readings as low as 1.9 mmol/L. Following a reluctant admission to the hospital on April 21, 2024, he underwent a 72-hour fast revealing a plasma glucose level of 2.2 mmol/L, elevated insulin and C-peptide levels, while tests for sulphonylurea were negative, indicating probable insulinoma. Dietary interventions were initially attempted, but due to recurrent hypoglycaemia, the patient was prescribed diazoxide. Subsequent imaging investigations, including CT and MRI, failed to locate the tumour, leading to a referral for a 68 Ga-Dota-Tate-PET-CT which also yielded no results. However, an endoscopic ultrasound on July 24, 2024, identified a subtle 13.1 x 4.8 mm isoechoic lesion in the pancreas, which upon biopsy confirmed a grade 2 neuroendocrine tumour. Post-biopsy, the frequency of hypoglycaemic episodes decreased, and the patient was successfully weaned off diazoxide. He was subsequently referred for endoscopic ultrasound and enucleation of the tumour.
Conclusion
Insulinomas can present diagnostic and management challenges and smaller tumours can be difficult to locate. Our case outlines the importance of pursuing investigations and the utility of endoscopic ultrasound in tumour localization.

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P326

Managing ROHHAD syndrome: a multidisciplinary approach to hypoventilation, partial diabetes insipidus, and desmopressin sensitivity

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A young female with ROHHAD syndrome first presented to Medway Hospital following a cardiac arrest caused by severe hypercapnia, a consequence of central hypoventilation. Since her admission, she has been under the care of a multi-disciplinary team, with key involvement from respiratory and endocrine specialists to address her complex needs. A particularly unique aspect of her case is her exceptional sensitivity to desmopressin, which has posed significant challenges in the management of partial diabetes insipidus (DI). Over time, the patient has had multiple hospital admissions due to electrolyte imbalances, particularly fluctuations in sodium levels. The frequency of these admissions increased following the death of her primary carer, a close family member. This rare finding in a ROHHAD patient underscores the critical importance of precise fluid and electrolyte management, requiring meticulous titration of treatment to avoid life-threatening sodium imbalances. Her case highlights the value of individualised care strategies and regular monitoring, alongside the need for clear escalation protocols to ensure timely intervention. This experience provides new insights into the management of ROHHAD patients with atypical presentations and reinforces the necessity of a collaborative, multidisciplinary approach for rare, multifaceted conditions.

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P327

Impact of somatostatin analogues on SSTR expression and Ki-67 expression marker in LCC-18 neuroendocrine tumour cells

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Introduction
Neuroendocrine neoplasms (NENs) comprise a heterogenous group of tumours with diverse clinical presentations and prognosis. Although significant progress has been made in treatment, a deeper understanding of somatostatin receptors (SSTRs) behaviour is essential to monitor disease progression and improve therapeutic strategies. This study investigates the effects of octreotide acetate (OA), lanreotide acetate (LA) and pasireotide (P) on LCC-18 cells, focusing on changes in SSTRs 2, 3, 4 and 5 and the proliferation marker Ki-67. Additionally, potential mechanisms behind drug resistance or loss of efficacy are explored.
Material and Methods
The LCC-18 cell line, derived grom a grade 3 NEN of colonic origin, was cultured and treated with increasing concentrations of OA, LA and P (6.25-100 μM) for 2 hours. Expression levels of SSTRs 2, 3, 4 and 5, and Ki-67 were evaluated using immunocytochemistry (ICC) and qRT-PCR. To assess potential cytotoxic effects, apoptosis induction was also examined following drug exposure.
Results
Preliminary results showed no significant induction of apoptosis with OA and LA treatment, while P demonstrated a mild apoptotic response at the highest concentration (100 μM). Early findings suggest differential effects of these analogues on SSTR and Ki-67 expression. However, detailed IC and qRT-PCR analysis are ongoing and will provide deeper insights into their respective mechanisms of action.
Conclusion
This study highlights the importance of evaluating early molecular changes following SSTR analogue treatment to identify biomarkers predictive of therapeutic efficacy. By elucidating alterations in SSTRs and Ki-67 expression, this research aims to enhance personalised treatment approaches for NEN patients. Such insights may lead to improved clinical outcomes by identifying early indicators of drug response and optimising future therapeutic strategies.

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P328

Unmasking a hidden insulinoma: a rare case of recurrent hypoglycemia

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Introduction
Insulinomas are rare, neuroendocrine tumors of the pancreas that cause recurrent hypoglycemia. Diagnosing them can be challenging due to nonspecific symptoms and difficulty in localizing the tumor. This case illustrates the difficulties in detecting an insulinoma over a prolonged disease course.
Case Presentation
A 56-year-old female presented with recurrent episodes suggestive of hypoglycemia. Her first episode occurred in 2018, with fainting and a blood glucose of 2.7 mmol/L. Prior to this, she experienced two episodes: one after a light lunch and walk with fatigue, blurred vision, imbalance, another after breakfast and cycling, where she became shaky 40 minutes later. Symptoms occurred at varying times, without a clear fasting-related pattern, she also noted weight gain. The patient was not on any medications and had no significant family history.
Examination
Her BMI was 33 kg/m^2, bp: 136/93 mmHg. Cardiovascular, respiratory, abdominal examinations were normal. No unusual rashes /acanthosis nigricans
Investigations
In 2018, oral GTT did not show reactive hypoglycemia, and C-peptide and insulin levels were appropriate for the glucose levels. Prolonged fasting revealed a glucose of 2.8 mmol/L but did not meet hypoglycemia criteria. She was advised to avoid prolonged fasting and consume low-GI foods. In 2022, the frequency of symptoms increased, prompting re-investigation. A 72-hour fasting test showed glucose 2.4 mmol/L elevated C-peptide (526 pmol/L), insulin (31 mU/L). Pancreatic CT was normal. She was discussed at Mdt. Doctate scan ordered and was normal. A year later abdominal pain and diarrhea revealed normal abdominal ct.
Management and Conclusion
The results suggested insulinoma but imaging did not reveal any lesion, she was referred to tertiary center. A repeat CT scan identified a small pancreatic lesion, Endoscopic US confirmed an insulin-secreting tumor, Ki-67 index 16%. Surgery was performed six years after the initial presentation. This case depicts challenges in diagnosing rare causes of hypoglycemia.

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P329

A rare case of persistent desmopressin intolerance across multiple formulations in arginine vasopressin deficiency (AVP-D)

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Arginine vasopressin deficiency (AVP-D), formerly known as central diabetes insipidus (CDI), is commonly treated with desmopressin, a synthetic analogue of antidiuretic hormone (ADH). While desmopressin is generally effective, rare adverse effects, including gastrointestinal upset and abdominal pain, may limit its use. Such symptoms are more commonly associated with oral formulations, less frequent with sublingual and intranasal routes, and exceedingly rare with subcutaneous delivery. We report a case of a 17-year-old female with familial arginine vasopressin deficiency (AVP-D) who was initially treated with oral desmopressin but she developed abdominal pain shortly after administration. The treatment was subsequently switched to a sublingual formulation, but the patient continued to experience similar abdominal discomfort. Attempts to use intranasal desmopressin were also unsuccessful, making it challenging to effectively manage her AVP-D symptoms over an extended period. Ultimately, a monitored inpatient trial of subcutaneous desmopressin was attempted; however, it also resulted in abdominal pain, confirming systemic intolerance regardless of the administration route. The symptoms resolved upon discontinuation of desmopressin. To effectively manage her symptoms, the patient was then transitioned to a thiazide diuretic, which reduces polyuria by inducing mild hypovolemia. This case highlights a rare, yet clinically significant, intolerance to desmopressin, marked by persistent gastrointestinal symptoms across multiple formulations, including the subcutaneous route. It emphasizes the need for individualized treatment strategies in managing AVP-D and supports thiazide diuretics as a viable alternative for patients who cannot tolerate desmopressin.

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P330

Trio of pituitary pathologies - a surprising revelation

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Introduction
Giant pituitary adenomas represent 6-10% of all pituitary adenomas. They are mostly nonfunctional and occur commonly in male. Surgical management to preserve the vision poses significant challenges.
Case Summary
65-year-old lady presented to the Ophthalmology with bitemporal hemianopia. On examination she had no neurological deficits and bitemporal hemianopia on confrontation and Goldmann visual field testing. Baseline investigations showed Free T4 10.6 pmol/L (11.5 – 22.7), TSH 2.79 mIU/L (0.55 – 4.78), 9am Cortisol 23 nmol/L (145 – 619), FSH was 16 IU/L, LH was less than 1 IU/L indicating secondary hypothyroidism, secondary adrenal insufficiency, and secondary hypogonadism, IGF-1 was normal. Pituitary MRI revealed a giant dumbbell shaped T2 hyperintense lesion, pituitary marco-adenoma causing expansion of sella turcica, displacing the optic chiasma superiorly and partially encasing the bilateral cavernous segment Internal carotid artery, measuring 5.3 cm in long axis. She underwent Stealth Guided Transsphenoidal extended approach endoscopic assisted pituitary adenectomy. Following which left eye vision deteriorated to light perception and patient had a further debulking of Pituitary adenoma via transcranial approach. Post-operative Pituitary MRI showed good resection of the lesion and vision improved.
Histopathology showed
1. A plurinominal adenoma with expression of SF-1, PIT-1 and FSH.
1. Meningioma CNS Grade 1.
1. Appearances compatible with degenerate benign cyst. Patient remains stable and has regular follow-up in the Pituitary clinic.
Conclusion
This case illustrates a unique trio of pathologies within a giant pituitary adenoma. The pituitary adenoma occasionally co-exists with another kind of intracranial tumour. Pituitary surgery remains the cornerstone of giant pituitary tumours management in multidisciplinary centres of excellence.

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P331

Postoperative adrenal atrophy: a rare twist in ectopic ACTH syndrome management

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Evaluation of the hypothalamic-pituitary-adrenal (HPA) axis using the short Synacthen test (SST) should only be performed during stable disease. Results correlate with insulin tolerance tests, provided the patient has not recently undergone surgery. In ACTH-dependent Cushings, adrenal hyperplasia occurs due to chronic ACTH stimulation. Following surgical removal of the ACTH source, only morning cortisol levels are reliable. A successful outcome in ACTH-dependent Cushings is indicated by undetectable cortisol levels, confirming the removal of the ACTH source. SST is not performed post-surgery as adrenal hyperplasia may cause a strong response to ACTH, even in the absence of endogenous ACTH. Glucocorticoid replacement is essential postoperatively, as suppressed corticotrophs require months to recover. We present a case of Cushing's syndrome due to ectopic ACTH production from a lung carcinoid tumor. Unlike the expected prolonged adrenal hyperplasia, this case demonstrated rapid adrenal atrophy postoperatively.
Case
A 36-year-old Saudi woman exhibited Cushingoid features for three years. ONDST was 488 nmol/L, and ACTH was 81.8 ng/L. Inferior petrosal sinus sampling (IPSS) with desmopressin confirmed ectopic ACTH production. Gallium-68-DOTATATE PET identified a gallium-avid lesion in the left lung.
Management
A 14 mm lesion was excised (13/03/2024) and confirmed as an atypical carcinoid (pT1b, N0, Mx). Postoperatively, cortisol levels were undetectable, and the patient was started on prednisolone (8 mg/day). Surprisingly, an SST at 8 weeks revealed undetectable cortisol levels even at 60 minutes, suggesting complete adrenal atrophy. By 6 months, cortisol levels remained suboptimal during a short Synacthen test (SST), with results of 29 nmol/L at 0 minutes, 108 nmol/L at 30 minutes, and 147 nmol/L at 60 minutes before prednisolone 3mg. The patient remains on low-dose prednisolone, with gradual weaning under supervision. Adrenal atrophy following ACTH source removal is rapid, and synacthen tests may be useful 8 weeks after surgery.

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P332

Cannulated prolactin – implementing a new cost-saving service pathway for hyperprolactinaemia

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Differentiating between true hyperprolactinaemia and stress induced hyperprolactinaemia can be difficult and may result in patients having unnecessary imaging and treatment.
Methods
The data for 89 patients who had a cannulated prolactin between January 2017 and September 2024 in the Royal University Hospital of Bath and Bristol Royal Infirmary has been analysed. The cannulated prolactin protocol used involved a cannula insertion and prolactin measurements at 0, 30, 60, 90 minutes.
Results
The mean baseline prolactin in this cohort was: Of the 89 patients, 70% (n = 62) had a normal prolactin. Interestingly, 45 patients had a normal prolactin at baseline. Of those where the prolactin normalised, the nadir occurred at 90min. This highlights the importance of doing a full 90minute test in order to avoid false positive results. Of those with a normal result, 8 patients had an MRI pituitary. 4 showed a non-functioning pituitary adenoma and 4 MRIs were normal. Thus 54 MRIs were saved. With the estimated cost of an MRI pituitary being £300 and cannulated prolactin being £76, the estimated cost saving was £16,200. If you add the cost of outpatient appointments, the potential cost saving might have exceeded £20,000.
Conclusion
We have introduced a new endocrine nurse-led hyperprolactinaemia pathway in our trust for GPs to access.
1. Prolactin raised on 2 occasions in the community.
2. If prolactin > 3000 mIU/l then MRI pituitary and urgent referral to Endocrinology clinic.
3. If prolactin level is between 700-3000 mIU/l then direct referral to endocrinology nurses to perform cannulated prolactin at 0 and 90 minutes. Lab only need to process the 90minute sample if the time 0 level is raised. If

cannulated prolactin is <700 mIU/l then patient to be discharged back to GP; if cannulated prolactin is >700 then MRI pituitary, pituitary panel and Endocrinology appointment.

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A rare case of recurrent episodes of severe hypoglycemia in an elderly patient secondary to insulinoma

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Insulinoma is a functional neoplasia from pancreatic beta cells and is the most common cause of organic hyperinsulinemic hypoglycemia in adults. Of these, 90% are benign, solitary, and intrapancreatic. Here we discuss a case of 93-year-old gentleman living in a care home, with Alzheimer's dementia, CKD, AAA, BPH. He had recurrent hospital admissions due to severe hypoglycaemia episodes treated with IV dextrose infusion. He was non-smoker and non-alcoholic. There were no family history of any hormonal problem or insulinoma or any NET. Examination was unremarkable except having intermittent confusion and reduced mobility likely due to Alzheimer's dementia. His observation was stable. Blood test showed HBA1c of 23mmol/mol, EGFR 54/min, Normal LFT's, Cortisol 534 nmol/l, TSH 0.49 mU/L, Insulin 549 pmol/L, C Peptide 5994 pmol/L.CTAP showed a well-defined rounded lesion measuring 23 mm in diameter at the neck of the pancreas with mild hyperenhancement in the arterial phase, suggestive of pancreatic NET with no evidence of distant metastasis. As he is very frail elderly gentleman, he was not suitable for surgical resection, hence, further investigations to localize the lesion was not considered. He was treated with injection octreotide, verapamil and diazoxide tablet initially. We managed to stop octreotide and verapamil after stabling blood sugar but continued with diazoxide 50 mg three times a day with blood sugar between 7.6 mmol/l to 15 mmol/L without further episodes of hypoglycemia. This case illustrates the importance of doing further investigations in elderly patients to identify the cause of recurrent hypoglycemia. Though hypoglycemia can be multifactorial for elderly patients including poor nutrition and organ failure but exploring further to identify any potential treatable cause likely insulinoma, can be rewarding. This may lead to improve morbidity and perhaps also helps to increase life expectancy with conventional medical treatment.

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P334

Rapid regression of pituitary metastasis from non-small cell lung carcinoma (NSCLC) treated with osimertinib

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Case Report
A 65-year-old woman presented with a 5 months history of severe headache, fatigue, nausea, vomiting, polyuria, and polydipsia. Biochemical investigations confirmed panhypopituitarism, including secondary adrenal insufficiency (cortisol <28 nmol/L, ACTH <5 ng/L) with Arginine Vasopressin Deficiency (AVD). Pituitary hormone replacement therapy was commenced (excluding growth hormone replacement). MRI demonstrated a bilobed sellar mass with suprasellar extension, with a partial bitemporal hemianopia observed on formal visual field assessments. The presence of profound hypopituitarism with AVD led us to consider metastatic disease as the most likely diagnosis with inflammatory conditions in the differential. FDG PET scan revealed a 4cm lung mass suspicious for primary lung cancer with multiple FDG-avid lymph nodes, including supraclavicular nodes. Biopsy of a left supraclavicular lymph node confirmed metastatic lung adenocarcinoma with an EGFR exon 19 deletion.
Treatment
She was treated with Osimertinib, a third-generation EGFR-Tyrosine Kinase Inhibitor. Three months following Osimertinib commencement, she experienced resolution of headaches with associated nausea. A marked reduction in the dimensions of the sella mass with resolution in the suprasellar component was visualised on repeat MRI. There was a retraction within the pituitary gland. The optic chiasm and pre-chiasmatic nerves were no longer compressed. These findings corroborated with ophthalmic assessments where normal visual fields were observed. Despite the significant radiological and ophthalmic improvements, hypopituitarism persisted for which she remained on pituitary hormone replacement.
Conclusion
Pituitary metastasis is rare, with lung and breast malignancies the commonest causes. Treatment approaches include surgery or radiotherapy focused on mitigating visual complications. This case highlights the importance of tissue diagnosis, enabling the use of targeted therapy, including Osimertinib, which has led to regression of the metastatic disease improving symptoms and visual function.

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P335

When size matters: the impact of a giant non functioning pituitary adenoma

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Giant pituitary adenomas present significant surgical challenges due to their size, invasive intracranial growth, and involvement of critical neurovascular structures. No consensus exists on the optimal surgical approach, often requiring multi-staged treatments. Most non-functioning adenomas measure 1–4 cm, with tumours over 4 cm being rare (10–15%). Tumours larger than 6 cm are classified as giant, while those exceeding 8 cm are extremely rare. Their asymptomatic, slow growth often leads to late presentation from mass effects. An 82-year-old male presented in 2009 with vision loss caused by a non-functioning pituitary macroadenoma (3x3.8x2.5 cm). Initial transsphenoidal surgery left a large residual mass in the sphenoid sinus and pituitary fossa, with mild chiasmal elevation. A second surgery, via a transoral/transmaxillary approach and palate splitting, significantly reduced the tumour. Follow-up showed stable MRI, visual fields, and no endocrine deficiencies. Histological analysis confirmed negative immunolabelling for ACTH, growth hormone, prolactin, and TSH. Despite subsequent growth, the tumour remained away from the optic chiasm until 2020, when its size increased from 4.9 cm in 2017 to 5.7 cm. While serial MRIs noted brainstem compression, there was no chiasmal involvement. By October 2024, the tumour had grown to 8.5 cm, significantly compressing the pontomedullary junction and optic chiasm, leading to visual field constriction, especially inferiorly and on the right. The Pituitary MDT ruled out radiotherapy (SRT and SRS) due to risks of tumour swelling and brainstem compression. Further surgery was postponed due to anaesthetic risks. Medical treatment with Cabergoline and Octreotide was recommended, with Temozolomide considered as a potential option based on its potential efficacy in improving clinical and radiological outcomes. Management requires expert team input, considering clinical findings, age, and comorbidities. Given the rarity of giant non-functioning pituitary adenomas, standardized protocols and research into predictive markers are essential to guide treatment decisions.

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P336

Cardio-metabolic effects of sesame-based functional diet on lipopolysaccharide-induced preeclampsia in wistar rats

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Preeclampsia (PE) also known as pregnancy-induced hypertension is a significant cause of maternal and fetal death (2-8% of pregnancies globally). Preeclampsia is linked to metabolic disorders such as obesity, dyslipidemia, and abnormal amounts of cardio-enzymes. Sesame (*Sesamum indicum*) seed contains beneficial phyto-compounds such as polyunsaturated fatty acids and minerals. This study investigated the effects of sesame-based diet (SBD) on cardio-metabolic parameters such as blood pressure, proteinuria, weight, angiotensin-converting enzyme (ACE), creatine kinase (CK), serum lipid profile (HDL, LDL, Trig, TC), kidney function indices (urea, creatinine, uric acid), and fasting blood sugar (FBS) concentration associated with lipopolysaccharide-induced preeclampsia in rats. The formulated diet was composed of sesame flour, maize flour, defatted soya bean, sesame oil, sugar, ginger, cloves, and garlic in the ratio of 0.35:0.29:0.25:0.05:0.1:0.006:0.002:0.002 respectively in 1 kg of the formulation. Thirty-five female Wistar rats (182.45±3.11g) were assigned into 7 groups (A-G) of 5 animals. PE was induced intraperitoneally with lipopolysaccharide (20 μ/kg b.wt.) in pregnant (gestation day (GD) 8) rats, except groups

A and F. Before and after PE induction, groups D and E were maintained on basal diets while groups A, B, C, F, and G were fed standard diet. Group C was administered the reference drug Amlodipine (5 mg/kg). The rats were sacrificed on GD 18. The result shows that rats fed SBD had significant reduction ($P<0.05$) in blood pressure measurement, proteinuria levels, FBS, and elevated body weight compared to the control rats. The serum ACE activity of sesame-fed rats compared favorably with control, while CK activity, creatinine levels, Trig and LDL-C concentrations were significantly decreased ($P<0.05$), and HDL-C, urea and uric acid levels significantly increased ($P<0.05$) in sesame-fed PE rats compared to the control. Therefore, SBD may be beneficial for the management of cardiometabolic dysfunctions associated with preeclampsia subject to further experimental validation.

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P337

The case for real world evidence for menopause outcomes

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Greater confidence in hormone replacement therapy (HRT) in clinical practice means that many women with complex comorbidities are now being offered HRT for menopause symptoms. Modern HRT formulations may be safer than older regimens, and accumulating evidence allows better risk stratification. However, there is a lack of outcome data for under-represented groups with complex health issues, particularly concerning cardiometabolic and gynaecological risks, oestrogen-related cancers, and testosterone use. The clinical outcomes associated with HRT regimens outside regulator-approved dosing are also unknown. Furthermore, there is a dearth of data to guide management for HRT-unsuitable women. The International Menopause Society has endorsed the case for real-world data collection in their 2024 White Paper, recognising that large-scale randomised trials using modern, novel or unconventional menopause treatments are unlikely to receive the necessary funding. The Society for Endocrinology (SfE) has also recognised the unmet need in menopause management and outcome data and the novel research opportunity to utilise innovative, secure online, real-world data collection platforms. In response, the SfE has founded the first UK women's health real-world data registry, aiming to capture critical outcomes across essential areas of women's health. The data collection process utilises an online platform accessed via site-specific QR codes. Following patient consent, relevant data from primary care records will be obtained through automation, with options for additional input from secondary care. The SfE will host this registry with unrestricted educational grant funding support. A steering group of leaders from endocrinology, allied specialities, affiliated charities, and patient groups underpin the registry's operational detail. The steering group chairs will share future developments and encourage SfE members to engage with this pivotal registry through research questions and data access requests. The SfE women's health registry is an ambitious long-term initiative aiming to support SfE members to help shape future women's health-related research and practice.

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P338

Aqueous extract of solanum nigrum leaf mitigates cardiometabolic and endocrine dysfunctions associated with anastrozole-induced polycystic ovarian syndrome in rats

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Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder characterized by hormonal imbalances, ovarian dysfunction, metabolic disturbances and cardiovascular disorders. This study investigated the therapeutic potential of aqueous extract of *Solanum nigrum* leaves (AESNL) on cardiometabolic and endocrine dysfunctions associated with PCOS in rats. Sixteen female Wistar rats (164.65 $\pm$3.44 g) were divided into four groups (A-D); A-control (n=4) and B, C and D- PCOS-induced (n=12). After induction with anastrozole (1mg/kg/day), PCOS animals (B-D) were orally treated for 14 days with distilled water (0.5ml), co-administration of metformin (7.14mg/kg/day) and clomiphene citrate (2mg/kg/day), and aqueous extract of *Solanum nigrum* (200mg/kg) respectively. The body weight, fasting blood glucose concentration, angiotensin-converting enzyme (ACE), creatine kinase (CK), lipid profile (total cholesterol, triglycerides, high-density lipoprotein-cholesterol, and low-density lipoprotein-cholesterol) and hormonal concentrations (testosterone, luteinizing hormone, estrogen, progesterone and insulin) were evaluated. Anastrozole administration resulted in impaired glucose tolerance, increased body weight, altered enzyme activity, hyperandrogenemia, hyperinsulinemia and dyslipidemia. The result revealed a significant decrease ($P<0.05$) in the total cholesterol, triglycerides, testosterone, LH and insulin concentration of AESNL-treated PCOS rats compared to the control rats. The administration of 200 mg/kg body weight of AESNL to PCOS rats significantly ($P<0.05$) improved fasting blood sugar (FBS), serum CK and ACE activity of PCOS rats compared to the control group. The aqueous extract of *Solanum nigrum* leaves has the potential to mitigate cardiometabolic and endocrine dysfunctions associated with PCOS. Therefore, it can be explored in novel drug design for the management of the endocrine and cardiometabolic dysfunctions associated with PCOS subject to further experimental validation.

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P339

Impact of occupational phthalate exposure on testosterone levels, and male sexual health questionnaire scores. a dose-response analysis

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Background
Phthalates are extensively used in industrial printing. Di-n-butyl phthalate (DnBP) is classified as an endocrine disruptor, negatively impacting testosterone levels in human males. This might contribute to an altered male sexual response, particularly in aging men. The Male Sexual Health Questionnaire (MSHQ) is a validated tool assessing male sexual function across various domains including scores for erectile function (MSHQ-E), sexual activity (MSHQ-S), and a total score (MSHQ-T).
Aim
Evaluate possible dose-response relationships between occupational phthalate exposures and testosterone levels, and MSHQ scores, using age-adjusted statistical models.
Methods
Sixty male printing workers donated urine samples post-shift over five consecutive days and blood samples in the morning on the first and last day of the workweek. Thirty-six urinary phthalate metabolites and serum total testosterone were quantified by liquid chromatography with mass-spectrometry detection and free testosterone by immunoassay. Calculated free testosterone (cFT) and bioavailable testosterone were derived. Dose-response relationships were modeled using multiple linear regressions, while Spearman correlations were used to assess testosterone-MSHQ scores.
Results
Negative associations were observed between cFT and DnBP metabolites; MnBP (β= -0.002, P=0.022), 3-OH-MnBP (β= -0.015, P=0.022), and $\sum$DnBP (β= -0.002, P=0.019). 3-OH-MnBP was inversely associated with MSHQ-S (β= -1.146, P=0.017). cFT was correlated negatively with MSHQ-E (β=-0.321, P=0.015), MSHQ-S (β=-0.298, P=0.026), and MSHQ-T (β= -0.388, P=0.003). Metabolites of newer-generation phthalates such as DiPeP (MiPeP, 4-OH-MiPeP, $\sum$DiPeP), DnoP (MnoP, 7-cx-MnHepP), DnHepP (6-OH-MnHepP, 6-cx-MnHepP), and DnPeP (MnPeP, 4-OH-MnPeP) were inversely associated with MSHQ-T.
Conclusion
Occupational exposure to DnBP negatively impacted both hormonal domain and sexual activity, even though recorded concentrations among workers were slightly above those of the general population. The MSHQ total score appears to be a sensitive marker of phthalate exposure. Comprehensive testosterone profiling, combined with clinical scores could be essential for clarifying the impact of endocrine disruptors on reproductive health.

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P340

A young female with gonadotropin resistance syndrome due to noval FSHR variants

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Background
Gonadotropin Resistance Syndrome (GRS), also referred to as ovarian resistance syndrome, is a rare condition caused by mutations in the Follicle Stimulating Hormone Receptor (FSHR) gene. It is characterized by primary amenorrhoea, elevated gonadotropins, low-normal oestradiol, and preserved ovarian reserve.
Case Presentation
A 17-year-old female presented with primary amenorrhoea and normal secondary sexual characteristics. Investigations revealed elevated Follicle Stimulating Hormone (FSH) levels (32–38 U/L), low-normal oestradiol (<92–128 pmol/L), and elevated Anti-Mullerian Hormone (AMH) levels (47.80 pmol/L), indicating preserved ovarian reserve. Whole-genome sequencing identified two heterozygous FSHR gene variants: c.1073A>T (p.Asp358Val) and c.854+5G>A, both classified as variants of uncertain significance. Parental genetic testing confirmed a compound heterozygous state. These findings were consistent with GRS.
Conclusion
This case underscores the importance of genetic testing in diagnosing rare causes of primary amenorrhoea. GRS, characterized by preserved ovarian reserve despite impaired FSH signaling, may allow for future fertility treatments. Identification of FSHR mutations aids in tailoring management and fertility planning.
Keywords
Gonadotropin Resistance Syndrome, FSHR mutation, primary amenorrhoea, ovarian reserve, fertility planning
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P341

A single centre study to describe the changes in serum testosterone concentration following application of testogel in post-menopausal women with hypoactive sexual desire disorder (HSSD) already receiving this as part of usual care in conjunction with estrogen containing hormone replacement treatment (HRT)

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Introduction
HSDD is characterized by long-term decrease in sexual desire (low-libido) causing personal distress. HSDD predominantly affects postmenopausal women or following oophorectomy. Despite the clear indication that testosterone supplementation could overcome the symptoms of HSDD by elevating testosterone levels, there is little research concerning this. For decades many post-menopausal women have been prescribed off-label testosterone, an approved therapy for men, at a modified dose. The purpose of this study was to determine the blood levels of testosterone in post-menopausal women with HSDD treated with Testogel©.
Methods
All 15 women were applying Testogel© via pump once every 3 days and had been prescribed Testogel© for at least 6 months. All were additionally taking estrogen based HRT. They attended for a testosterone day curve with Testogel© at the dose of 20.25 mg applied after an initial blood test. Samples were taken 2 hourly for 10 hours and at 24 hours post-Testogel-application. Testosterone was measured by mass spectrometry. The Female Sexual Functioning Index (FSFI) was completed by the women.
Results
Female Sexual Functioning Index (FSFI) median score was 26.5/36 (25-75% interquartile range 18-30) with highest domain scores for sexual satisfaction and arousal (4.2/6) and slightly lower scores for orgasm and desire (4.0/6) and no reported issues re pain on intercourse. All women subjectively reported an improvement in sexual function with Testogel©. Maximum testosterone varied from 1.3-10.3nmol/L with the time maximum level was reached varying from 2-24 hours. Area under curve (AUC) testosterone varied substantially from 23.4 to 222.6. Half-life of testosterone also varied from 22 to 40 hours. There was a positive correlation between BMI and AUC testosterone beta=7.54 (95%CI 4.39-10.7) $P<0.001$. No symptoms of hyperandrogenism were reported.
Conclusion
We found considerable variation in all parameters relating to testosterone pharmacokinetics in women applying Testogel©. All women reported clinical benefit with no reports of androgen related side-effects.
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P342

Preventing laryngeal nerve palsy during thyroidectomies – a non-systematic review of the surgical anatomy literature

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Background
Recurrent laryngeal nerve palsy (RNLP) is an established morbidity in thyroidectomy with a variable prevalence. Many risk factors are associated with RNLP and several common mechanisms of injury need to be considered by surgeons. Various anatomical landmarks are used to identify the recurrent laryngeal nerve (RLN) intraoperatively with differing levels of prevalence and significance. Variations of the nerve can complicate the procedure for many surgeons and are associated with nerve injury. Preventative methods can be used to mitigate against RNLP, although considerable controversy exists as to the most effective method.
Methods
A literature search was carried out using PubMed, to identify relevant papers using Boolean operators, such as AND and OR. Key words were utilised, for example, "variations", "landmarks" and "preventative methods".
Results
Repeat goiter operations and malignancy have the highest rates of palsy and the most common mechanisms of injury are traction and thermal injuries. The tracheooesphageal groove (TOG) and inferior thyroid artery (ITA) have a higher variability in their relationship to the nerve, whereas the Zuckerkandl tubercle (ZT) and Berry's ligament (BL) have higher consistent relationships. Extralaryngeal branching poses a high risk of palsy due to their high prevalence. Intraoperative visualisation (IOV) is the gold standard currently for preserving the nerve, but certain injuries can only be detected by intraoperative neuromonitoring (IONM). However, there are no statistically significant differences in palsy rates between either method.
Conclusions
The ZT and BL are effective landmarks to identify the nerve by surgeons. IOV is still the main method to preserve the nerve but IONM may play a role as an adjunct. Further studies with larger sample sizes are needed to reduce biases.
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P343

Lithium-induced thyroiditis presenting as thyroid storm: a case report and review

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Goitre and hypothyroidism are well-established complications of lithium therapy; however, lithium-induced hyperthyroidism (LIH) is rare, with an incidence of 1.0–1.7%. First reported in 1976, the mechanism underlying this paradoxical phenomenon remains poorly understood. Hypotheses suggest autoimmune overactivity or direct lithium-induced thyroid destruction. We present the case of a 32-year-old gentleman with schizoaffective disorder and ADHD, on lithium carbonate and clozapine, who presented with a 2-week history of vomiting, agitation, and confusion. He denied thyroid hormone use or any personal or family history of thyroid disease. On presentation, his vital signs were HR 131 bpm, temperature 38.4°C, BP 138/72, RR 21, and oxygen saturation 95% on room air. Clinical examination revealed hypovolemia, though his thyroid exam was unremarkable. Initial management targeted acute kidney injury and dehydration. Lithium toxicity was ruled out with levels at 0.5 mmol/L (0.4–1). Persistent fever, psychotic deterioration, and confusion led to thyroid testing, showing T4 > 100 pmol/L (11–22) and TSH 0.02 mU/L (0.27–4.2). Negative thyroid antibodies and reduced uptake on radioactive thyroid imaging suggested destructive thyroiditis. A Burch-Wartofsky score of 65 confirmed thyroid storm secondary to thyroiditis. The patient was treated with carbimazole 40mg daily, prednisolone 30mg daily, propranolol 40mg twice daily, and clonazepam 2mg three times daily, replacing lithium. His symptoms improved after 6 days of treatment. In summary, lithium-induced hyperthyroidism (LIH) poses challenges due to its unpredictable onset, lack of management consensus, and potential need to discontinue lithium. Diagnosis is complicated as LIH symptoms often overlap with mania, and lithium levels are frequently within normal range. Treatment is further complicated by interactions between antithyroid and psychiatric medications, which can lead to the re-emergence of psychotic symptoms. These challenges highlight the urgent need for further research into risk factors and the development of tailored monitoring and treatment approaches.
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P344

Evaluating the incidence of hypothyroidism and its associated factors within one-year post radioactive iodine (RAI) therapy for benign thyroid disease; a single centre experience

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RAI is a definitive treatment option for benign thyroid disease aiming for euthyroidism. In practice, incidence of subsequent hypothyroidism is 5–50%, with potential for significant symptoms and exacerbation of thyroid eye disease (TED). NICE guidance recommends close monitoring of thyroid function (TFT) following RAI therapy with prompt initiation of levothyroxine; however, practice varies and there is no consensus RAI dosage algorithm.

Aims

1. Assess effectiveness of centre doses (400 MBq -Graves' disease (GD)/ multinodular goitre, 200 MBq -toxic adenoma). 2. Evaluate frequency of abnormal TFT post RAI and adherence to NICE guideline, following implementation of automated EPR requesting for 6 weekly TFT monitoring at point of RAI consent.

Method

Retrospective data analysis (OUHFT registered audit) of patients undergoing RAI (April 2021-April 2022).

Results

Of 84 patients identified, 40 were excluded as followed-up by referring centre. The majority of patients received RAI for relapsed GD (80%). Outcome: 25 patients (57%) hypothyroid, 10 euthyroid (23%) and 6 remained hyperthyroid; mean time to hypothyroidism 3 months. 79% of 400 MBq dose patients were rendered euthyroid/ hypothyroid and 5 patients had treatment failure. Elevated TRAB was associated with treatment failure. 3 patients received prophylactic steroid; no patient developed/worsened TED. Adherence to NICE guidelines was 93% at 6 months, 78% at 12 months.

Discussion

Lower than national average RAI dose led to comparable outcomes for euthyroidism (23%) and hypothyroidism (57%). The lower doses allow reduced radiation protection precautions which is of practical benefits to patients' day-to-day life post-treatment. We find that hypothyroidism within 6 months of RAI is captured by the NICE monitoring regime. Using prophylactic steroid/avoidance of RAI in those with active TED led to no worsening of TED. Adherence to NICE guidelines was encouraging and demonstrated the electronic change to arranging this works effectively. Realistic consent for hypothyroidism is important.

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P345

Lost time. a year without treatment in graves' thyrotoxicosis leading to cardiogenic shock: a case of resilience

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Introduction

Thyrotoxicosis can have profound systemic effects, with rare cases progressing to severe cardiac failure and multi-organ dysfunction. This report presents a 21-year-old female with untreated Graves' disease who developed thyroid storm, leading to life-threatening complications. The case underscores the catastrophic consequences of untreated hyperthyroidism and the importance of timely intervention.

Case

The patient, diagnosed with Graves' disease at 15 years and non-compliant with treatment for over a year, presented with fever, abdominal pain, and non-bloody diarrhoea following travel from Singapore. Investigations revealed TSH <0.01, FT4 >100 pmol/L, FT3 >50 pmol/L and TSH RAb 14.73 IU/L. She had a calculated Burch-Wartofsky Point Scale (BWPS) score of 80. She rapidly deteriorated, including cardiogenic shock, two pulseless electrical activity (PEA) arrests, and the need for veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Her course was complicated by severe left ventricular dysfunction (ejection fraction 15%), ECMO related ischemic calf muscle injury necessitating bilateral fasciotomies, rhabdomyolysis, acute renal failure, bilateral femoral deep vein thromboses, and infections requiring multiple debridement. Tracheal stoma breakdown and critical illness myopathy further prolonged her recovery. With aggressive thyroid management, including propylthiouracil, steroids, and beta-blockers, her cardiac function improved significantly, with an ejection fraction of 55% by day 20.

Blood test	On admission (20/9)	26/09	30/09	07/10	22/10	7/11	1/12
Free T4 (pmol/L)	>100	51.0	21.2	12.5	11.6	38.3	7.2
Free T3 (pmol/L)	>50			-	3.3	-	4.0
TSH (mIU/L)	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
NT Pro BNP (ng/L)	454			1879	-	669	-

Conclusion

This case highlights the severe systemic consequences of untreated hyperthyroidism, notably its impact on cardiac function. It also emphasises the potential for recovery with timely, targeted thyroid management, even in the setting of critical illness. The interplay between thyroid dysfunction and multi-organ failure underscores the need for greater awareness and early intervention.

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P346

Inceptor is essential to maintain thyroid function in mice

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Insulin inhibitory receptor (inceptor) is highly expressed in various secretory cells and plays an important role in granule formation. The thyroid consists of secretory cells including thyrocytes and c cells which produce thyroxin and triiodothyronine to regulate and maintain metabolic homeostasis. However inceptor expression and function has never been investigated in thyroid. Inceptor-KO mice shows higher FT3 levels comparing to WT mice but doesn't show any proliferation difference. And isolation thyrocytes for 3D culture, inceptor-KO has more thyroid follicles formation at day 6 and thyroid-related markers (PAX8 and Nis) expression is higher, indicating inceptor-KO thyroid organoid more mature than WT. Inceptor-KO promotes hyper functional thyroid, and inceptor expression in thyroid is important to maintain thyroid function balance.

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P347

Co-administration of levothyroxine and iron tablets, are we following the guidelines?

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Background

Recent studies have indicated impairment in levothyroxine absorption when administered simultaneously with iron tablets. This clinical audit aims to prevent the impact of this interaction on our patients to optimize therapeutic outcomes.

Standard

The National Institute for Health and Care Excellence (NICE) guidelines recommend maintaining an interval of at least four hours between levothyroxine and ferrous sulfate tablets on administration. The British National Formulary (BNF) suggests separating the two medications by at least four hours and giving levothyroxine 30-60 minutes before breakfast.

Target

Separating levothyroxine and iron administration by at least 4 hours.

Method

This is a cross-sectional audit that included 50 patients admitted at North Cumbria Integrated Care NHS Trust, taking levothyroxine and iron salt tablets. Data on iron preparation, the timing of administration of the two medications, and the time interval between them were documented and compared to the NICE guidelines.

Results

Out of the 50 patients included, 84% were prescribed levothyroxine and iron at the same time with no interval. Of the 11 patients taking ferrous sulfate and levothyroxine, 10 patients took both without a time interval.

Action plan

1. A presentation was done to raise awareness of this necessary change. 2. A poster was created to remind clinicians of the time interval on prescribing. 3. The electronic prescription system team was involved to display an alert on the system when the two medications are prescribed simultaneously.

Conclusion

These audit findings highlight the necessity for clinicians to be aware of this interaction and to consider alternative timing strategies according to the guidelines to

optimize the efficacy of levothyroxine therapy to ensure the highest standards of patient care.

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P348

Levothyroxine pseudo-malabsorption: a difficult pill to swallow

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We describe five patients (four female, one male) aged 24-58 years who, despite being prescribed oral levothyroxine (250-400 µg daily), remained biochemically hypothyroid and were referred for investigation by Endocrinology. Initial review included assessment for history of diarrhoea; coeliac screen; review of possible competing medications; and investigation of potential assay interference. After these causes of true malabsorption, physiological and analytical interference were excluded, patients underwent levothyroxine absorption test. Patients received a weight-dependent levothyroxine bolus (650-1900 µg) administered orally under supervision. Blood samples for thyroid-stimulating hormone (TSH) and free thyroxine (FT4) were collected at baseline and hourly for at least four hours, FT4 concentration increase was assessed against published criteria. All patients demonstrated adequate levothyroxine absorption, exceeding criteria defined by Walker et al. (2013) and Caron et al. (2023); FT4 increase of $>54\%$ at 2 h, or FT4 $+5.14$ pmol/L at 4 h, respectively. Malabsorption was therefore excluded as the cause of refractory hypothyroidism, with poor compliance the most likely explanation. Weekly supervised bolus levothyroxine administration with baseline and 2 h bloods further demonstrated adequate absorption; significant improvement in TSH concentration was observed in four of five patients (mean pre-test TSH 187.3 mU/L vs mean TSH following final supervised dose 4.4 mU/L). Dose adjustments were made as required, one patient remained on a consolidated weekly levothyroxine dose due to persistent vomiting. At subsequent follow-up, four of five patients were biochemically euthyroid. Based on our experience, we have proposed a harmonised approach to levothyroxine absorption test at our centre: supervised weight-dependent levothyroxine dose with blood samples at baseline, and hourly up to 4 h. Adequate absorption is assessed using the criteria defined above, with malabsorption excluded if either criterion is met. Supervised levothyroxine administration with bloods at baseline and 2 h is continued for 5 weeks to ensure compliance.

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ePoster Presentations

Adrenal and Cardiovascular

EP1

Case report – a case of carotid body paraganglioma due to chronic hypoxic state

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A 68 year old gentleman was referred to the endocrine service with a large right sided neck mass of which MRI neck showed findings consistent with carotid body tumour. He has a significant background history of atrial septal defect with shunt reversal and resultant Eisenmenger's syndrome. The patient denied any symptoms of catecholamine excess and was normotensive. Physical examination also revealed stage 4 finger clubbing. Biochemical analysis revealed unremarkable plasma metanephrines; normetanephrine 1050 pmol/l (0-1180), metanephrine 759 pmol/l (0-510), 3-methoxytyramine <100 pmol/l (0-180). Genetic analysis of inherited phaeochromocytoma and paraganglioma gene panel did not identify a cause for the tumour. The impression was this is a non-secretory parasympathetic carotid body paraganglioma secondary to chronic hypoxic state from his underlying congenital heart disease. MDT discussion concluded that the patient was not a surgical candidate. He underwent 25 sessions of radiotherapy resulting in tumour shrinkage. Carotid body tumours are the most common form of head and neck parasympathetic paraganglioma. It can arise as part of a genetic syndrome or sporadically. Sporadic carotid body paragangliomas are more common in people living at high altitude and in those with chronic hypoxic state. The absence of a known genetic predisposition to this gentleman's carotid body paraganglioma strengthens the hypothesis that it is the result of a chronic hypoxic state. There is a growing body of evidence to suggest a link between hypoxia and carotid body paraganglioma. However, our understanding of the underlying pathophysiological process remains limited and is an area for further investigation.

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EP2

An interesting case of adrenal insufficiency in pregnancy

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Case Presentation

A 29-year-old G2 P0 woman at 8weeks of gestation presented with **hyperemesis gravidarum** and **electrolyte imbalance** (hyponatremia and hyperkalemia). Despite copious intravenous fluid resuscitation and antiemetics, her symptoms persisted. Notable clinical findings included generalized tanning, **postural hypotension**, and **vomiting**, led to a suspicion of **adrenal insufficiency**.

Endocrine evaluation revealed:

- **Random Cortisol**: 181 nmol/L
- **Sodium**: 114 mmol/L (Normal: 133-146 mmol/l)
- Potassium: 6.1 mmol/L (Normal: 3.5-5.3 mmol/l)
- **Adrenal Cortex Antibodies**: Positive

Short Synacthen Test

- **0 Minute Basal Cortisol**: 208 nmol/L
- 30 Minute Cortisol: 211 nmol/L
- **60 Minute Cortisol**: 203 nmol/L
- **Plasma ACTH**: 1298 ng/L (elevated) Up to 50ng/L

These findings confirmed the diagnosis of **Addisonian crisis**. The patient was treated with **glucocorticoid therapy**, resulting in marked symptom improvement. She was followed up in the endocrine clinic, continued on **hydrocortisone**, and started on oral fludrocortisone for postural hypotension.

Discussion

The Early Pregnancy Unit did not initially consider adrenal Insufficiency due to symptom overlap with hyperemesis gravidarum, a common condition in early pregnancy. Both conditions cause **nausea, vomiting, and dehydration**, complicating the diagnostic process. Pregnancy-related physiological changes, such as increased metabolic demand and stress responses, can unmask or exacerbate **adrenal insufficiency**, triggering a crisis. This patient had a history suggesting that she may have had adrenal insufficiency for at least one year before the pregnancy. Awareness of signs like **unexplained tanning** is crucial for early detection as in this case.

Conclusion

This case emphasizes the importance of early recognition of adrenal insufficiency in pregnancy. **Prompt referral** to an endocrinologist can prevent complications and ensure optimal treatment, improving outcomes for both mother and fetus. This case highlights the intersection of **obstetrics** and **endocrinology Multi-Disciplinary Team** in managing complex pregnancy-related conditions.

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EP3

Pheochromocytoma: a case of recurrent takotsubo cardiomyopathy

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Background

Phaeochromocytoma is a rare neuroendocrine tumour of the adrenal medulla, accounting for less than 0.2% of hypertension cases. Classic symptoms include episodic headache, sweating, and tachycardia.

Aims

1. To raise awareness of the symptoms and early diagnosis of pheochromocytoma. 2. To discuss management of phaeochromocytoma-related hypertension.

Case Presentation

A 75-year-old woman presented with intermittent dizziness, headaches, and elevated blood pressure (185/82 mmHg) four years ago. She was started on Amlodipine. One year later, her symptoms worsened, with erratic BP (170/105 mmHg), dizziness, diaphoresis, weight loss, and falls. Ramipril was added. After presenting with decompensated heart failure, she had multiple hospital admissions for chest pain, initially treated as acute coronary syndrome. However, coronary angiography showed normal arteries, and she was diagnosed with Takotsubo cardiomyopathy. A CT scan incidentally found a 4 cm adrenal nodule, which had grown since a previous scan. MRI confirmed a 4.2 cm adrenal mass suspected to be phaeochromocytoma. Urine metanephrines were elevated at 12.94 and 10.38 μmol/24h (normal <2 μmol/24h). She was started on phenoxybenzamine and is awaiting adrenalectomy.

Discussion

1. Phaeochromocytoma should be suspected in patients with hypertension, headaches, and sympathetic hyperactivity. 2. Diagnosis is confirmed by measuring urine or plasma metanephrines. 3. Incidental adrenal tumours require endocrine evaluation. 4. Delayed diagnosis can lead to complications like hypertensive crises and Takotsubo cardiomyopathy. 5. Treatment involves alpha-adrenergic blockers and adrenalectomy where indicated.

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EP4

Adrenal cushing syndrome in a nigerian female

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Introduction

Cushing syndrome is a rare endocrine disorder caused by excess cortisol production, leading to a constellation of symptoms and physical features. Primary adrenal tumors account for 10-20% of cases of Cushing syndrome. Most of these patients have benign adrenocortical adenomas, and rarely adrenal carcinoma or nodular adrenal hyperplasia

Case report

A 25-year-old female undergraduate presented with a six-month history of unintentional weight gain. There was associated easy fatigability, especially when climbing the stairs. There is no history of cough, orthopnea, paroxysmal nocturnal dyspnea, or leg swelling. There was a positive history of easy bruising and purplish stretch marks on her tummy. She admits to a history of abdominal pain, located on the right side of her tummy. No diarrhoea, vomiting, darkening of the skin, excessive acne, or male pattern of hair distribution. No history of exogenous steroid use or family history of similar symptoms. Examination revealed a young woman, with moon-face, facial plethora, buffalo hump, truncal obesity, and multiple purplish striae on her abdomen. Her weight was 80 kg and height 1.63m with a body mass index (BMI) of 30.1 kg/m^2, with a waist-hip ratio of 0.92. Gowers' sign was positive and blood pressure was 110/90mmHg. The investigations' results show non-suppression of cortisol following overnight low-dose dexamethasone suppression test, failure of cortisol suppression by 50% or more following overnight high-dose dexamethasone suppression test, and inappropriately low basal ACTH. Abdominal MRI revealed a near oval-shaped mass measuring 14.8mm x 25.4mm (TxAP) in the right suprarenal region separate from the right kidney. Cortisol secretion was controlled before surgery, open right adrenalectomy, with histologic confirmation of adrenal adenoma. Clinical symptoms improved with the normalisation of basal serum cortisol.

Conclusion

Adrenal Cushing's syndrome is a rare but important diagnosis in patients with hypercortisolism. Early recognition and surgical intervention can significantly improve the quality of life.

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EP5

Cardiovascular risk evaluation based on lipid levels in geriatric patients in rural colombia

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Introduction
Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality in the geriatric population. Identifying risk factors, especially lipid levels, is crucial for preventing adverse cardiovascular events. In rural communities, where access to healthcare may be limited, it is essential to assess the cardiovascular health of the elderly to implement appropriate preventive and treatment measures.
Objective
To evaluate cardiovascular risk according to lipid levels in geriatric patients in a rural Colombian population.
Methodology
A clinical, instrumental, and laboratory examination was performed on 100 patients with an average age of 68.7 $\pm$ 4.7 years. Cardiovascular risk stratification was carried out using the Systematic Coronary Risk Assessment Score. High risk was defined by the presence of cardiovascular disease and diabetes mellitus, age over 65 years, hypertension, or isolated/mixed dyslipidemias. Anthropometric data (height, weight, BMI), vital signs, blood pressure readings, and laboratory data (total cholesterol, LDL, HDL, lipoprotein A, triglycerides, creatinine, blood urea nitrogen) were analyzed.
Results
The nosological composition of the examined patients ($n = 100$) shows that the study mainly included individuals with hypertension (60%), obesity (24%), and stable types of coronary artery disease (34%). The proportions of patients with type 2 diabetes, primary kidney disease, and chronic obstructive pulmonary disease were 21%, 17%, and 14%, respectively.
Conclusion
The presence of elevated serum triglyceride levels in individuals at high cardiovascular risk is associated with obesity, type 2 diabetes, hypertension, and coronary artery disease.
Keywords
obesity, diabetes, hypertension, arterial disease, cholesterol.
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EP6

Prevalence of cardiometabolic disease in a municipality of northwestern colombia

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Introduction
Cardiometabolic diseases, including hypertension and dyslipidemia, represent a significant public health concern, particularly in rural areas where healthcare access may be limited. Identifying the prevalence of these conditions in specific populations can inform targeted interventions and improve health outcomes.
Objective
To evaluate the prevalence of cardiometabolic disease in a municipality in northwestern Colombia.
Methodology
This descriptive study aimed to identify cases of diseases linked to cardiovascular risk. Patients aged 40 to 95 years were included, provided they had recorded cardiometabolic variables, including lipid profiles, glucose levels, renal function, blood pressure readings, and body mass index (BMI).
Results
Among the participants, 58.5% were female and 41.5% were male. Hypertension emerged as the most prevalent condition within this population. This finding aligns with reports from urban settings, highlighting a consistent trend in the prevalence of hypertension across different demographics. Given this high prevalence, there is a pressing need to optimize the biopsychosocial management of these patients to prevent cardiometabolic repercussions due to poorly controlled blood pressure levels.
Conclusion
Primary and secondary prevention efforts are essential in rural municipalities in Colombia to mitigate long-term cardiometabolic consequences associated with prolonged hypertension. Addressing these health issues can significantly enhance the quality of life and reduce healthcare costs in the community.
Keywords
metabolic syndrome, hypertension, epidemiology, metabolic repercussions.
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EP7

Prevalence of metabolic disorders in patients with chronic venous insufficiency in a latin american institution

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Introduction
Chronic venous insufficiency (CVI) is a common condition that can lead to significant morbidity. Understanding the prevalence of metabolic disorders in patients with CVI is crucial for effective management and prevention of cardiovascular complications.
Objective
To evaluate the prevalence of metabolic alterations in patients with chronic venous insufficiency at a Latin American institution.
Methodology
This retrospective study involved reviewing medical records of 100 patients diagnosed with CVI, following the CEAP classification criteria. Patients over 65 years old with isolated or mixed dyslipidemia and alterations in plasma glucose levels were included. The FINDRISC score was utilized to estimate the risk of developing type 2 diabetes mellitus in these patients.
Results
The mean age of participants was 65.5 $\pm$ 5.3 years, with a female predominance of 71% compared to 29% male. The average duration of diagnosed chronic venous insufficiency was 11.5 $\pm$ 4.3 years. Elevated BMI was the most prevalent criterion for metabolic syndrome, followed by increased abdominal circumference and elevated low-density lipoprotein (LDL) cholesterol as risk factors. These findings indicate a high prevalence of metabolic syndrome criteria, contributing to an increased risk as indicated by the FINDRISC score.
Conclusion
Metabolic syndrome significantly increases the risk of cardiovascular disease in the studied population. Early identification and management of metabolic disorders in patients with chronic venous insufficiency are essential for reducing associated health risks.
Keywords
metabolic syndrome, diabetes, cholesterol, venous insufficiency.
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Bone and Calcium

EP8

A clinical case report highlighting the side effects of steroid therapy in ankylosing spondylitis: iatrogenic cushing's

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A 37-year-old man of Romanian descent presented with complaints of back pain and was found to be HLA B27 positive. Subsequently, he was diagnosed as having Ankylosing spondylitis and he was initiated on high-dose steroids. The duration of regular steroid therapy lasted for more than ten years. After his move to the United Kingdom, he was referred to endocrinology outpatient clinic for symptoms of weight gain, muscle weakness, postural light-headedness, sexual dysfunction, fatigue, and skin striae. Examination revealed significant abdominal striae, a cushingoid appearance, and proximal muscle weakness, which is typical of Cushing's syndrome. The biochemical tests showed hypogonadotropic hypogonadism, secondary hypothyroidism, and a positive short Synacthen test with an insulin stress test suggestive of inadequate cortisol and growth hormone response, A diagnosis of iatrogenic Cushing's syndrome with secondary adrenal insufficiency was made. The patient was started on a tapering regimen of prednisolone to restore adrenal function, with doses reduced bi-weekly. Subsequently, he developed complications of Cushing's syndrome, namely-osteoporosis, steroid-induced diabetes, hypercholesterolemia, and anemia for which he was treated. These were the significant side effects due to prolonged

steroid use and the effect on the individual's health and further requiring the use of medications to tackle the issues following the use. This case highlights the risks associated with long-term steroid therapy, the importance of appropriate tapering as well as close monitoring of steroid treatment to prevent complications and improve the patient's quality of life.

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EP9

The impact of long-term intranasal steroid therapy on adrenal function: a clinical case report

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We present the case of a gentleman who was investigated in the Endocrine clinic for chronic fatigue and adrenal insufficiency secondary to prolonged use of nasal steroid sprays. Nasal steroids were initially prescribed due to asthma and were discontinued in 2013. This is a 53-year-old patient with intermittent complaints of fatigue, which were alleviated by taking hydrocortisone. The initial dose of hydrocortisone was 20 mg, later reduced to 5 mg. Multiple Short Synacthen Tests (SST) consistently reflected suboptimal cortisol responses, strongly indicating a diagnosis of adrenal insufficiency. There were no gastrointestinal or cardiovascular issues, and no significant changes in weight or appetite. Following multiple endocrinology appointments and a seemingly successful trial of hydrocortisone replacement, the patient frequently altered his doses—either reducing or omitting them altogether—with no additional medical repercussions. At 5 mg of hydrocortisone, the patient experienced reduced exercise tolerance, while at doses of 15 mg or higher, he complained of worsening symptoms including headaches, hypertension, and further lethargy. Iatrogenic Cushing's was considered and ruled out by normal renin-aldosterone levels, plasma metabolites, and the absence of any Cushingoid features. The concomitant nature of this gentleman's chronic fatigue and adrenal insufficiency has proven to be a challenge when determining the best approach to managing his hypoadrenalism secondary to exogenous steroid use

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Endocrine Cancer and Late Effects

EP10

A novel clinical case demonstrating the efficacy of Sestamibi scans in identifying parathyroid adenoma concurrently with metastatic breast cancer

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We present the case of a 60 year old female, who was referred from the breast clinic after having a radical mastectomy and radiotherapy with a raised calcium of 2.78. She had a negative CT chest/abdomen/pelvis and her parathyroid hormone was raised at 19.7. She had a previous history of renal cancer treated with nephrectomy and was known to have the variant of the BRCA 1 gene. Her main symptom was fatigue post treatment. Her calcium: creatinine clearance ratio was 0.0104. The vitamin D was initially 44 but post treatment it increased to 54 but PTH remained raised at 23.5. Her calcium remained raised 2.68-2.83. The ultrasound of her parathyroid and kidneys did not reveal any abnormalities. Her DEXA scan showed osteopenia in her forearms only. In view of her BRCA gene she was keen for bilateral mastectomy and was on the waiting list. A Sestamibi scan was requested but due to shortage of the assay there was a delay in her getting this. She proceeded to have the breast surgery. Post operatively the Sestamibi showed a functioning parathyroid adenoma posterior to the lower pole of the right thyroid lobe. It also showed a non-avid hypoattenuating liver lesion and a T9 sclerotic bone lesion, suggestive of metastasis. MRI spine and liver confirmed the appearances were in keeping with multiple vertebral and hepatic metastases. We believe that this is the first reported case of sestamibi detecting a functioning parathyroid adenoma as well as liver and bone metastasis. Previous case reports found metastatic disease in sestamibi scans for other conditions but none with a functioning parathyroid adenoma and metastatic disease reported. Her calcium has normalised and she is on denosumab every 6 weeks.

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EP11

A challenging case of parathyroid cancer

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Parathyroid carcinoma (PC) is a rare malignancy, with fewer than 1,000 cases reported since 1904. It accounts for approximately 0.005% of all cancers and 0.5–1% of parathyroid disorders.

Case

A 52-year-old male was referred to the Endocrine clinic in 2023 for severe hypercalcemia (Ca 3.2 mmol/l). Biochemistry: Ca 3.2mmol/L PTH 32.42 pg/mL, Creatinine at 130 μmol/l. He had a background of primary hyperparathyroidism treated with L parathyroidectomy with concordant pre-operative U/S in 2019 at a different center. Surgical notes suggested the lesion was adherent to surrounding structures, with histology confirming atypical features. Hypercalcemia recurred 1 year post surgery, unfortunately patient did not engage with specialist services. Patient underwent localization studies, while suspecting parathyroid malignancy. MRI neck, 4D CT, ultrasound neck repeated on 2 occasions were inconclusive. CT-TAP identified bilateral pulmonary nodules suggestive of metastasis, confirmed by a Choline PET scan. A diagnosis of metastatic parathyroid cancer was confirmed in a multidisciplinary meeting. The metastatic lesions are unresectable currently. The management of hypercalcemia has been challenging, requiring multiple admissions, however he is responding to Denosumab injections currently.

Discussion

Parathyroid carcinoma often presents with severe hypercalcemia, frequently exceeding 3.5 mmol/l, and elevated PTH $>$ five times the normal. There is significant renal and bone disease compared to those with parathyroid adenoma. The diagnosis of parathyroid carcinoma can be challenging histologically, but macroscopic features intraoperatively and clinical progression can support the diagnosis.

Conclusion

Our case is quite unusual and challenging in view of the presentation with distant metastasis with no localized disease. It highlights the importance of considering parathyroid carcinoma in patients with persistent severe hypercalcemia. Early diagnosis and surgical intervention are essential for improving patient outcomes. The management of refractory hypercalcemia remains a significant challenge.

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EP12

Recurrent pituitary macroadenoma due to secondary resistance to cabergoline

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This is a case presentation of macroprolactinoma, the most common type of functional tumour among pituitary adenomas. The typical presentation of pituitary macroadenomas (PA) is either due to mass effect, hormonal excess or deficit. It is vital to evaluate the pituitary axis and visual field assessment to know the extent of the local compression effect. The imaging fine-cut computer tomography or MRI helps to see the tumour burden. It is generally recommended to begin treatment with dopamine agonists for prolactinomas. All other pituitary adenomas are typically treated with trans-sphenoidal surgery, with medical therapy reserved for those who are not cured by surgery. About 5-18% of prolactinoma patients show resistance to dopamine agonists. In this case, pituitary macroadenoma (prolactinoma) recurred after eight years of complete response to CBG. There is a discussion of Dopamine agonist resistance and other management options for pituitary macroadenoma in cases of DA resistance. The patient developed central hypothyroidism and hypoadrenalism due to the mass effect of PA. A multidisciplinary team approached the patient.

Conclusion

The most common functional pituitary tumours are pituitary adenomas. The most effective treatment for these tumours is dopamine agonists. It's worthwhile to note that resistance to dopamine agonists can be primary or secondary. Secondary resistance can occur after one year of the initial response. It is advisable to conduct further biochemical and radiological tests to determine the response of the tumour to DA. For managing pituitary macroadenomas, surgery is the most effective treatment. Radiotherapy or Chemotherapy may be considered when surgery is not feasible. New therapeutic options such as Tyrosine kinase inhibitors (lapatinib) and Octreotide therapies can be considered for treating PA.

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Metabolism, Obesity and Diabetes

EP13

Risk factors for impaired glucose tolerance: a cross-sectional study

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Background
This study aims to analyze the risk factors for elevated fasting plasma glucose (FPG) and 2-hour post-load plasma glucose (2hPG) in IGT patients respectively.
Methods
A cross-sectional study was conducted with 463 IGT patients in China between January 2021 and August 2021. Data collected included demographics and medical history, blood glucose, glycated hemoglobin, liver function, renal function, and blood lipids. Univariate and multivariate regression analyses were used to evaluate the associated risk factors for FPG and 2hPG. Finally, the patient's information was entered into an EXCEL table, and the data were analyzed using SPSS 26.0 statistical software.
Results
Male gender, older age, and higher 2hPG were independent risk factors for elevated FPG levels. Higher FPG, higher LDL-C, and a history of hypertension were independent risk factors for elevated 2hPG levels.
Conclusions
Male gender, older age, higher FPG, higher 2hPG, higher LDL-C, and history of hypertension were independent risk factors for IGT patients. We need to pay attention to 2hPG and recommend OGTT as an early screening tool to identify high-risk individuals.

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EP14

Cholestyramine could be a good choice for difficult to control type 2 diabetes on optimal oral therapy

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Introduction
Type 2 diabetes mellitus (T2DM) poses a significant challenge when optimal oral therapies fail to achieve adequate glycemic control. This study explores the potential of cholestyramine, a bile acid sequestrant traditionally used for lowering cholesterol, as auxiliary therapy for patients with T2DM on maximized oral medication regimens. Despite the effectiveness of various oral medications, some individuals with T2DM experience persistent hyperglycemia. Cholestyramine's mechanism of action in T2DM management is not fully elucidated. While its primary function is to bind bile acids in the intestine, potentially improving glp1 secretion, more research research is needed to understand the specific pathways involved in glycemic control.
Materials and Methods
This retrospective cohort study followed 200 patients with poorly controlled type 2 diabetes in a private clinic. All participants were on maximized oral therapy with HbA1c levels exceeding 8.6%. One hundred patients (Group 1) received cholestyramine 4 grams daily for hypercholesterolemia alongside their existing treatment regimen, which included metformin XR 2 grams daily, sitagliptin 100 mg daily, empagliflozin 25 mg daily, and pioglitazone 30 mg daily. The remaining 100 patients continued on maximized oral therapy alone.
Results
Findings demonstrate a statistically significant decrease in HbA1c levels ($P < 0.0001$) within group 1 patients following 3 months of cholestyramine treatment. Conversely, group 2 displayed no significant change in HbA1c ($P < 0.7750$). The results show that cholestyramine 4 gm once daily can lead to control of blood glucose in difficult to control type 2 diabetes patients.
Conclusion
This review investigates the possibility of cholestyramine as an additional treatment option for individuals with T2DM struggling to achieve glycemic control despite optimized oral therapies. By analyzing existing research and highlighting areas for further investigation, this review aims to contribute to the ongoing exploration of novel therapeutic approaches in T2DM management.

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EP15

Post parathyroidectomy severe rhabdomyolysis due to the synergistic effects of statins and general anaesthetic agents

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Introduction
Rhabdomyolysis, myocyte injury with the release of intracellular contents into the circulation, can result from various causes, the commonest being trauma or a fall with a long lie, less commonly statins or general anaesthetic agents (GAA), but literature on rhabdomyolysis due to the synergistic effects of statins and GAA is limited.
Case Report
A 75-year-old female with known ischemic heart disease, familial hypercholesterolemia, pre-diabetes, chronic kidney disease IIIa, osteoporosis and primary hyperparathyroidism. Medications included Aspirin, Ramipril, Ezetimibe and Rosuvastatin (40 mg) for the past 15 years without any hepatotoxic or myotoxic side-effects. Two-weeks before the presentation, she had an uneventful parathyroidectomy but developed generalised myopathy, progressive weakness and pain predominantly in the legs. She had proximal myopathy but no other features of endocrinopathy. There was no history of trauma, long-lie, strenuous exercise, seizures or electric shock injury. No personal or family history of autoimmune conditions.
Investigations
The baseline investigations were normal (including full blood count, renal and thyroid functions, C-reactive protein, bone, coagulation, and lipid profiles). However, Creatine Kinase (CK) was very high, 27096 (25-200U/l), and Alanine transaminase was 717 (0-34 U/l). Extensive autoantibody profile was negative, including antinuclear and anti-Jo antibodies.
Management
Conservative management, including intravenous fluid and suspending statins, resulted in clinical improvement and normalisation of liver functions and CK.
Conclusion
Since she tolerated the statins very well for more than 15 years without any side effects and symptoms started right after the surgery, we consider this was most likely due to the synergistic effects of statins, surgery and GAA (Sevoflurane & Propofol, both of which are known cause of rhabdomyolysis).
Learning points
Patients undergoing general anaesthesia while on statins are at a higher risk of rhabdomyolysis due to the synergistic effects. Whether statins should be withheld preoperatively remains a clinical decision depending on individualised cardiovascular risk.

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EP16

First case of cushing's disease associated with pheochromocytoma in the colombian northwest

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Introduction
Endogenous hypercortisolism (EH) is a serious condition caused by an excess of glucocorticoids in the body, classified into ACTH-dependent and ACTH-independent variants, occurring in 70-80% and 20-30% of cases, respectively. A rare cause of ACTH-dependent EH is ectopic ACTH syndrome (ACTH-ES), accounting for approximately 15-20% of cases. ACTH-ES is characterized by the hyperproduction of adrenocorticotropic hormone (ACTH) from neuroendocrine tumors outside the pituitary gland, including pheochromocytoma (PC).
Case Report
We present the first case of Cushing's disease associated with pheochromocytoma in the Colombian Northwest. The patient, a male in his thirties, exhibited clinical signs of hypercortisolism and sought care at the region's most complex hospital. Laboratory tests revealed urinary cortisol levels exceeding five times the normal range, with normal ACTH levels. Further examination confirmed ectopic Cushing's syndrome (CS). Multislice computed tomography (MSCT) of the abdomen identified a mass in the left adrenal gland. Urine tests showed a significant increase in methylated catecholamine derivatives. The patient underwent left adrenalectomy, and the diagnosis of pheochromocytoma was confirmed morphologically and pathologically. An immunohistochemical study demonstrated intense expression of chromogranin A and ACTH in the tumor cells.

Discussion
This case highlights the rare occurrence of paraneoplastic ACTH production by pheochromocytoma. The patient's presentation with hypercortisolism and the confirmation of ectopic ACTH production emphasize the complexity of diagnosing adrenal tumors.
Conclusion
This report underscores the importance of considering pheochromocytoma in patients with hypercortisolism and elevated urinary cortisol levels. Early identification and surgical intervention are crucial for effective management and improved patient outcomes.

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EP17

Report of the first case of Wiedemann-Rautenstrauch syndrome in a patient from a South American hospital

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Introduction
Wiedemann-Rautenstrauch syndrome, also known as neonatal progeroid syndrome, is an ultra-orphan disease classified among premature aging syndromes with an autosomal recessive inheritance pattern. It is associated with mutations in the POLR3A, POLR3B, and POLR3GL genes, which encode RNA polymerase III. The incidence of this syndrome is currently unknown.
Case presentation
We present the first clinical description of an 8-year-and-9-month-old patient with Wiedemann-Rautenstrauch syndrome in a South American hospital. The patient exhibited progeroid features, including edentulism, growth retardation, low weight, and generalized lipodystrophy. Genetic testing revealed compound heterozygous mutations in the POLR3A gene. The patient was observed for three years, allowing for dynamic follow-up and comprehensive assessment.
Discussion
This case contributes to the limited worldwide experience in monitoring patients with neonatal progeroid syndrome. It highlights the importance of differential diagnosis in such complex cases, considering the clinical overlap with other premature aging syndromes. As there is currently no specific treatment available for this condition, the patient is managed by a multidisciplinary team of healthcare providers, focusing on supportive care and monitoring for associated complications.
Conclusion
This report is the first of its kind in our region and one of the few globally, emphasizing the need for increased awareness and understanding of Wiedemann-Rautenstrauch syndrome. Future research and collaboration are crucial for developing effective management strategies and improving the quality of life for affected patients.

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EP18

Report of the first case with NF1 gene mutation with deletion of exon 16 and 22 in a patient with neurofibromatosis type 1 and pheochromocytoma

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Introduction
The association between neurofibromatosis type 1 (NF-1) and neuroendocrine tumors, particularly pheochromocytoma (PC), has not been well characterized in our populations. NF-1 is a genetic disorder that presents with various clinical manifestations, and understanding its relationship with neuroendocrine tumors is essential for effective management.
Case presentation
We describe a clinical case of a 52-year-old man from Venezuela diagnosed with NF-1 in 2019. The diagnosis was based on the presence of four hallmark signs: café-au-lait skin lesions, scoliosis, multiple neurofibromas, and Lisch nodules. The diagnosis of pheochromocytoma was established through significantly elevated levels of free metanephrines and normetanephrines in a 24-hour urine collection, as well as the identification of a malignant phenotype in the right adrenal gland tumor via CT scan. This diagnosis was confirmed by pathomorphological examination. During genetic analysis, a novel mutation classified as of uncertain significance was identified in one of the NF1 gene alleles: a 482 bp deletion that included exons 16 and 22. This mutation caused splicing alterations, resulting in a reading frame shift and premature termination of protein synthesis. Additionally, a study of the transcription levels of genes associated with pheochromocytoma (RET, TMEM127, MAX, FGFR, MET, MERTK, BRAF, NGFR, PI3K, AKT, MTOR, KRAS, MAPK) revealed a significant decrease in KRAS and BRAF transcripts and an increase in TMEM127 transcripts, categorizing the pheochromocytoma in this case as associated with the second group of genetic abnormalities in paragangliomas.
Conclusion
This case underscores the importance of timely recognition of NF-1 and the need for a multidisciplinary approach to manage catecholamine-secreting tumors effectively. Early diagnosis is crucial for developing appropriate follow-up strategies for affected patients.

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EP19

Double diabetes: when autoimmunity and insulin resistance co-exist

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Introduction
Type 1 diabetes (T1DM) is characterised by autoimmune destruction of pancreatic β-cells, which results in insulinopenia. Type 2 diabetes (T2DM) is caused by insulin resistance associated with pancreatic β-cell dysfunction. The combination of these two conditions is classed as double diabetes.
Case report
Female patient aged 16 years with a history of gestational diabetes in her mother. She presented with profound asthenia associated with a cardinal syndrome of 1 month's duration. Emergency investigations revealed inaugural ketosis (capillary glycaemia of 2.87g/L and positive acetonuria on urine dipstick, alkaline reserves of 17 mEq/l). Clinical examination revealed a BMI of 29 kg/m^2 and a waist circumference of 90 cm, with acanthosis nigricans on the neck. Paraclinical investigations showed an HbA1c of 14%, a negative infectious workup, a C-peptide of 79 pmol/l ($<$200 pmol/l) and anti-GAD antibodies $>$280 IU/ml. Given this clinical and biological picture, the diagnosis of double diabetes was accepted and the patient was started on basal bolus insulin therapy with metformin.
Discussion
Double or hybrid diabetes is a condition characterised by the coexistence of autoimmune T1DM and T2DM, accompanied by the presence of insulin resistance and metabolic syndrome. Initial epidemiological studies have indicated that 4% of patients with T1DM may also develop T2DM. A study led by Mishra in 2018 found a 7% prevalence of double diabetes in young diabetics with an average age of 22. The latest hypotheses suggest that obesity, by promoting insulin resistance, induces glucotoxicity and accelerates β-cell apoptosis. Furthermore, inflammatory phenomena due to excess adipose tissue and the resulting dysregulation of the immune system can trigger T1DM.

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EP20

It's hypoglycaemia o'clock – iatrogenic hypoglycaemia on an insulin pump due to time reversal

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Introduction
Hyperglycaemia, the result of under-treating diabetes mellitus, is associated with long-term complications. On the contrary, hypoglycaemia (the result of over-treatment), can lead to sudden harm; the latter of which can be due to a myriad of causes. We present a case of a patient on an insulin pump with recurrent nocturnal hypoglycaemia from an error in the settings of her pump that has not previously been described within the literature.
Case Presentation
A 36-year-old female with Type 1 Diabetes Mellitus presents to the clinic. Although she had a history of poor compliance with insulin (with recurrent admissions for diabetic ketoacidosis), she had recently improved her adherence to treatment, and was now being upgraded to an insulin pump. Following this transition, she

demonstrated multiple episodes of nocturnal hypoglycaemia, requiring intranasal glucagon. She feared entering automatic mode on the pump (despite reassurance), and therefore her nocturnal basal rate was reduced. Despite this adjustment, she had three further admissions for nocturnal hypoglycaemia. Upon closer inspection of the pump, it appeared that the programmed time had been reversed by 12 hours. It appeared that the reduced basal rate set for night-time had erroneously been delivered throughout the day; moreover, the cause of her nocturnal hypoglycaemia was simply the elevated day-time basal rate being delivered overnight. Following the correction of the time programmed on the pump, no further nocturnal hypoglycaemia was noted.

Conclusion

This case is serves as a reminder of the importance of considering all causes of hypoglycaemia. Despite the many points of contact with a medical professional, the cause of the hypoglycaemia was missed. It was later found to be iatrogenic due to improper time programming. This case has not been described previously in the literature and serves to avoid overlooking common areas for fallacies with diabetes technology.

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EP21

Insulin modulates macrophage inflammation in a time and sex-dependent manner

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Background

Insulin is well-known as an anabolic hormone and growth factor that mediates glucose and lipid metabolism. Insulin signaling dysregulation causes a cascade of adverse effects, leading to development of cardiometabolic diseases such as type 2 diabetes mellitus (T2DM) and atherosclerotic cardiovascular disease. Men and women are noted to have different disease progression and outcomes with T2DM women having increased relative risk for fatal and non-fatal cardiovascular disease compared to men. These differences have been suggested to stem from sex differences in insulin resistance. With insulin resistance and inflammation being a common phenome underlying cardiometabolic disease pathophysiology, it has been increasingly recognized insulin plays a major role in macrophage mediated-inflammation. Published studies are contradictory in opinions if insulin primes macrophages to be proinflammatory or anti-inflammatory with limited studies investigating female macrophages. We aim to investigate if male and female macrophages respond differently to insulin.

Methods

Bone-marrow derived macrophages (BMDM) from wild-type C57BL/6J male and female mice (n = 4-6) were harvested and stimulated with 0.1-100 nM of insulin for 2- or 24-hours. RT-qPCR was used to analyze changes in mRNA expression. Results were analyzed using a two-way ANOVA using fisher's least significant difference test.

Results

2-hour stimulation showed insulin increased female *Ccl2*, *Tnf-a* and *Il-10* and decreased *Il-1b* mRNA expression compared to males. 24-hours stimulation showed insulin increased female *Akt2, Nf-kB*, *Ccl2*, *Il- 1b*, *Il-10* and *Tnf-a* and decreased *Tlr4* mRNA expression.

Conclusion

Our results demonstrate male and female BMDMs respond differently to insulin. Female BMDMs showed increased pro-inflammatory gene expression when stimulated for 24-hours. Female BMDMs also displayed increased *Il-10* gene expression at 2- and 24-hours. This points to female macrophages response being more sensitive to insulin signaling. These results could be used to inform current therapeutic strategies and with the view to improve cardiometabolic disease outcome in females.

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EP22

A quality improvement project (QIP) evaluating inpatient diabetic foot care using the SINBAD scoring system at a district general hospital (DGH)

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Introduction

The National Diabetes Foot Care Audit (NHS Digital, 2019) employs the SINBAD score to evaluate patient care. According to NICE guidelines (2016), any patient with an ulcer should be referred to specialist services within one working day. This project aims to implement a systematic clinical assessment of diabetic foot patients using the SINBAD scoring system, develop appropriate investigation and management plans based on severity, and facilitate timely referrals to specialist teams to improve clinical outcomes, particularly in limb preservation.

Methodology

A retrospective data collection of 32 diabetic foot patients was conducted using Electronic Patient Records over three months from June to August 2024. Data included documenting risk factors, wound evaluation using the SINBAD score, necessary investigations, initiation of antibiotics within 1-2 hours, specialist consultations, and podiatrist/TVN review within 12 hours of presentation.

Results

Good practices identified included evidence of infection documented in 86% of patients, antibiotics initiated within 2 hours for 76%, and wound swabs sent for 64% of the cohort, with 72% receiving appropriate antibiotic reviews. Additionally, 69% were streamed directly to the Endocrine Ward from the Emergency Department. However, concerns arose with only 45% receiving X-rays upon admission, 55% lacking documented specialist discussions within 2-4 hours, and only 31% seen by a podiatrist/TVN within 12-24 hours. Nutritional blood and HbA1c checks were not performed for 72% and 79% of patients.

Conclusion

Our findings emphasise the need for structured assessment and timely intervention in managing diabetic foot patients. We developed a diabetic foot care pathway now accessible on the hospital intranet and integrated the SINBAD scoring system into the clerking document. Additionally, we displayed posters in clinical areas and organised teaching sessions for resident doctors. We aim to enhance clinical outcomes and reduce limb loss risk by implementing the SINBAD scoring system and improving referral processes.

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EP23

The curious case of hypoglycaemia in the older person without diabetes-conservative management of insulinoma

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82-year-old female presented with new onset seizures and confusion. The paramedical team found the capillary blood glucose (CBG) to be 2.1mM which was treated. She had a past medical history of gastrointestinal stromal tumour (GIST) which was surgically treated and being followed up by the oncology team. There was no other past history. She was caring for her disabled husband and was independent with ADLs. During admission, hypoglycaemic episodes which consistently occurred between 0300 and 0700hrs was noted. After several unsuccessful attempts at taking blood samples during the hypoglycaemic episode, one sample captured a plasma glucose value of 2.5mM with C-peptide of 862 pmol/l. HbA1C prior to the admission was 41mmol/mol. A diagnosis of 'possible insulinoma' was made. CT pancreas was normal (MRI not tolerated). Delirium persisted for 2 months. Due to level of frailty, she was not a candidate for surgical intervention. She was commenced on libre 2 sensors and set up on low glucose alarms. She was started on diazoxide (300 mg/day) and was discharged home with stable CBGs. One month later, she was admitted after a fall. CBG was 15 to 20mM and HbA1C was 74mmol/mol. Cognition was normal. Dose of diazoxide was reduced to 100 mg/day and due to recurrence of hypoglycaemic episodes, increased to 200 mg/day. She was discharged home with low GI dietary advice and CBG $<$18mM This case highlights the advantages of using alarmed flash glucose monitor in an older person **without diabetes,** challenges with diazoxide and the rare association of insulinoma with GIST.

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EP24

Characterization and stratification of familial hyperlipidemia using the dutch clinical criteria in a south american population

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Introduction
Familial hyperlipidemia (FH) refers to inherited genetic disorders that lead to elevated serum cholesterol levels, primarily low-density lipoprotein (LDL) cholesterol. Early detection is essential to prevent cardiovascular disease (CVD). The prevalence of FH in Colombia is unknown, and the Dutch Lipid Clinic Network (DLCN) criteria are widely used for diagnosis.
Objective
This study aimed to identify FH cases in a population from northwestern Colombia using the DLCN criteria and describe associated clinical characteristics.
Materials and Methods
A retrospective study included patients aged 18 to 95 years with available lipid profiles and cardiometabolic data. The DLCN criteria were applied to identify FH. Patients with incomplete data or secondary causes of hyperlipidemia (e.g., hypothyroidism or nephrotic syndrome) were excluded.
Results
Of 25 patients meeting the DLCN criteria, 56% were male, with the highest prevalence between the fourth and fifth decades. Most (80%) were classified as having very high cardiovascular risk, and 70% had a history of coronary or cerebrovascular disease, aligning with existing literature.
Discussion
These findings reveal a significant cardiovascular burden in individuals with FH, emphasizing the need for early detection, particularly in middle-aged men. The strong association between FH and CVD highlights the importance of targeted screening and timely intervention.
Conclusion
Greater awareness of FH is needed to promote early diagnosis, especially in individuals with a family history of hyperlipidemia or premature CVD. Expanding screening efforts in primary care is essential to improve patient outcomes and prevent cardiovascular complications.

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EP25

Long-term efficacy of pharmacological and non-pharmacological therapies in the development of type 2 diabetes in south american patients

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Introduction
The underdiagnosis of early carbohydrate metabolism disorders, such as impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), delays type 2 diabetes (T2DM) diagnosis and reduces the effectiveness of oral antidiabetics. Early pharmacological intervention in individuals with IGT/IFG can delay the onset of T2DM and, in some cases, prevent it.
Objective
To evaluate the long-term efficacy of metformin in reducing the conversion rate of IGT/IFG to T2DM in South American patients.
Materials and Methods
A non-randomized, prospective observational study included patients newly diagnosed with IGT/IFG. Metformin was prescribed for 5 to 10 years, and the conversion to T2DM was assessed after 10 years of follow-up.
Results
Among the 1000 patients evaluated, 500 received metformin and 500 did not. The sample included 786 men and 214 women, aged 40 to 80 years, with no significant differences in age or gender between groups. Many patients discontinued treatment after the observation period.

Group	Patients (n)	Conversion to T2DM (%)
Metformin (Treated)	500	2%
No Treatment (Untreated)	500	49%

After 10 years, the conversion rate to T2DM was significantly lower in the metformin group (2%) compared to the non-treated group (49%) ($P < 0.001$).

Discussion
The long-term use of metformin significantly reduced the risk of T2DM in patients with IGT/IFG, demonstrating the value of early pharmacological intervention. These findings highlight the importance of sustained treatment to prevent diabetes progression.
Conclusion
Prolonged metformin use provides effective secondary prevention of T2DM in high-risk patients. Tools like FINDRISK are recommended to identify at-risk individuals and guide preventive efforts.

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EP26

Clinical variables in hyperestrogenism and hypogonadism in obese patients from a south american hospital

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Introduction
Epidemiological data on the incidence of hyperestrogenism is scarce and is typically assessed indirectly through the prevalence of gynecomastia.
Objective
To evaluate the prevalence of hyperestrogenism, androgen deficiency, and the combination of testosterone deficiency with hyperestrogenism in obese men through a retrospective analysis. The study also examines the influence of body mass index (BMI) and age on estradiol and testosterone levels.
Materials and Methods
A retrospective review of 100 medical records from men categorized as normal weight, overweight, or obese was conducted. The statistical analysis was performed using IBM SPSS Statistics 23.0.
Results
Hyperestrogenism was diagnosed in 34% of patients, based on estradiol levels exceeding 47 pg/ml. As BMI increased, the incidence of hyperestrogenism rose from 19% in men with normal BMI to 42% in those with grade III obesity. Testosterone deficiency was observed in 61% of patients. A significant reduction in blood testosterone levels was noted as BMI increased, from 12.5 nmol/l in men with normal BMI to 8.6 nmol/l in those with grade III obesity. The combination of testosterone deficiency and hyperestrogenism was present in 58% of the patients examined.
Discussion
The study highlights the significant impact of hormonal imbalances, particularly hyperestrogenism and hypogonadism, in obese patients. These conditions are associated with reduced quality of life, sexual performance, and an increased cardiometabolic risk, aligning with findings from other studies.
Conclusion
Hormonal conditions such as hypogonadism and hyperestrogenism play a critical role in the health of obese patients, contributing to significant declines in quality of life and increased cardiometabolic risk.

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Neuroendocrinology and Pituitary

EP27

Panhypopituitarism - a case with an unusual cause

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Introduction
This case outlines a rare cause of Pan-hypopituitarism in a patient with HIV on anti-retroviral treatment.
Case Study
A 74-year-old man of African-origin was diagnosed with HIV in 2002. He presented with Pneumocystis carinii pneumonia, low CD4 count, and high viral load. He was managed with anti-retrovirals leading to excellent response. Since 2002, he has been on various anti-retrovirals including Emtricitabine, Tenofovir, Efavirenz, Zidovudine, Abacavir, and Lamivudine. His thyroid functions became abnormal in June 2020, showing a reduction in Free Thyroxine (FT4) levels with inappropriately normal thyroid stimulating hormone (TSH) (Table 2). Further investigations showed low testosterone with normal gonadotrophins. The Synacthen stimulation test showed borderline normal results (Table 1).
Results
Testosterone – 6.4 nmol/l (8.7-29) Luteinising hormone (LH) – 4.0 u/L (1-10) Follicular Stimulating Hormone (FSH) – 5.0 u/L (1-8)
Discussion
There is good evidence in literature pointing towards HIV disease process and anti-retrovirals being associated with pituitary and endocrine dysfunction in

Synacthen Stimulation Test (Table 1)

Time (minutes)	0	30	60
Cortisol (nmol/l)	140	343	446

Adequate response either >420 at 30 minutes or > 430 at 60 minutes

Table 2.

Date	TSH (0.2-5 mu/l)	FT4 (10-24 pmol/l)
Dec-19	1.04	11.1
Aug-20	1.07	8.9
Apr-22	1.44	6.2
Mar-23	1.23	8.2
Jul-24	1.11	6.7

Magnetic Resonance Imaging of pituitary was normal.

patient with HIV. HIV with high viral load can lead to hypopituitarism due to the immunosuppressant effect and hypophysitis. Anti-retrovirals can interfere with the hormone metabolism leading to hormonal abnormalities. As MRI pituitary was normal and there was no history of intracranial surgery, radiotherapy, injury, or apoplexy, we suspect the pituitary insufficiency is related to HIV.

Conclusion

Pituitary insufficiency in patients with HIV is unusual but recognized. The need for monitoring of pituitary hormones in HIV is not entirely clear and needs more research.

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EP28

A rare case of fsh-secreting pituitary adenoma (FSHoma): clinical presentation, diagnosis, and management

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Background

FSH-secreting pituitary adenomas (FSHomas) are rare gonadotroph adenomas accounting for less than 3% of all pituitary adenomas. These tumors typically present with mass effects such as visual disturbances or symptoms of hypopituitarism, with minimal clinical manifestations of hormone excess. Their rarity and subtle presentation often delay diagnosis.

Case Presentation

A 48-year-old male presented with progressive visual impairment and decreased libido over the course of two years. Ophthalmologic evaluation revealed bitemporal hemianopia. Magnetic resonance imaging (MRI) identified a 25 mm pituitary macroadenoma impinging on the optic chiasm. Endocrine workup revealed hypogonadotropic hypogonadism, elevated serum follicle-stimulating hormone (FSH) levels (28 IU/l), and mildly elevated prolactin due to the stalk effect.

Management

Transsphenoidal surgery was performed to relieve optic chiasm compression and achieve tumor debulking. Postoperatively, the patient exhibited partial recovery of visual function. Histopathology confirmed the diagnosis of an FSHoma. Further immunohistochemical analysis of the resected tumor confirmed FSH secretion. Due to incomplete tumor resection, the patient was referred for adjuvant radiotherapy.

Discussion

This case highlights the diagnostic challenge of FSHomas, which often present with non-specific symptoms due to their relatively silent hormonal activity. Surgery remains the cornerstone of treatment, with adjuvant radiotherapy considered in cases of incomplete resection. This report contributes to the limited literature on FSHomas and underscores the importance of considering pituitary adenomas in patients with unexplained hypogonadism and visual field defects.

Conclusion

FSHomas are rare, and early identification is crucial to prevent irreversible visual damage. This case underscores the importance of a multidisciplinary approach in managing complex pituitary adenomas.

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EP29

A case of acute onset severe headache - an important differential of SAH

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A sudden and severe headache caused by spontaneous pituitary apoplexy (PA) in a previously undiagnosed pituitary adenoma is a rare but potentially life-threatening condition that can also result in permanent vision loss. We present the case of a 70-year-old man who presented with a thunderclap headache persisting for four days, along with nausea and meningism, his vision was unaffected. A CT scan, initially done to exclude subarachnoid haemorrhage, showed a hyperdense mass in the suprasellar region. An MRI of the pituitary confirmed haemorrhage within a macroadenoma, confirming PA. Biochemically a globally low pituitary profile was seen with TSH: 0.22, T4:10.4, Random cortisol: 34, FSH:2.7, IGF-1 89.3, Testosterone:1.8, LH:1.0, Prolactin of <6, patient was also hyponatremic. The patient was given a stat dose of 100 mg IV hydrocortisone to prevent adrenal crisis. He was then started on a stress dosing of hydrocortisone (40, 20, 20), thyroxine and testosterone replacement. His hyponatremia was corrected once he was started on treatment. The above approach was taken as clinically stable patients with mild symptoms and the absence of neuro-ophthalmologic symptoms can be managed conservatively as per Society of Endocrinology guidelines. Conservative management involves starting steroids, thyroid, and hormone replacement as required. Management of unstable patients requires early surgical intervention. Criteria for surgical intervention would be reduced visual acuity, visual field defects, and deteriorating level of consciousness. Patients with PA will also require repeat assessment of pituitary and visual function at 4-6 weeks. Thereafter they will be followed up at 6-12 month intervals to titrate treatment and to monitor progression or re-occurrence on imaging. The case highlights the importance of considering PA as a differential in presentations of severe headaches, visual disturbances, and meningism. It also acts as a reminder of the guidelines for the management of pituitary apoplexy.

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EP30

An uncommon cause & presentation of cranial diabetes insipidus

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72 year old female patient admitted with constipation and vomiting. Whilst admitted to hospital, the patient was found to have significant hypernatraemia with a sodium level of 174 with reduced GCS. The patient had been under endocrine service and was being investigated for suspected cranial diabetes insipidus, having missed two doses of desmopressin due to being unwell she developed this significant hypernatraemia. She was treated with a complex fluid regime and desmopressin which gradually decreased her sodium to within normal range over 48 hours. With treatment, her GCS significantly improved and she returned back to her baseline. The patient had a background of central nervous system (CNS) vasculitis which was likely the cause of the cranial diabetes insipidus. CNS vasculitis is a rare disorder with an estimated annual incidence rate of 2.4 cases per 1 million person-years (Goads, Chauhan & Bollu, 2023). Immune system activation results in inflammation and damage to the blood vessels and brain structure, this damage and insult to the brain likely led to the pituitary gland being compromised. The patient experienced a life-threatening emergency as a result of this insult which conclusively proved that she did indeed have cranial diabetes insipidus.

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EP31

Non functioning pituitary macroadenoma mimicking as pituitary hypophysitis

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32 years old female referred with headache which developed post-partum with a CT head initially showed heterogeneous hyper dense 2.2 cm supra sellar lesion further confirmed with MRI pituitary, confirming a pituitary macroadenoma. In her first clinic review in March 2023, she was lactating with a normal menstrual cycle but complained of continuous headache and no double vision or visual field abnormality noted. Her 09am pituitary profile in March 2023 showed TSH: 1.34 Miu/L FT4: 12.3 pmol/l LH: 4.1 IU/L FSH: 8.0 IU/L Prolactin: 2408 mIU/L Oestradiol <92 pmol/l Cortisol N/A Growth hormone:0.08 ug/L IGF: 19.5 nmol/l. Cabergoline 0.5 mg once a week commenced considering functioning adenoma. Formal visual field noted to be normal. In August 2023, she reported increasing dizziness and irregular menses with intermittently blurred, double vision reported. Repeat prolactin was 17mIU/L and cortisol 146 at 0730. ACTH 9ng/l. Blood tests were consistent with hypophysitis than an adenoma and

Pituitary MDT advised commencing Prednisolone 5 mg OD. ITT in Sept '23 showed a normal peak cortisol 752 and Peak GH 8.35 ug/L - Nadir Glucose 2.1 and Prednisolone was stopped along with Cabergoline. Her prolactin rose again to a similar level in December 2023 and she was restarted back on Cabergoline 250 mg once weekly. Surveillance MRI Pituitary March 2024 showed no change in size of adenoma and prolactin was noted to be low on cabergoline. Due to lack of response to treatment, cabergoline was stopped. MDT in March 2024 favoured Pituitary macroadenoma and recommended ongoing surveillance with regular eye checks and MRI scans or proceeding to surgery to obtain a histological diagnosis. It's unusual to see a non functioning pituitary macroadenoma presenting as hypophysitis post-partum and how these two clinical conditions over played making diagnosis and management slightly complicated.

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EP32

Panhypopituitarism - an unusual cause of physiological decline

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Case
A 68-year-old gentleman presented to A&E with a 6-month history of physical and cognitive decline, on a background of learning disability, autism spectrum disorder and schizophrenia. His mobility had deteriorated from being mobile without aid, to mobilising with a stick and having multiple falls, with associated cognitive decline. His care needs had increased from 4 carer visits/day to requiring 24-hour care. He had no history of headaches, or visual disturbance.
Investigations
Admission bloods showed normal inflammatory markers, electrolytes, liver function and PSA. Free T4 was 3.6 pmol/l (normal range 10.5-24.5 pmol/l), with an inappropriately normal TSH of 2.05mU/L (NR 0.27-4.2mU/l), consistent with secondary hypothyroidism. CT Brain demonstrated a 25mm sellar lesion. Pituitary MRI was of suboptimal quality due to movement artefact and confirmed a 31x16x16mm pituitary macroadenoma, with no optic chiasm involvement. Anterior pituitary function tests demonstrated panhypopituitarism, with ACTH, growth hormone and gonadotropin deficiencies: 9am Cortisol 25nmol/l (NR 133-537nmol/l), ACTH 4ng/L (NR $<$50ng/l), FSH 1.8u/L (NR 1.5-12.4u/l), Testosterone $<$0.5nmol/l (NR 6.7-25.7nmol/l), IGF1 43ug/L (NR 38.6-230.8ug/l). Prolactin was mildly increased (560mU/l; NR 0-323 mU/l) in keeping with antipsychotic medication use and stalk effect. FBC demonstrated a mild normocytic anaemia consistent with testosterone deficiency.
Treatment
The patient was commenced on physiological hydrocortisone replacement, followed by levothyroxine and testosterone gel. Within a few weeks, his carers had noticed an improvement in his mobility and cognition and reduced falls. He is scheduled for repeat pituitary imaging in 12 months.
Conclusion and discussion points
Hypopituitarism typically presents with non-specific symptoms including fatigue and erectile dysfunction in men. The diagnosis can be particularly challenging in patients with learning disabilities. This case highlights the importance of considering a diagnosis of hypopituitarism in adults with learning disabilities presenting with physical and cognitive decline, as treatment reduces morbidity and mortality and improves physical and cognitive function.

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Reproductive Endocrinology

EP33

Serum progesterone level on embryo transfer day is linearly correlated clinical pregnancy rate in fresh IVF-ET cycle, but not in frozen ET cycle

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This is a retrospective study performed by single physician at single primary fertility center. From January 2023 to September 2024, 994 cycles of ET procedures were performed. They were 648 fresh ET cycles, 346 ET cycles. For fresh ET, Q1 contained P4 level between 5.65 to 32.9ng/dl. Their age was 39.7$\pm$4.6 years old, and 4.44$\pm$5.60 oocytes were obtained, 1.87$\pm$0.74 embryos were transferred and clinical pregnancy rate were 27.2% (44/162). Q2 contained P4 level between 33.2 to 54.5ng/dl. Their age was 38.8$\pm$4.3 years old, and 6.26$\pm$4.29 oocytes were obtained, 2.28$\pm$0.71 embryos were transferred and clinical pregnancy rate were 33.9% (55/162). Q3 contained P4 level between 54.7 to 97.0ng/dl. Their age was 37.6$\pm$4.3 years old, and 9.43$\pm$4.53 oocytes were obtained, 2.27$\pm$0.65 embryos were transferred and clinical pregnancy rate were 46.9% (77/162). Q4 contained P4 level between 97.2 to 405.0ng/dl. Their age was 36.1$\pm$4.0 years old, and 14.15$\pm$5.86 oocytes were obtained, 1.99$\pm$0.66 embryos were transferred and clinical pregnancy rate were 55.6% (90/162). Clinical pregnancy rate was statistically different between quartile groups. ($P <$ 0.01) For frozen ET, Q1 contained P4 level between 2.90 to 13.78ng/dl. Their age was 36.3$\pm$4.2 years old, 1.95$\pm$0.74 embryos were transferred and clinical pregnancy rate were 48.3% (42/87). Q2 contained P4 level between 13.79 to 18.80ng/dl. Their age was 36.6$\pm$4.2 years old, 1.95$\pm$0.73 embryos were transferred and clinical pregnancy rate were 50.6% (44/87). Q3 contained P4 level between 18.81 to 26.10ng/dl. Their age was 36.3$\pm$3.8 years old, 1.82$\pm$0.75 embryos were transferred and clinical pregnancy rate were 43.7% (38/87). Q4 contained P4 level between 26.11 to 113.0ng/dl. Their age was 35.8$\pm$4.2 years old, 1.75$\pm$0.66 embryos were transferred and clinical pregnancy rate were 52.9% (46/87). Clinical pregnancy rate was not statistically different. ($P >$ 0.01)

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EP34

A rare cause of primary amenorrhoea: leydig cell hypoplasia - inactivating homozygous mutation in the luteinizing hormone chorionic gonadotropic receptor (LHCGR) in an XY genotype individual

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A 26-year-old female of Asian origin presented with primary amenorrhoea. She was born at full term. Her milestones were normal. She had history of gonadectomy at age 14. She had not started her periods but had no symptoms to suggest hyperandrogenism. She had history of consanguinity as her parents are cousins. She had five sisters of which only two had started their periods. On examination, she was normotensive. She had complete absence of breast with absent axillary and pubic hair. She had female external genitalia with a blind vaginal pouch. Her baseline bloods were suggestive of hypergonadotropic hypogonadism. She had a normal short synacthen test, and a 24-hour urine steroid profile to rule out congenital adrenal hyperplasia. An MRI of the pelvis which confirmed the blind vagina about 3 cm in length. There was no uterine tissue or ovarian or any other inguinal mases. Her Karyotype analysis confirmed the presence of an XY genotype consistent with a male sex chromosome. Further genome sequencing confirmed the presence of an inactivating homozygous LHCGR variant consistent with the diagnosis of Leydig cell hypoplasia. In humans luteinizing hormone/ chorionic gonadotropin receptor (LHCGR) plays a pivotal role in sexual differentiation and maturation in both males and females. Inactivating mutations of these receptor may present with various phenotypic spectrum depending on the sex and the degree of receptor defect. Amenorrhea is a common presentation to an endocrinologist. A structured approach can help reveal the underlying diagnosis. Patients with disorders of sexual development should be managed as a multidisciplinary team with ongoing psychological support.

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Thyroid

EP35

Pituitary hyperplasia secondary to uncontrolled primary hyperthyroidism: a case report

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This case reports a 38-year-old woman with poorly controlled hypothyroidism who developed pituitary hyperplasia as a secondary complication. She initially presented with intermittent headaches, and MRI imaging revealed an enlarged pituitary gland with suprasellar extension compressing the optic chiasm. Her medical history included Hashimoto's thyroiditis followed by a total thyroidectomy. Despite this, her thyroid function remained highly variable, with thyroid-stimulating hormone (TSH) levels often exceeding 100 mIU/l, indicating inadequate control of her hypothyroidism. Upon further evaluation, a multidisciplinary team decided to increase the patient's levothyroxine dose and provided counselling on proper medication administration to optimize absorption and adherence. Subsequent MRI imaging, following improved thyroid function, demonstrated a reduction in the size of the pituitary swelling, correlating with lower TSH levels. Pituitary hyperplasia, a non-neoplastic enlargement of pituitary

cells, can occur in patients with primary hypothyroidism due to insufficient negative feedback from thyroid hormones. This results in increased secretion of thyrotropin-releasing hormone (TRH), which stimulates pituitary growth. Unlike pituitary adenomas, which are tumours potentially requiring surgical intervention, pituitary hyperplasia due to hypothyroidism is generally reversible with optimized thyroid hormone replacement therapy. Imaging modalities such as CT and MRI reveal an enlarged pituitary gland. Differentiating between a pituitary adenoma and hyperplasia is essential and requires a multidisciplinary team discussion. Prior to contemplating surgical intervention, it is imperative to thoroughly assess both radiographic imaging findings and biochemical test results. For individuals with hypothyroidism in whom pituitary enlargement is incidentally detected during unrelated brain imaging, the recommended approach involves initiating thyroid hormone replacement therapy, closely monitoring the condition, and periodically conducting follow-up imaging studies. Patient adherence to thyroid hormone therapy is crucial as non-compliance can lead to persistent or recurrent elevated TSH levels, potentially causing the hyperplasia to return or worsen and prompting consideration of unnecessary surgical interventions if misinterpreted as a tumour.

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EP36

Challenging management of graves' disease: a case of antithyroid medication resistance leading to thyroidectomy

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Grave's disease is one of the autoimmune diseases with autoantibodies stimulating the TSH receptors and causing thyroid hyperplasia and leading to hyperthyroidism. Hyperthyroidism can lead several complications that can be fatal like arrhythmias, heart failure and pulmonary hypertension. Grave's disease can also be associated with orbitopathy. Management of Grave's disease include medical treatment with antithyroid medications, radioactive iodine that can reduce the thyroid tissue or surgical resection. Antithyroid resistant Grave's disease is a recognized condition that might need surgical approach with total thyroidectomy. There are few case reports about this condition. We, hereby, are reporting a case of carbimazole resistant Grave's disease that required total thyroidectomy.

Case report

This 26 year old lady with background of Systemic Lupus Erythematosus, Rheumatoid arthritis, Asthma and Personality disorder was diagnosed with Grave's disease in October 2020 after having symptoms of extreme tiredness, unintentional weight, heat intolerance and loose stools. Her TSH was 0.01 mU/L and FT4 was 50.7 pmol/l and FT3 was 21.60 pmol/l. Thyrotropin receptor antibody was 18.34 U/L and Thyroid peroxidase antibody was >600 IU/ml. She has family history of thyrotoxicosis. CT neck showed diffusely enlarged thyroid gland with no retro-sternal extension. She was started on Carbimazole which was up titrated to 40 mg twice daily and Propranolol MR 80 mg BD but with no effect clinically or biochemically. Propylthiouracil was tried but patient didn't tolerate it. So, she was referred to ENT and underwent a total thyroidectomy in June 2023 and histology showed diffuse benign hyperplasia and was started on Levothyroxine 150 mg per day.

Conclusion

It can be challenging to recognize and treat carbimazole resistant Grave's disease. Non compliance and malabsorption should be excluded. Once recognized, patient should be referred for definitive treatment to avoid life threatening complications.

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EP37

A rare case of hypothyroidism-induced rhabdomyolysis

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We present a case of a 65-year-old man who arrived at the emergency department after falling and lying for a long time at home. Relevant past medical history includes asthma, previous myocardial infarction, rheumatoid arthritis, and hypertension. Biochemically, he had a creatine kinase (CK) of 7461, normal renal function, and deranged thyroid function with a thyroid stimulating hormone (TSH) of 95.9 and thyroxine (T4) of 9. Subsequently, the patient was treated for a long lie causing high CK with aggressive intravenous crystalloids. Patient was then referred to rheumatology for possible polymyositis given persistently raised CK despite fluids and absence of dermatological lesions. Myositis screen requested, and it was negative. However, an MRI of the hip and femur revealed possible diffuse myositis. We requested an EMG and excluded polymyositis. Given the absence of polymyositis and deranged thyroid function tests, another possible diagnosis of thyroid myopathy emerged. Further immunological tests revealed positive thyroid peroxidase and negative rheumatoid factor. The patient's CK levels continue to deteriorate, reaching a level above 10,000. After consulting with the endocrinology team, they started the patient on a low dose of Levothyroxine. After a week of levothyroxine, the patient's CK levels improved dramatically to 4000 from 10,000. The dose of levothyroxine was then doubled on discharge, and the CK levels were subsequently normalised. Rhabdomyolysis brought on by hypothyroidism is a recognised but rare condition. Very few cases of hypothyroidism causing rhabdomyolysis have been reported in the literature. The pathophysiology of rhabdomyolysis in hypothyroidism remains unclear, and various hypotheses have been postulated. Screening for hypothyroidism in patients with elevated muscle enzymes should be considered, since an early diagnosis and prompt treatment of hypothyroidism are essential to prevent rhabdomyolysis and its consequences.

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EP38

Hypokalaemic periodic paralysis and graves' disease: triggered by steroids – a rare case report

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Background

Hypokalemic thyrotoxic periodic paralysis (HTPP) is a rare but potentially life-threatening complication of hyperthyroidism, characterized by episodic muscle weakness or paralysis. It is primarily associated with Asian populations, although cases have been reported worldwide. The exact pathophysiology of HTPP remains unclear, but it is believed to involve a combination of factors, including hyperthyroidism, genetic predisposition and various triggers such as stress, infection, medications including steroids.

Case Presentation

A 51-year-old male Asian presented to the emergency department with acute onset of generalized weakness affecting both upper and lower limbs. He mentioned receiving an intra-articular corticosteroid injection several hours before the onset of weakness for knee pain in GP Surgery. Physical examination revealed global weakness with reduced power in all limbs. Deep tendon reflexes were diminished. Laboratory tests showed Potassium levels of 1.5mmol/L (3.5-5.3), Thyroid functions TSH <0.01mIU (0.35-4.94), T4 24 pmol/l (9-19.1), T3 22.4 pmol/l (2.4-6), TSH receptor antibody came back positive as 5.2IU/l(0-2.9). The patient was managed with Intravenous potassium, oral Carbimazole 40 mg and propranolol. His weakness was subsequently improved following potassium replacement. A NM thyroid scan revealed diffuse increased uptake with no nodules which was keeping with graves' disease. On follow up, thyroid functions were improved as T4 13.5, T3 5.5 hence, Carbimazole was reduced to 20 mg. A 6 month follow up revealed complete normalization of thyroid function as TSH 0.36, T4 11.

Conclusion

This case highlights the importance of recognizing HTPP as a potential complication of hyperthyroidism, especially in patients with risk factors such as Asian ethnicity and recent exposure to triggers. Early diagnosis and prompt treatment are essential for preventing severe complications such as arrythmias and ensuring a favourable outcome. Further research is needed to elucidate the precise mechanisms underlying steroid-induced HTPP in Graves' disease.

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EP39

Thyrotoxic hypokalaemia periodic paralysis

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Background

Thyrotoxic hypokalemic periodic paralysis (THPP) is a rare complication of hyperthyroidism, primarily reported in Asian populations, affecting about 2% of hyperthyroid individuals. In non-Asian populations, its incidence is considerably lower, estimated at 0.1% to 0.2%. THPP typically presents with muscle weakness and hypokalemia, predominantly in males aged 20 to 40.

Case Presentation
We describe a 38-year-old male patient of African descent who presented to the Accident and Emergency department with progressive weakness of the lower limbs, which subsequently affected his upper limbs. Neurological examination revealed diminished reflexes in the lower limbs, while reflexes in the upper limbs were normal, with no other neurological deficits observed.
Investigations
Laboratory tests indicated a critically low serum potassium level of 2.2 mmol/l, signifying severe hypokalaemia. Thyroid function tests showed undetectable thyroid-stimulating hormone (TSH), elevated free thyroxine (T4) at 30 pmol/l, and undetectable high free triiodothyronine (T3). Diffuse thyroid enlargement was noted, prompting further evaluation for autoimmune thyroiditis, Grave's thyrotoxicosis with thyroid antibody testing pending.
Discussion
This case illustrates the atypical presentation of THPP in a non-Asian patient and emphasizes the importance of timely diagnosis. The combination of acute muscle weakness and specific laboratory findings should prompt clinicians to consider THPP in hyperthyroid patients, particularly in the context of acute paralysis. This is a condition which can cause significant morbidity with muscular paralysis and respiratory arrest secondary to respiratory muscular paralysis. Our patient did not have any reparatory issue on admission. He was treated with antithyroid medications, betablockers and Potassium.
Conclusion
The rarity of THPP in non-Asian populations highlights the need for increased awareness among healthcare providers. Prompt recognition and management of this condition can improve patient outcomes and prevent complications related to hypokalemia and thyroid dysfunction. Further research is needed to enhance understanding and treatment strategies for THPP across diverse populations.

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EP40

A case of hypothyroidism following paclitaxel and carboplatin chemotherapy

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Hypothyroidism has been a common side effect of newer antineoplastic agents used for non-thyroid cancer treatment including tyrosine kinase inhibitors, bexarotene, Ipilimumab etc. However, we have not had any case reported with hypothyroidism following the treatment with Paclitaxel and Carboplatin in patient with non-thyroid cancer treatment. There has been the earlier onset and higher incidence of hypothyroidism observed in concomitant therapy with paclitaxel and radiation as compared with radiation alone in treatment of locally advanced head and neck cancer. A 64-year-old lady with known metastatic breast cancer to bone, omentum, right pleural and right sided pleural effusion with suspected malignant cells was started on the chemotherapy regime of Paclitaxel followed by Carboplatin: Paclitaxel cycles initiated in April 2024 followed by Carboplatin in August 2024. She had normal thyroid function test: TSH 3.10 mU/l, free T4 14.3 pmol/l in November 2023 prior to the start of the chemotherapy. She presented to the emergency department with generally unwell, loose stool, slurred speech, and generalised weakness in October 2024. She was found to have bradycardic at 42 beats per minute and marked hypothyroidism: TSH 37.85 mU/L and free T4 $<$5.4 pmol/l. She was found to have small right cerebellar enhancing lesion on CT head during admission, in addition to her progressive disease on recent CT scan in June 2024. Her heart rate appeared to vary between 35 to 71 and stable blood pressure prior to the start of liothyronine 10 micrograms twice daily. She was subsequently put on palliative with her progressive metastasis disease, extreme frailty a few days following admission and had passed away peacefully. This case highlights that hypothyroidism could be the potential side effect of Paclitaxel and Carboplatin chemotherapy and would be beneficial for the patient to have monitored the thyroid function test during treatment.

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EP41

Hypothyroidism during pregnancy and the challenges associated with non-compliance: a case report

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Background
Hypothyroidism, if overt and untreated during pregnancy, is linked to both adverse maternal outcomes, including increased risk of miscarriage, pre-eclampsia and post-partum haemorrhage, but also to poor neonatal outcomes, including respiratory distress, low birth weight and impaired cognitive development.
Case presentation
32-year-old diagnosed with hypothyroidism in 2007, first seen by endocrinology after her 5th pregnancy where TSH remained $>$130mu/l. The patient has experienced complications attributed to hypothyroidism, including pericardial effusion, renal impairment, constipation and gestational diabetes. Her eldest children require additional educational support, and her twins (born 37+5) were assessed to have developmental delay. Furthermore, one of her twins who was borderline low birth weight required NICU admission with respiratory distress and neonatal jaundice. There are complex social circumstances compounding this case, with safeguarding concerns regarding possible child neglect. She has represented during her eighth pregnancy after failed sterilisation, despite TSH 89mu/l, T4 7.0 pmol/l and T3 $<$ 1.5 pmol/l. She was only taking 100 mg of expired levothyroxine once a week. Complications to her unborn child's health were discussed, and she had capacity. Her levothyroxine dose was increased to 150mcg, with 2 months supply given directly to her. However, TSH remained raised and she was offered further support to aid compliance. A subsequent echocardiogram reported left ventricular global systolic impairment, with cardiology additionally concerned about right ventricle non-compaction due marked trabeculation. After this review, compliance improved and at 32 weeks her TSH was 6.34mu/l, T4 15.6 pmol/l and T3 3.4 pmol/l.
Discussion and learning points
This case highlights the relationship between maternal and foetal health and emphasises the importance of medication adherence and control of hypothyroidism during pregnancy. Unfortunately, this case encompasses complex medical and ethical challenges that the endocrinology team have managed with input from multiple specialties, and given the patient's grand multiparity, the concerns extend to the impact on her unborn child's health.

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EP42

Raised thyroid free hormones with unsuppressed stimulating hormone: a case report of resistance to thyroid hormones

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A 30-year old young man attended A&E with palpitation. He had history of ADHD with learning difficulty. Provisional diagnosis was made as hyperthyroidism. He received treatment with anti-thyroid medication and beta-blocker. On follow up, his free hormones (FT4 & FT3) were nearly unchanged with slowly rising TSH. He remained asymptomatic following the first episode of palpitation. Following cessation of treatment with anti-thyroid medication, his TSH returned to normal with high free thyroxine. Patient was subsequently discharged with advice. This case highlights the importance of early suspicion in relatively asymptomatic patient, early genetic test in young patient with relevant history and biochemical abnormality.

TFT	12/06/2021	31/08/21
TSH (m IU/l)	1.07	2.08
FT4 (pmol/l)	43	42
FT3 (pmol/l)	9.3	9.5
TRab *(IU/l)		$<$1.10

*Thyroid receptor antibody

TFT	07/09/22	22/11/22	13/12/22	30/12/22	31/05/23 (After stopping Carbimazole)
TSH (m IU/l)	9.72	12.33	16.95	31.20	3.54
FT4 (pmol/l)	33	31	26	23	41
FT3 (pmol/l)	9.5	9.5	8.0	8.9	12.9

Genetic test warranted, which confirmed THRβ-related thyroid hormone resistance.

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Late Breaking

EP43

A case study of a 73 old with indeterminate stable adrenal lesion progressing to metastatic adrenal carcinoma

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74 years old female admitted to orthopaedic ward following hip pain. She was unable to weight bear and hence x ray and subsequently a CT scan was done too which showed large destructive lucent lesion in left femoral neck with pathological fracture. There was a suggestion of her having malignancy, so a CT TAP was arranged which showed that she has got large ovoid mass in the upper abdomen which most likely is malignancy and had multiple metastatic bony deposits. On reviewing her previous notes, she was under endocrinology. At that time there was no adrenal MDT in the hospital. A scan was done in 2017 which showed that she had large heterogenous lesion arising from the left adrenal gland. This was in keeping with adenoma. Two ODSTs were done and the results were 54 and 62 respectively. The scan was rediscussed and there was a small indeterminate lesion in the inferior aspect of the gland. In 2018 the scan remained unchanged. In 2021 another scan was, and the presumed adenoma remained unchanged. The hormone profile in 2023 showed 24 hr UFC to be 338 and low dose dexamethasone suppression test was arranged. On this occasion she had operation done to excise the tumour and total hip replacement. The histology showed metastatic adrenocortical carcinoma. Retrospectively a lesion had been present since 2017 but it was very slow growing. This case highlights the importance of close working with MDT colleagues, review suspicious lesions in the MDT and be aware of dual pathologies as in this case we can see that she had an adenoma in the super aspect of left adrenal gland and an indeterminant lesion in the inferior aspect.

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EP44

Pheochromocytoma: beyond a life-threatening emergency

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Introduction
Pheochromocytoma is a neuroendocrine tumor that develops in the chromaffin cells of the adrenal medulla. It is a potentially serious pathology that can be responsible for sudden death and also alter quality of life, particularly when it is part of a genetic syndrome. We describe the case of a patient with neurofibromatosis type 1 with severe visual acuity impairment secondary to optic nerve glioma.
Observation
This 20-year-old patient was diagnosed with pheochromocytoma as part of the investigation of secondary arterial hypertension. A meticulous examination revealed several lentiginous skin lesions, several neurofibromas and cafés au lait spots, enabling us to classify the pheochromocytoma as part of neurofibromatosis type 1. In addition, the patient presented with severely impaired visual acuity, with papilledema at the fundus, which prompted a chorioorbital MRI in favor of an optic nerve glioma, one of the manifestations of neurofibromatosis. The patient underwent both types of treatment, with marked clinical and biological improvement.
Discussion
Pheochromocytoma is a serious pathology that can be life-threatening and functionally compromising. Once this pathology has been diagnosed, management must be based both on hemodynamic emergencies and on genetic studies, in order to manage certain disorders that are part of this genetic syndrome at an earlier stage.

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EP45

Prevalence and risk factors for lithiasis in primary hyperparathyroidism

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Introduction
Primary hyperparathyroidism is a frequent pathology due to inappropriate PTH secretion. Its seriousness lies in the occurrence of multiple cardiovascular, bone and renal complications responsible for recurrent urinary lithiasis.
Patients and methods
In order to better assess the prevalence and to understand the factors favouring the occurrence of renal calculi, 60 patients were evaluated in a prospective study conducted at the Rabat military hospital in the endocrinology department over a 7-month period from January 2024 to July 2024. Patients with a primary hyperparathyroidism profile were included in the study. Patients with secondary hyperparathyroidism, tertiary hyperparathyroidism or marx syndrome, as well as patients with stones from another cause: hyperuricemia, medical
Results
The prevalence of subjects with kidney stones was around 30%. The mean age was 51.9 ± 14.3 years, and the gender ratio (women/men) was 5.4. Compared with those without renal calcifications, the group with renal calcifications had: - low creatinine levels (67 ± 25.1 vs. 74.6 ± 17.5 µmol/l, $P = 0.03$). -In addition, their fractional calcium excretion (calcium/creatinine excretion ratio) was elevated (0.91 ± 0.28 vs. 0.74 ± 0.40 µmol/, $P = 0.02$). -Calcemia was higher ($P = 0.03$). -Natriuresis: higher above 8 mmol/ kg/24h ($P = 0.02$) The other variables measured were similar in both groups. No biochemical was predictive of renal calcifications in multiple regression analysis.
Conclusion
This study confirms that the occurrence of calcifications in primary hyperparathyroidism is associated associated with lower creatinemia and higher fractional calcium excretion, as well as elevated as well as elevated calcemia.

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EP46

A case of severe agranulocytosis induced by carbimazole in a patient with graves' disease requiring thyroidectomy

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74 year old lady with a background of rheumatoid arthritis and Felty's syndrome was diagnosed as having Grave's Thyrotoxicosis few months back in Australia. She was commenced on Carbimazole. She came back to UK and had repeat bloods done with GP which showed neutropenia. The levels of neutrophils were 0.01 and WCC was 0.4. She was otherwise asymptomatic, her weight had been stable and there were no concerns regarding any infection. Rest of her infectious screen including blood cultures, Respiratory screening and COVID were all negative. The cause of the neutropenia was Carbimazole. She was also on Hydroxychloroquine due to her Rheumatoid Arthritis which was stopped along with Carbimazole. After stopping her Carbimaozle, her T4 started rising and it was 45 at one point. In order to maintain euthyroidism she was started on Lugol's iodine, potassium iodide, propranolol and colestyramine. These medications were not initiated all at once but were introduced gradually over time. She also developed AF due to her hyperthyroidism and was needing anticoagulation. She was also given filgrastim to help with the levels of neutrophils. Her thyroid functions improved, and she was transferred to ENT unit for total thyroidectomy. She had successful thyroidectomy done and was started on Levothyroxine. Previous studies have demonstrated that risk of developing agranulocytosis is higher in the first two to three months and patients aged >40. This was the classical case where she was in her 70s and recently diagnosed as having Grave's disease. It is important to recognize the medications as a cause of neutropenia and also to look for any effects of neutropenia experienced such as infections.

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EP47

From hashimoto's thyroiditis to graves' disease: the transformer

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Transformation of Hashimoto's thyroiditis to Graves' disease is rare and can occur at any point during autoimmune hypothyroidism. We present a 50-year-old lady, who presented with palpitations and fatigue. Initial thyroid function tests showed hyperthyroidism with elevated thyroid peroxidase (TPO) (146.48 IU/ml, reference range 0 to 5 IU/ml) but negative TSH receptor antibodies (TRAb).

Thyroid uptake scan revealed features consistent with Hashitoxicosis, and ultrasound (thyroid) demonstrated diffusely heterogeneous echotexture and features suggestive of thyroiditis. She was a non-smoker with family history of lupus. She was started on low-dose carbimazole and beta-blocker, with regular monitoring. On follow-up, TPO antibodies were elevated (654 IU/mL) and, interestingly, TSH receptor antibodies became raised (7.8 IU/L, reference range <0.4 units/ L) after 9 months. Pathophysiology of this transformation remains unclear. However, potential mechanism could be conversion or change in quantity from blocking to stimulating subtypes of TRAb. Literature review identified higher prevalence of smoking among individuals transitioning from Hashimoto thyroiditis to Graves' disease and these switchers significantly showed higher prevalence of personal and familial history of non-thyroidal autoimmune disorders. However, our patient was a non-smoker but had family history of lupus. This case highlights Hashimoto's thyroiditis transforming into Graves' disease, in which TSH receptor antibody turns from negative to positive during its interesting clinical course.

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EP48

An interesting case of amiodarone-induced thyroiditis

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Amiodarone is an effective anti-arrhythmic drug but is associated with significant side effects, including thyroid dysfunction due to its high iodine content and direct toxic effects on the thyroid. We present a 74-year-old gentleman with asymptomatic hyperthyroidism (TSH < 0.01 mU/L, free T3 6.1 pmol/L, free T4 30.2 pmol/L) while on long-term amiodarone therapy. His medical history included ventricular tachycardia (VT), atrial fibrillation, implanted cardioverter defibrillator (ICD), myocardial infarction, and coronary artery bypass grafting (CABG). He had been on amiodarone for five years, with unsuccessful attempts at discontinuation due to arrhythmia recurrence necessitating its reintroduction. Initially managed with carbimazole for suspected amiodarone-induced thyroiditis (AIT), further investigations revealed negative TSH receptor antibody and thyroid peroxidase (TPO) antibodies (0.63 IU/mL, reference range 0–5 IU/mL). ESR was moderately raised while awaiting interleukin-6 results. Inflammatory thyroiditis with normal vascularity was identified on thyroid ultrasound. Thyroid uptake scan was deemed unreliable due to ongoing amiodarone therapy, which was continued per cardiology recommendations to mitigate the risk of recurrent VT. On clinical suspicion, prednisolone 40 mg/day was initiated, leading to very good initial response, further supporting the diagnosis of amiodarone-induced thyroiditis (AIT) type 2. However, patient admitted discontinuing prednisolone after taking only 20 mg/day for two weeks. His thyroid function worsened after stopping the steroids. Prednisolone was subsequently restarted with a plan for close monitoring of thyroid function tests. This case highlights the diagnostic and management challenges of amiodarone-induced thyroiditis in patients requiring ongoing amiodarone therapy due to high risk of VT recurrence.

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