# Endocrine Abstracts

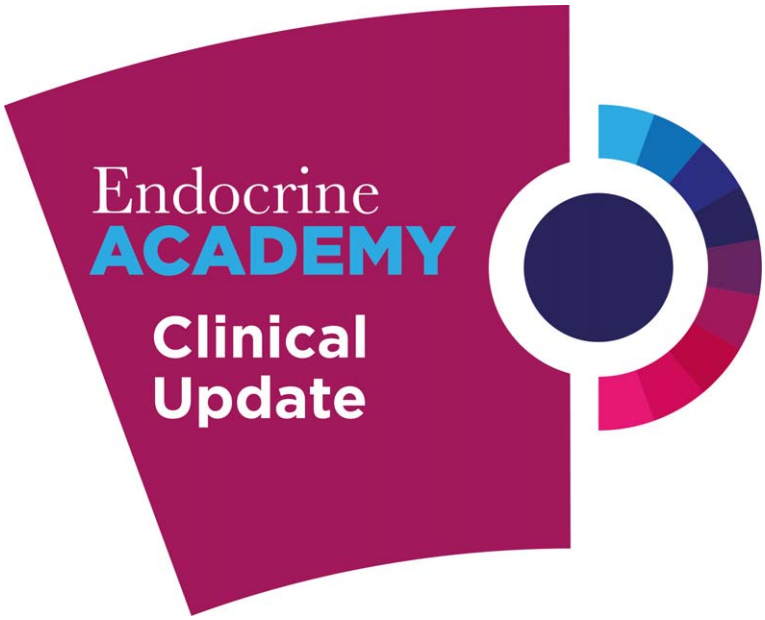
**November 2025** Volume 113
ISSN 1479-6848 (online)

## Society for Endocrinology Clinical Update 2025

Society for Endocrinology

published by bioscientifica

Online version available at
**www.endocrine-abstracts.org**




# Society for Endocrinology Clinical Update 2025

# CONTENTS

***Society for Endocrinology Clinical Update 2025***

# Workshop A: Disorders of the hypothalamus and pituitary

## WA1.1

**Adrenal insufficiency assessment after transsphenoidal surgery: caution with SST and the recommended role of ITT – a case report**

Idowu Olaogun
Bristol Royal Infirmary, Bristol, United Kingdom

Background
The insulin tolerance test (ITT) is widely regarded as the gold standard for assessing central adrenal insufficiency in patients undergoing pituitary surgery. However, due to its higher cost, time burden, and potential risks such as hypoglycaemia, the short Synacthen test (SST) is often used instead. While convenient, SST may have limitations in the peri-operative period, particularly early after surgery when the hypothalamic–pituitary–adrenal (HPA) axis may be suppressed. We present a case illustrating the risk of relying solely on SST, leading to missed adrenal insufficiency.
Case Presentation
A 23-year-old woman presented with headaches and secondary amenorrhoea. She had no significant past medical history, had never used exogenous steroids, and was not on any regular medications. Initial pituitary MRI demonstrated a 2.7 cm macroadenoma without optic chiasmal compression or cavernous sinus invasion; a repeat MRI at six months showed interval growth to 3.1 cm. Visual fields were normal to confrontation, and she exhibited no features of Cushing's syndrome or acromegaly. Baseline biochemistry showed hypogonadotropic hypogonadism (FSH 2.1 IU/l, LH 1.6 IU/l, oestradiol 54 pmol/l), normal prolactin, IGF-1 26 nmol/l, TSH 2.3 mU/l, FT4 11 pmol/l, and 9 am cortisol 465 nmol/l. She underwent elective transsphenoidal surgery. On postoperative day two, cortisol was borderline at 187 nmol/l; hydrocortisone replacement was commenced with plans for reassessment. At six weeks, SST showed an apparently adequate cortisol response (peak 490 nmol/l at 60 minutes), and hydrocortisone was discontinued. Subsequently, she developed progressive symptoms of adrenal insufficiency including dizziness, nausea, vomiting, and unintentional weight loss. Repeat SST again showed a "normal" peak cortisol, creating diagnostic uncertainty. A therapeutic trial of hydrocortisone led to marked symptomatic improvement. Although ITT was not performed in this case, it remains the reference standard for evaluating central adrenal function and would likely have clarified the diagnosis earlier.
Discussion
This case highlights that SST performed early after pituitary surgery may yield falsely reassuring results. The adrenal glands can respond adequately to Synacthen even when ACTH secretion is impaired, leading to under-recognition of central adrenal insufficiency. Persistent symptoms should prompt reassessment and, in equivocal cases, dynamic testing with ITT where feasible.
Conclusion
SST results should be interpreted cautiously in the early postoperative period after TSS. Clinical judgement remains essential, and ITT continues to have an important role when there is diagnostic uncertainty. Early recognition and treatment of adrenal insufficiency can significantly reduce morbidity.

DOI: 10.1530/endoabs.113.WA1.1

## WA1.2

**Acromegaly in the diabetes clinic**

Emma Lydon[1] & Craig Thurtell[2]
[1]NHS Education for Scotland, Glasgow, United Kingdom; [2]NHS Lanarkshire, Airdrie, United Kingdom

55 year old male with 5 years of type 2 diabetes mellitus referred to clinic for consideration of Glucagon-like peptide-1 (GLP-1) agonist therapy. BMI of 45 kg/m$^2$, asthma, depression, hypertension and obstructive sleep apnoea (intolerant of CPAP). Noted to have large boggy feeling hands and feet, mild acanthosis nigricans and a deep voice. On enquiry, shoe size had increased from 8 to 12, wedding ring did not fit and weight gain and jaw protrusion had been noticed. Insulin-like growth factor 1 (IGF-1) was raised at 984 µg/l (49-191), Growth Hormone (GH) did not suppress with oral glucose tolerance testing: 3.9µg/l at 0 h and 2.8 µg/l at 2 h. Pituitary hormone screen showed no suppression. MRI of pituitary with contrast showed an expanded pituitary fossa with the normal pituitary on the right and a 15 x18 mm less enhancing lesion to the left, lying close to the optic nerve and slight extension towards the left cavernous sinus, in keeping with a pituitary macroadenoma, functioning as a GH secreting Pituitary Neuroendocrine Tumour (PitNET). Complications screen showed no formal visual field defect, echocardiogram showed no structural abnormalities, colonoscopy revealed a likely benign polyp (with a plan for biopsy) and there were no palpable thyroid nodules. Ongoing optimisation of diabetes management (GLP-1 agonist has improved HbA1 c to 47). The patient was discussed at pituitary MDT and seen by neurosurgeons, and has presently been waiting 13 months for operative management. IGF-1 was initially suppressed to 450µg/l on the somatostatin analogue Lanreotide 120 mg monthly. After several months the efficacy has reduced; IGF-1 was not suppressed at 950µg/l. He has now developed the complication of cholecystitis, so Lanreotide has been suspended and expedition of his surgery has been requested from the neurosurgeons.

DOI: 10.1530/endoabs.113.WA1.2

## WA1.3

**Missed diagnosis of mild autonomous cortisol secretion (MACS) in a patient with pituitary macroadenoma presenting as steroid withdrawal syndrome following transsphenoidal surgery**

Idowu Olaogun & Rami Fikri
Bristol Royal Infirmary, Bristol, United Kingdom

Background
Mild autonomous cortisol secretion (MACS) is most frequently associated with adrenal incidentalomas and is seldom considered in the context of pituitary incidentalomas. Patients with overt Cushing's syndrome are well recognised to develop steroid withdrawal symptoms following curative surgery; however, the timing and recognition of such symptoms in MACS are less well established. We report a case of a missed MACS diagnosis in a pituitary incidentaloma presenting with delayed onset steroid withdrawal symptoms after transsphenoidal surgery (TSS).
Case Presentation
A 34-year-old woman was referred to endocrinology with irregular menses, headaches, and right-sided visual field impairment. She reported recent weight gain but lacked overt cushingoid or acromegalic features. Imaging demonstrated a pituitary macroadenoma compressing the right optic chiasm. Baseline investigations revealed hypogonadotropic hypogonadism (FSH 1.1 IU/l, LH 1 IU/l, oestradiol 97 pmol/l), mild hyperprolactinaemia (650 mIU/l), and secondary hypothyroidism (TSH 1.3 mU/l, FT4 7.3 pmol/l). Morning cortisol was 588 nmol/l; ACTH was insufficient for interpretation, and an overnight dexamethasone suppression test (ODST) was not performed. IGF-1 was normal. She commenced levothyroxine and underwent TSS two weeks later. Initial postoperative recovery was excellent with rapid improvement in energy and functional status. However, four weeks postoperatively she developed progressive fatigue, dizziness, poor appetite, and unintentional weight loss. Postoperative short Synacthen testing (SST) was normal on two occasions, although SST is recognised to have limited specificity in this context. Due to worsening symptoms, a trial of hydrocortisone was initiated with marked clinical improvement. Unexpectedly, histopathology confirmed a corticotroph adenoma. Subsequent ACTH and 24-hour urinary free cortisol were normal.
Discussion
This case illustrates that MACS can occur in pituitary incidentalomas and may be missed if routine preoperative screening for cortisol excess is not undertaken. Importantly, steroid withdrawal symptoms can present later than classically expected and may occur despite apparently normal postoperative dynamic adrenal testing. Histopathology remains essential when biochemical results are inconclusive.
Conclusion
Cortisol excess should be thoroughly excluded in all patients with pituitary masses, even in the absence of classic cushingoid features. Preoperative screening with ODST or equivalent is critical for surgical planning, patient counselling, and postoperative care. Early recognition of subtle cortisol excess may prevent significant morbidity related to delayed steroid withdrawal syndromes.

DOI: 10.1530/endoabs.113.WA1.3

## WA1.4

**Post-operative management of salt & water disturbances: a triple-phase response to transsphenoidal surgery for craniopharyngioma**

Wut Yee Win & Andrew Powlson
Cambridge University Hospitals NHS Foundation Trust, Cambridge, United Kingdom

Introduction
Pituitary tumours, and perhaps particularly suprasellar tumours or where surgery threatens the infundibulum, require vigilant peri-operative monitoring for salt and water complications such as arginine vasopressin deficiency (AVP-D), and syndrome of inappropriate antidiuretic hormone secretion (SIADH). In this case, an 18-year-old male with a craniopharyngioma demonstrates a potentially challenging example, with a distinct 'triple-phase' AVP response to transsphenoidal surgery (TSS).

Case Summary
A 15-year-old male presented with partial hypopituitarism. MRI demonstrated a suspected craniopharyngioma (cystic lesion with calcification and heterogeneous enhancement). Growth hormone and testosterone were replaced and, in the absence of compressive symptoms (vision was intact), conservative management (surveillance) was favoured. In view of subsequent growth of the lesion (8 x9 mm to 23 x13 mm over a 2-year interval), he underwent transsphenoidal cyst decompression with partial tumour resection at age 18.
Post-operative Course and Timeline
**Day 1:**
Postoperatively, he developed significant polyuria(>400 mL/hour) with thirst and polydipsia (24-hour intake 5194 mL; urine output 6380 mL/24 h). With this negative balance, serum sodium transiently rose to152 mmol/l (reference133–146 mmol/l). With urine osmolality 89 mOsm/kg and serum osmolality 306 mOsmol/kg, post-operative AVP-D was diagnosed and dDAVP (0.5 mg SC) was given. Continued oral desmopressin and drinking to thirst (his thirst was intact) led to normalisation of balance and biochemistry.
**Day 6:**
Serum sodium dropped to a nadir of 126 mmol/l, with elevated urine sodium, no thirst, little urine output and modest reported positive balance (albeit with suboptimal records initially). DDAVP was stopped and it was then with fluid intake restriction (to 750 mL/24 hours) for presumed SIADH. Serum sodium normalised by day 8, with appropriate off-loading of excess water.
**Day 11:**
After a period of stability, polyuria recurred (fluid intake 2050 mL/24 h; urine output 5123 mL/24 h) with significant thirst and serum sodium rising within the reference range. Recurrence of AVP-D was diagnosed, and he was started on oral dDAVP 100 mg twice daily. With this, his salt and water balance remains controlled. He has also required ongoing glucocorticoid and thyroxine replacement.
Discussion
This case illustrates the 'triple-phase' AVP response following TSS in pituitary tumours.
1. **Transient AVP-D phase:** Polyuria, thirst and hypernatremia, requiring dDAVP.
1. **SIADH phase:** Hyponatremia due to inappropriate ADH secretion, managed with fluid restriction and stopping dDAVP.
2. **Permanent AVP-D:** Ongoing dDAVP requirement.

Conclusion
This case underscores the potentially complex salt and water disturbances after peri-operative surgery. Close monitoring of fluid balance and serum sodium, with appropriate response is crucial. Management is aided by awareness of the potential for such a triphasic response.

DOI: 10.1530/endoabs.113.WA1.4

## WA2.1

### When erectile dysfunction hides a deeper cause: pituitary hypophysitis in a young male

Maria Omer & Scott Williams
Countess of Chester Hospital, Chester, United Kingdom

A 35-year-old male was evaluated for a five-year history of erectile dysfunction (ED) and reduced libido. His past medical history included asthma, post-traumatic stress disorder, tinnitus, vitamin D deficiency and mumps infection during adolescence, he was uncertain whether this was complicated by orchitis. Current medications included Fostair inhaler and intermittent salbutamol. He presented with erectile dysfunction and complete absence of morning erections, showing transient improvement with a short course of testosterone gel. There were no additional features suggestive of either primary or secondary hypogonadism. He has three children and no desire for further fertility. Initial workup revealed borderline low testosterone (7.7–10 nmol/l) with inappropriately normal follicle-stimulating hormone (FSH) at 6.1 IU/l and luteinizing hormone (LH) at 4.7 IU/l. Thyroid function test was normal and prolactin was 434 mIU/l. Glucagon test showed inadequate GH and cortisol response. Magnetic resonance imaging (MRI) of the pituitary demonstrated focal nodular enhancement of the pituitary stalk with slight T1 hyperintensity post-contrast. Multidisciplinary team (MDT) review suggested differential diagnoses of pituitary hypophysitis with infiltrative or infective underlying cause, versus pituitary stalk adenoma. Given the radiological and hormonal profile, the patient was initiated on hydrocortisone replacement therapy to address possible secondary adrenal insufficiency. Further work-up excluded systemic infection: serology for hepatitis B, hepatitis C, HIV, and QuantiFERON-TB testing were negative. Autoimmune screening including ANA, ENA, anti-mitochondrial, anti-dsDNA, anti-liver kidney microsomal, and anti-smooth muscle antibodies was negative. Full blood count and ESR were normal. IgG4 levels were within the normal range. Serum ACE was elevated (78 U/l; normal <50), raising the possibility of sarcoidosis, but calcium level was normal and CT thorax-abdomen-pelvis (CT-TAP) showed no lymphadenopathy or systemic involvement. Thus, granulomatous disease was considered unlikely. A subsequent MRI three months later, demonstrated mild reduction in both pituitary height and stalk thickness, suggesting interval improvement. These findings, together with negative systemic investigations, supported the working diagnosis of idiopathic pituitary hypophysitis.
Conclusion
This case highlights the diagnostic challenges of pituitary stalk lesions presenting with endocrine dysfunction. The presence of focal pituitary stalk thickening, together with the exclusion of alternative etiologies, supported a diagnosis of pituitary hypophysitis of unknown origin. Management focused on hormone replacement and close surveillance. This case underscores the need to consider hypophysitis in patients with pituitary stalk abnormalities and unexplained hypopituitarism, while ensuring thorough evaluation for potential underlying causes.

DOI: 10.1530/endoabs.113.WA2.1

## WA2.2

### Cyclical vs evolving cushing's disease: the diagnostic conundrum and endless investigation

Bijal Patel, Deborah Papadopuolou, Salaj Masand, James Wilkinson, Risheka Walls, Florian Wernig, Niamh Martin, Emma Hatfield, Karim Meeran & Anjali Amin
Imperial College NHS Trust, London, United Kingdom

Background
Cyclical Cushing's syndrome is a rare condition marked by fluctuating episodes of cortisol excess (peaks) followed by periods of normal or low cortisol levels (troughs). These intermittent features can make diagnosis challenging and can often overlap with evolving Cushing's disease.
Clinical Case
A 30-year-old female self-reported features of hypercortisolaemia including intracapsular adiposity, a round facial appearance and abdominal hirsutism. She was recently also diagnosed with type 1 diabetes and commenced on insulin. Her biochemistry demonstrated elevated late-night salivary cortisol (6.0 nmol/l, RR < 2.6) and cortisone (37.9 nmol/l, RR < 18) levels, and a raised 24 hr-urinary free cortisol (UFC, 212 nmol/l, RR 0-164). Additionally, she failed to suppress cortisol (228 nmol/l, RR < 50) after an overnight dexamethasone suppression test (ONDST). An MRI demonstrated a normal pituitary with a small area of non-enhancement on the left side suggestive of a microadenoma. However, at the time of performing these tests she was also diagnosed with Graves' disease, and there were some concerns that her thyrotoxic state could impact her cortisol levels and her ability to process dexamethasone, causing misleading results. Given her mild clinical features, ambiguous biochemistry and inconclusive MRI findings, repeated testing was warranted. Over the next 9-months, her late-night salivary cortisol and cortisone levels fluctuated from raised (peak: cortisol 6.0 nmol/l, cortisone 37.9 nmol/l) to normal (nadir: cortisol 1.6 nmol/l, cortisone 12 nmol/l). Her ONDSTs continued to demonstrate failure of cortisol suppression. However, her paired dexamethasone levels were low at times (2.0 nmol/l and 1.7 nmol/l; RR < 3), suggesting impaired absorption of or poor compliance with dexamethasone. Furthermore, during a time where she had positive salivary and ONDTs results, her 24 hr-UFC level remained normal (94 nmol/l), which resulted in diagnostic uncertainty. Despite her variable biochemistry, her appearance began to change, and she was now considered to be clinically Cushingoid. Furthermore, her DEXA scan revealed osteoporosis of the spine and osteopenia of the hips. As a result, she was commenced on rivaroxaban for VTE prevention and referred for inferior petrosal sinus catheter sampling (IPSS). Her IPSS excluded an ectopic source of ACTH production, and she is currently awaiting a repeat MRI +/- methionine PET/CT.
Questions for Discussion
How does thyrotoxicosis impact biochemical testing for hypercortisolaemia? Does she have cyclical Cushing's or evolving Cushing's disease? Are her fluctuating dexamethasone levels due to excess metabolism or poor absorption/ non-compliance of dexamethasone? How useful is a methionine PET/CT scan for diagnosing Cushing's disease in a patient without a clear lesion on MRI?

DOI: 10.1530/endoabs.113.WA2.2

## WA2.3

### Arginine vasopressin deficiency after craniopharyngioma surgery: a complex multidisciplinary challenge

Hafiz Muhammad Zubair Ullah & Natasha Sawhney
Aberdeen Royal Infirmary, Aberdeen, United Kingdom

Background
Arginine vasopressin deficiency (AVP-D), is a recognized complication of surgery for suprasellar tumours such as craniopharyngioma, where disruption of the hypothalamic–neurohypophyseal axis may occur. AVP-D manifests with polyuria, polydipsia, and risk of profound hypernatraemia if fluid intake is insufficient or desmopressin therapy is suboptimal. Management is particularly challenging in patients with cognitive impairment, as in this case, where self-regulation of fluid balance was compromised, necessitating careful biochemical monitoring, medication titration, and family or carer support.
Case Summary
We present a case of 43-year-old woman with a history of adamantinomatous craniopharyngioma, initially diagnosed in Nigeria, complicated by hydrocephalus requiring bilateral ventriculoperitoneal shunts (2022). She subsequently underwent cyst debulking at our centre in May 2025 after radiological progression & clinical decline. Post-operatively, she developed persistent AVP-D, presenting with polyuria & recurrent hypernatraemia (peak 176 mmol/l), necessitating multiple hospital admissions & desmopressin dose adjustments. Four weeks later, she was re-admitted with confusion and diagnosed with hyperosmolar hyperglycaemic state (HHS), with sodium of 176 mmol/l & serum osmolality of 413 mmol/kg, precipitated by infection. She was initially started on insulin alongside glimepiride for newly diagnosed type 2 diabetes, with good response and improvement in HbA1 c from 72 to 49 mmol/mol. She has since been weaned off insulin & is currently maintained on glimepiride alone. Subsequent endocrine follow-up revealed evolving panhypopituitarism with secondary adrenal insufficiency, central hypothyroidism, and hypogonadism, for which she was optimized on oral hormone replacement. Further inquiry revealed that she had an ongoing neurocognitive decline, over several years, manifesting as poor short-term memory, disorientation, and reduced ability to perform daily activities. This had been compounded by treatment burden & social challenges, particularly childcare responsibilities. Social care support, neurorehabilitation, and psychological input have been central to her ongoing care alongside endocrine & neurosurgical follow-up.
Discussion points
1. Management of AVP-D – This case underscores the difficulty in balancing desmopressin dosing & fluid intake, especially when cognitive impairment limits self-management. Early recognition of hypernatraemia & close electrolyte monitoring are critical.
2. Metabolic complications – The development of HHS illustrates the increased risk of metabolic decompensation in patients with complex neuroendocrine disease. Coordinated diabetes input is essential to reduce morbidity & hospitalizations.
3. Neurocognitive and psychosocial impact – Beyond medical stabilization, quality of life and functional independence are major concerns.

This case highlights the complexity of managing post-surgical AVP-D in a patient with multiple pituitary hormone deficits, metabolic complications, and cognitive impairment, emphasizing the need for a multidisciplinary approach.

DOI: 10.1530/endoabs.113.WA2.3

## WA2.4

**Acromegaly with pituitary stalk involvement: multidisciplinary challenges in management**

Haider Imtiaz[1], Shailesh Gohil[1], Narendra Reddy[1,2] & Miles J Levy[1,2]
[1]University Hospitals of Leicester, Leicester, United Kingdom; [2]University of Leicester, Leicester, United Kingdom

A 45-year-old HGV driver was referred with a five-year history of reduced libido and erectile dysfunction. He was found to have gonadotrophin deficiency with consistently low testosterone levels on multiple occasions. On clinical assessment, he exhibited classical features of acromegaly, including coarsening of facial features and acral enlargement, although he reported no symptoms suggestive of growth hormone (GH) excess. Laboratory investigations confirmed acromegaly with elevated insulin-like growth factor 1 (IGF-1) levels and a failure to suppress GH on an oral glucose tolerance test. Additionally, he was found to have TSH deficiency. Testosterone replacement and levothyroxine therapy were initiated. MRI demonstrated a pituitary macroadenoma measuring 11.5 × 8 × 18.5 mm, with suprasellar extension, contacting the right optic nerve and optic chiasm. The lesion exhibited an unusual morphology, extending beyond the pituitary stalk. Methionine PET imaging showed tracer by the entirety of the pituitary gland. The multidisciplinary team (MDT) concluded that surgical resection would carry a very high risk of cerebrospinal fluid (CSF) leak and permanent arginine vasopressin (AVP) deficiency. Given these risks, medical therapy with lanreotide was initiated. However, IGF-1 and GH levels remained persistently elevated despite treatment. This case raises a critical management dilemma: Should medical therapy with somatostatin receptor ligands be continued, or should alternative approaches such as pegvisomant, radiotherapy, or high-risk surgical intervention be considered for better disease control or potential cure?

DOI: 10.1530/endoabs.113.WA2.4

## WA3.1

**A case of panhypopituitarism**

Ebony Sciberras Giusti & Mark Gruppetta
Mater Dei Hospital, Msida, Malta

A 13- year-old boy presented with a 5-day history of fronto-parietal headaches and low-grade fever. He complained of a 3-month history of polyuria and polydipsia; with a daily oral intake of 4 litres per day, mild weight loss, reduced concentration and reduced exercise tolerance. Examination was unremarkable. Biochemical work-up revealed a picture consistent with Arginine Vasopressin deficiency: Hypernatraemia 150 mmol/l, Serum hyperosmolality 302 mOsm/kg, Urine hypoosmolality 155 mOsm/kg, 24-hour urine output >4 litres/day. MR Pituitary reported a 5 x 4 mm solid mass lesion of the pituitary stalk with an intermediate T1 and T2 signal as well as homogenous and avid enhancement on contrast administration. There was no evidence of optic nerve compression. A skeletal survey reported a 2.5 cm lytic focus in the mid shaft of the left femur with prominent established cortical thickening, implying chronicity. MR Left femur suggested this lesion to be longstanding in nature and consistent with Langerhans' cell histiocytosis. However, both a CT guided and open biopsy resulted negative for malignancy. This was followed by a negative Bone marrow aspirate and Lumbar puncture. PET CT showed increased uptake in the left femoral lesion. Biochemical surveillance uncovered development of secondary hypothyroidism: TSH 0.018 mU/l and a fT4 15.10 pmol/l. An endoscopic trans-nasal trans-sphenoidal biopsy of the pituitary gland was performed. Post operatively the patient was kept on a hydrocortisone regimen whose need was challenged 6 weeks post-operatively. Due to a poor response to a trial off hydrocortisone and skirting level of cortisol past the 60-minute mark of 536 mmol/l on synacthen test, it was decided to continue the patient on hydrocortisone in view of probably imminent secondary hypocortisolism. The patient moved on to develop secondary hypogonadism with down trending testosterone, FSH and LH levels of < 0.69 mmolL, <0.1 U/l and <0.1 U/l respectively. This was then followed by down trending IGF-1 levels and signs suggestive of GH deficiency. 2 years later, an Image guided right parietal craniotomy and biopsy of thickened pituitary stalk was positive for CD1 a positive cells, confirming a diagnosis of multisystem risk organ negative LCH. Primary management involved chemotherapy alongside ensuing obesity and hyperglycaemia. Reactivation of right frontal skull LCH which necessitated an excision biopsy. DDAVP, Levothyroxine, Hydrocortisone, Testosterone undecanoate and Vitamin D supplementation form part of his current treatment regimen with follow-up at a Young Adult Clinic.

DOI: 10.1530/endoabs.113.WA3.1

## WA3.2

**Unusual presentation of adrenal insufficiency with weight gain and atypical diabetes**

Aparajita Roy, Pallavi Agarwal, Sarah Hammett & Mohamed Bakhit
University Hospital Lewisham, London, United Kingdom

Background
Adrenal insufficiency and diabetes mellitus occasionally coexist, but unusual presentations can complicate diagnosis. We present a case of adrenal dysfunction with atypical autoimmune diabetes in a patient with severe obesity.
Case Presentation
A 51-year-old Afro-Caribbean woman with body weight of 156 kg and BMI 56.9, with no prior medical history was referred by the GP for rapid weight for 5 months. Random cortisol was low at 56 nmol/l. She was urgently reviewed in the ambulatory care unit. She had central and peripheral fat distribution and round face. There was no history of previous steroid exposure of any form. Hydrocortisone was started empirically and the following blood tests were requested.
Investigations

| Test | Result | Reference Range |
|---|---|---|
| HbA1 c | 39 mmol/mol | <42 |
| FSH | 4.7 IU/l | 1.7–7.7 |
| LH | 1.5 IU/l | 1–9 |
| Oestradiol | <19 pmol/l | 45–854 |
| GH | 0.77 μg/l | 0–10 |
| IGF-1 | 190 μg/l | 65.6–249.2 |
| ACTH | <3 ng/l | 10–50 |
| Prolactin | 260 mU/l | 0–495 |
| TFTs | Normal | – |

A short Synacthen test showed inadequate cortisol response (0 min = 8 nmol/l, 30 min = 112 nmol/l), confirmed onrepeat testing. She had low androstenedione and DHEAS (undetectable). Pituitary MRI demonstrated an expanded bony fossa with near-empty sella. Two months later, she was admitted in a different hospital with osmotic symptoms, fatigue and blurred vision, Serum glucose was 27 mmol/l, and ketones were 0.3. HbA1 c was 101 mmol/mol. Anti-GAD65 antibody was markedly raised (1683.4 U/mL; <5), while IA2 and ZnT8 were negative. She was treated as type 1 diabetes and commenced on Glargine and Aspart insulin.

Management and Outcome

At follow-up, she was found to have recurrent prolonged hypoglycaemia despite basal insulin reduction to 4 units. Repeat antibody testing showed anti-GAD65 > 2000 U/mL, but HbA1 c normalised to 39 mmol/mol. After multidisciplinary review, insulin was stopped. She has remained off insulin to date (3 months). Her glucose control has remained good as evident by time in target of >90% on her most recent Freestyle Libre data.

Discussion

The clinical, radiological and biochemical findings suggest adrenal insufficiency, possibly from a burnt-out pituitary adenoma or silent pituitary apoplexy. Her diabetes course is atypical: anti-GAD65 was strongly positive but there was rapid insulin independence and stable glucose afterwards.

Conclusion

This case highlights the complexity of overlapping endocrine disorders. Ongoing monitoring remains crucial, with adequate patient's education and follow up.

DOI: 10.1530/endoabs.113.WA3.2

## WA3.3

**A case of acromegaly, with review of perioperative monitoring for risk of hypopituitarism and disease recurrence**

Niamh Ryan, Claire McHenry & Philip Weir
Royal Victoria Hospital, Belfast, United Kingdom

A 52 year old man presented to his GP due to an increase in the size of his hands and feet. His wedding ring had become too tight and his shoe size had increased by three sizes. He had a change in his bowel habit but no headache or visual disturbance. Insulin-like growth factor-1 (IGF-1) was raised at 166 (9.8-26.3)nmol/l. He was referred to endocrinology. In clinic IGF-1 remained raised at 121 nmol/l, growth hormone (GH) was 40 ng/mL, and he was noted to have profound acromegalic features. Cortisol, TSH, T4, prolactin, LH, FSH, and testosterone were normal. MRI scan pituitary gland showed a macroadenoma with extension into the cavernous sinus, but no compression of the optic chiasm. He was diagnosed with acromegaly and referred for neurosurgery. He underwent transphenoidal resection of the pituitary adenoma. Post operatively he was started on hydrocortisone as per pituitary surgery protocol. His fluid input and output were monitored, with no evidence of AVP (arginine vasopressin) deficiency. Day 5 morning cortisol was 286 nmol/l. Daily steroids were stopped and he was discharged with steroids for sick days only. GH day 1 post operatively had reduced to 3.0 ng/ml. He re-presented two weeks later with dizziness, and was found to be hyponatremic at 126 mmol/l, with serum osmolality 272 (275-295)mOsm/kg, urine osmolality 183 mOsm/kg, and he was commenced on hydrocortisone daily. At follow up in endocrine clinic, he clinically felt well with no headaches, had some regression of his acromegalic features, and reduction in his blood pressure. His post-operative visual fields remained intact. Short synacthen test showed cortisol at T=0 at 311 nmol/l rising at T=30 to 523 nmol/l, following synthetic ACTH, and his daily steroids were stopped. Other pituitary blood tests remained in normal limits, and IGF1 now normalised to 33.5 nmol/l. Histopathology of his pituitary lesion was of somatotroph lineage, with no aggressive features, in keeping with a diagnosis of acromegaly. Repeat MRI pituitary scan did show an area of high signal reported as likely residual tumour. Oral glucose tolerance test found a growth hormone level of 2.8 ng/ml at 2 hours (<0.5 ng/ml) which was evidence of ongoing excess growth hormone secretion. He was discussed at a complex case meeting with the Neurosurgeon, with no further surgery planned at present. He will require ongoing monitoring of his biochemical markers for acromegaly recurrence, as well as screening for associated co-morbidities such as diabetes, hypertension, and obstructive sleep apnoea.

DOI: 10.1530/endoabs.113.WA3.3

## WA3.4

**Challenges in the perioperative management of a young adult with suprasellar craniopharyngioma, panhypopituitarism, and AVP deficiency**

Maha Khalid & Ma'en Al-Mrayat
University Hospital of Southampton, Southampton, United Kingdom

The perioperative management of pituitary tumours presents complex challenges, particularly when complicated by panhypopituitarism and arginine vasopressin deficiency (AVP-D). We present the case of a 22-year-old male referred by ophthalmology with rapidly progressive visual loss. Orbital MRI revealed a large predominantly cystic suprasellar mass with internal calcification, compressing the optic chiasm and displacing the midbrain. Differential diagnoses included craniopharyngioma, germinoma, and optic pathway glioma. On endocrine review, the patient demonstrated florid features of AVP-D, reporting polyuria of 8–10 L/day and severe polydipsia, which had been previously misattributed to behavioural causes. Initial investigations confirmed panhypopituitarism, with very low thyroid hormones, testosterone, prolactin, and a random cortisol of 76 nmol/l. He was commenced on hydrocortisone and desmopressin (AVP analogue) with clinical improvement. Neurosurgical intervention included preoperative external ventricular drain, subsequent craniotomy, tumour debulking, and shunt insertion. Postoperative imaging confirmed a small residual tumour, hypothalamic involvement, and no significant hydrocephalus. Complications included severe bilateral visual loss, hypothalamic syndrome, and Charles Bonnet visual hallucinations. The patient was placed on active radiological surveillance with consideration of postoperative radiotherapy, including proton beam therapy, pending recovery. A significant perioperative learning point arose when omission of desmopressin during an admission with intercurrent infection led to profound hypernatraemia (serum sodium 195 mmol/l), manifesting as irritability and confusion. He required intensive care admission for careful correction of hypernatraemia and reinstatement of desmopressin. This incident highlighted the critical importance of meticulous perioperative endocrine management and the need for heightened awareness among general medical teams of the potentially fatal consequences of desmopressin omission in AVP-D. This case underscores the multi-disciplinary complexities of managing large suprasellar tumours with hypothalamic and pituitary involvement. It reinforces the necessity of proactive endocrine input throughout the perioperative pathway, strict protocols for AVP-D management, and robust communication across teams. Recognition of AVP-D as a life-threatening condition is paramount, as failure to provide timely replacement can result in catastrophic outcomes. In conclusion, our patient illustrates the spectrum of challenges in the perioperative care of pituitary tumours: balancing neurosurgical intervention, long-term surveillance, and rigorous endocrine replacement. Vigilance in AVP-D management, alongside comprehensive multidisciplinary collaboration, is crucial to optimising patient safety and long-term outcomes.

DOI: 10.1530/endoabs.113.WA3.4

## WA4.1

**Pembrolizumab-associated hypophysitis and diabetes insipidus in a patient with metastatic lung adenocarcinoma: a case report**

Halem Hussein[1], Ahmed Abdelaal[2] & Ahmed Ahmed[2]
[1]Great Western Hospital, Swindon, United Kingdom; [2]Yeovil Hospital, Yeovil, United Kingdom

Background

Immune checkpoint inhibitors such as pembrolizumab can cause immune-related adverse events (irAEs), including endocrine dysfunctions. While thyroiditis and adrenal insufficiency are more common, hypophysitis is rare with PD-1 inhibitors. Central diabetes insipidus (DI) is even more unusual.

Case

We report a 67-year-old female with metastatic lung adenocarcinoma (T4 N0 M1 c) on pembrolizumab who developed dual endocrine toxicities—ACTH deficiency (secondary adrenal insufficiency) and central diabetes insipidus. She presented with polyuria and polydipsia during ongoing immunotherapy (Cycle 12), and was diagnosed via hormonal testing and osmolality studies. Treatment with prednisolone and desmopressin resulted in rapid symptomatic improvement.

Conclusion

This case highlights the importance of vigilance for rare endocrine irAEs such as diabetes insipidus in patients receiving PD-1 inhibitors. Early recognition and hormone replacement allowed continuation of pembrolizumab with maintained disease control. A 67-year-old female with stage T4 N0 M1 c right lung adenocarcinoma was initiated on palliative pembrolizumab following initial chemoradiotherapy. She had no prior history of endocrine or autoimmune disorders.

Disease Status

- She was approaching Cycle 13 of pembrolizumab.
- A recent CT chest/abdomen/pelvis (May 2025) demonstrated a partial response with no evidence of progression.

Presenting Symptoms

- The patient developed polyuria, polydipsia, and mild fatigue over several weeks.
- She remained weight stable and was wheelchair-dependent due to prior cancer-related deconditioning.

Endocrine Workup
- Morning cortisol: Low
- ACTH: Low-normal → consistent with secondary adrenal insufficiency
- Plasma osmolality: High
- Urine osmolality: Inappropriately low
- Response to desmopressin: Immediate clinical and biochemical improvement, confirming central diabetes insipidus

Diagnosis
- Pembrolizumab-induced hypophysitis, presenting with:
- ACTH deficiency (Addison's disease)
- Central diabetes insipidus

Management
- Initiated on prednisolone 5 mg once daily (maintenance glucocorticoid)
- Desmopressin 100 mg twice daily (oral)
- Provided with hydrocortisone emergency kit for intercurrent illness

Outcome
- Rapid symptom relief
- Stable biochemical parameters
- Continued pembrolizumab without interruption
- Imaging follow-up confirmed ongoing tumor control without new lesions

Discussion
Immune-related endocrine toxicities are increasingly recognized with checkpoint inhibitor therapy. While thyroiditis and primary adrenalitis are common, hypophysitis is less frequently seen with PD-1 inhibitors and more classically associated with CTLA-4 blockade. Central diabetes insipidus is exceedingly rare as an irAE. The posterior pituitary is less susceptible to autoimmune inflammation, making isolated or combined anterior/posterior involvement unusual. Only a handful of cases combining ACTH deficiency and DI have been reported with anti–PD-1 therapy. In this patient, early recognition of symptoms and prompt hormonal evaluation were key. The dual endocrine dysfunction was effectively managed with steroid and desmopressin replacement, allowing continuation of pembrolizumab and preservation of quality of life.

DOI: 10.1530/endoabs.113.WA4.1

## WA4.2

**Giant prolactinoma presenting with central hypopituitarism: a case of dramatic medical response**

Andrew Gerges[1], Suresha Muniyappa[2] & Paula Marchetti[3]
[1]Sheffield Teaching Hospitals NHS Trust, Sheffield, United Kingdom; [2]Doncaster and Bassetlaw Teaching Hospitals NHS Trust, Doncaster, United Kingdom; [3]Doncaster and Bassetlaw Teaching Hospitals NHS Trust, Sheffield Teaching Hospitals NHS Foundation Trust, United Kingdom

Introduction
Prolactinomas are the most common hormone-secreting pituitary tumors, accounting for up to 40% of pituitary adenomas. They are classified into microprolactinomas (<10 mm), macroprolactinomas (≥10 mm), and giant prolactinomas (≥40 mm). Symptoms may arise from hyperprolactinemia or mass effect. Differential diagnoses for hyperprolactinemia include physiological states, medications, hypothyroidism, and non-functioning adenomas. We report a case of a giant prolactinoma with central hypothyroidism and hypogonadism, showing a remarkable response to medical therapy.

Case Presentation
A 45-year-old male was evaluated for ejaculatory dysfunction. Initial testing revealed low testosterone (1.70 nmol/l), prompting pituitary hormone assessment:
- Prolactin: 220,948 mU/l
- FSH: 1.53 IU/l
- LH: 1.10 IU/l
- TSH: 0.96 mU/l
- Free T4: 7.5 pmol/l
- Cortisol: 327 nmol/l

He reported fatigue, aches, headaches, visual blurring, dizziness, and low libido but denied galactorrhea, rhinorrhea, or erectile dysfunction. Past medical history included atrial septal defect, pulmonary valve stenosis, and chronic hepatitis B. Visual fields by confrontation were initially normal. MRI revealed a large pituitary macroadenoma remodeling the clivus, displacing the optic chiasm, encasing the left internal carotid artery, and invading both cavernous sinuses. The patient denied any CSF leak. He was started on Cabergoline (250 mg twice weekly) and referred urgently to the Pituitary MDT and Ophthalmology. Formal testing revealed grossly depressed visual fields bilaterally, and the patient was advised not to drive. Baseline echocardiography was stable.

After one month:
- Prolactin: 19,526 mU/l
- TSH: 1.75 mU/l
- Free T4: 10.4 pmol/l
- Cortisol: 396 nmol/l
- Testosterone: 2.19 nmol/l

Cabergoline was uptitrated to 500 mg TDS, reducing prolactin to 2,000 mU/l, and is being increased to 1 mg BD. Testosterone replacement was initiated. Levothyroxine was started for central hypothyroidism. The patient is awaiting a repeat MRI scan to assess tumor size and further guide management.

Conclusion
This case demonstrates the potential for dramatic prolactin reduction and symptomatic improvement in giant prolactinomas with high-dose dopamine agonists alone. Surgery may be avoidable even in large, invasive tumors. Treatment goals include rapid tumor shrinkage, visual recovery, and full hormonal restoration.

DOI: 10.1530/endoabs.113.WA4.2

## WA4.3

**Severe catatonia as a rare neuropsychiatric manifestation of ACTH-dependent cushing's syndrome**

Kavya Rajendran, Omar Mohammed, Mamta Joshi, Steve Hyer, Giuseppe Maltese, Nikhil Johri & Tharani Jasmine Tharma
Epsom and St Helier University Hospital, London, United Kingdom

Cushing's syndrome is a multisystem disorder with hallmark metabolic features, but its neuropsychiatric manifestations—particularly catatonia—are under-recognised. We present a 38-year-old woman with no prior endocrinopathy admitted with acute confusion, persecutory delusions, and catatonia. Labs showed hypercortisolaemia (serum cortisol 1544 nmol/l), elevated ACTH (64 ng/l), raised urinary cortisol (>3300 nmol/l) and hypokalaemia (2.9 mmol/l). Adrenal androgens were raised (testosterone 2.9 nmol/l, androstenedione 22.6 nmol/l), while other anterior pituitary hormones were normal, suggesting preserved pituitary function aside from corticotrophin hyperactivity. A pituitary MRI revealed a 4 mm microadenoma and ^68 Ga-DOTATATE PET excluded ectopic sources. Despite partial cortisol suppression on high-dose dexamethasone, ACTH levels stayed elevated, supporting pituitary-origin ACTH-dependent Cushing's syndrome. She was started on metyrapone (1 g TDS), benzodiazepines, and treated with insulin and electrolytes. Antipsychotics were avoided due to risk of worsening catatonia. Apixaban was initiated for thrombotic risk. Psychiatric input was sought early and integrated into multidisciplinary care to guide benzodiazepine use and provide psychological support. She underwent trans-sphenoidal resection; histology confirmed an ACTH-positive corticotroph adenoma with Ki-67 <3%. Given her substantial cortisol burden, peri-operative care included stress-dose hydrocortisone. Although biochemical remission was achieved post-operatively, she developed steroid withdrawal symptoms—fatigue, myalgia, mood lability—indicating higher supplementation than standard dosing was required. Glucagon stimulation confirmed secondary adrenal insufficiency and GH deficiency, prompting tailored hydrocortisone replacement with gradual weaning. Anticipatory counselling before surgery helped mitigate psychological distress during withdrawal. The literature suggests a mechanistic link between hypercortisolaemia and catatonia via GABAergic and dopaminergic dysregulation. Gunther *et al*. report 80% zolpidem response [1]. Catatonic episodes show elevated ACTH and DHEAS [2], exacerbated by cortisol surges [3]. The Endocrine Society recommends surgical resection as first-line, with medical therapy for pre-operative control or inoperable cases [5]. Cognitive deficits may persist post-remission [4]. Only one prior case of catatonia in Cushing's syndrome is reported (Yamaguchi *et al*., 2019); ours is the second [6]. This case highlights recognition of catatonia as manifestation of endocrine disease. Interpreting pituitary function, anticipating steroid withdrawal, and individualised hydrocortisone dosing—essential to manage high-burden cortisol states. Early endocrine input and multidisciplinary care are vital to optimise outcomes.

References
1. Gunther M *et al*. Zolpidem in catatonia. *J Acad Consult Liaison Psychiatry*. 2025;66(1):49–56.
2. Muneoka K *et al*. Neurosteroids in periodic catatonia. *JCEM Case Rep*. 2023;1(1):luad009.
3. Zwiebel S *et al*. Catatonia with hypercortisolaemia. *Case Rep Psychiatry*. 2018;2018:4264763.
4. Katragadda A *et al*. Cognitive decline in Cushing's. *J Neuroendocrinol*. 2025;37(1):e13466.
5. Nieman LK *et al*. Cushing's treatment guideline. *J Clin Endocrinol Metab*. 2015;100(8):2807–13.
6. Yamaguchi H *et al*. Subclinical Cushing's catatonia. *Psychogeriatrics*. 2019;19(4):402–3. doi:10.1111/psyg.12394.

DOI: 10.1530/endoabs.113.WA4.3

## WA4.4

**Arginine vasopressin deficiency perioperatively in a patient with pituitary apoplexy**

Muhammad Siddique
Aberdeen Royal Infirmary, Aberdeen, United Kingdom

Background
Arginine Vasopressin (AVP), also known as antidiuretic hormone (ADH), is secreted from posterior pituitary and plays a vital role in regulating water balance and serum sodium levels. Arginine Vasopressin Deficiency (AVP-D) previously known as central diabetes insipidus is well recognized complication following pituitary surgery. Perioperative monitoring of urine out and sodium levels is essential. When patient produces excessive urine for more (>50 ml/kg/hour for more that 2 hours, AVP-D is suspected. Patient needs urgent endocrine review and treatment with desmopressin. This case illustrates a patient developed AVP Deficiency on the third postoperative days following pituitary surgery for pituitary apoplexy.
Case
A 68-year-old male was admitted under the neurosurgical team for semi urgent Trans sphenoidal surgery. He presented with sudden onset headache and bitemporal visual loss in a regional hospital ad he was diagnosed with pituitary apoplexy leading to partial hypopituitarism and development of severe hyponatremia. He was managed with levothyroxine, and his sodium was normalized at the time of review by neurosurgical team. He did not require hydrocortisone given normal morning cortisol. He had MRI guided Endoscopic trans sphenoidal hypophysectomy (ETSH) on 26/06/2025. He received glucocorticoid cover perioperatively. Surgery was uneventful. He was monitored post operatively by daily endocrine review. On post operative day three, he developed significant polyuria, producing 400-500 ml/ hours for several hours equating to >50 ml/kg/hour for three consecutive hours. The patient reported increased thirst and was allowed to self-regulate fluid intake.
Laboratory tests showed:
- Serum sodium:145 mmol/l
- Serum Osmolality: 296 mOsm/kg
- Urine osmolarity: 83 mOsm/kg and
- Urine specific gravity was <1.005

These findings were diagnostic of AVP deficiency was given a single dose of intravenous desmopressin 1.0 ug IV which resulted in rapid symptomatic and biochemical improvement. He could not wait for further monitoring and was discharged on hydrocortisone, levothyroxine and desmopressin 100 microgram with clear instructions to use only if urine output exceeds 50 ml/kg/hr for > 2 hours. with advice to monitor input and output and repeat sodium in 2-3 days. His followed up back in regional hospital demonstrated stable electrolytes, normal urine output and good recovery.
Discussion Points
AVP deficiency often rises after surgery, but it can be delayed –how long monitoring must be continued? Pituitary apoplexy cases may have variable recovery of pituitary function, including transient or permanent AVP deficiency. Should we measure co peptin post pituitary surgery as it has good but no excellent accuracy.

DOI: 10.1530/endoabs.113.WA4.4

## WA5.1

**Ironing out hypogonadotropic hypogonadism – haemochromatosis affecting the pituitary gland**

Salaj Masand[1,2], Apichaya Amrapala[1], Philippa Mallon[1], Agnes Johnson[1] & Mushtaqur Rahman[1]
[1]Northwick Park Hospital, London, United Kingdom; [2]Charing Cross Hospital, London, United Kingdom

Case Report
A 25-year-old man presented in 2018 with 3-year history of severe hypogonadism symptoms (fatigue, difficulty concentrating, low libido and mood). His initial investigations indicated hypogonadotropic hypogonadism (HH): virtually undetectable serum testosterone (1.4 nmol/l) with inappropriately low gonadotrophins (FSH 1.4 IU/l, LH 2.0 IU/l). The serum prolactin level and the rest of the pituitary profile were in the normal ranges; while a pituitary MRI scan was also reported as normal. He had well developed secondary sexual characteristics. His haemoglobin was 121 g/l (130-170) with low haematocrit, consistent with the effect of androgen deficiency on haemopoiesis, while osteopenia was reported on a bone-density scan. He responded impressively to testosterone replacement therapy. 18 months later, he developed arthralgia, prompting further investigation. He was found to have a markedly elevated serum ferritin of 3,957 μg/l. Genetic testing confirmed a homozygous HFE gene mutation, therefore confirming a diagnosis of hereditary hemochromatosis. He commenced regular venesections in 2019. Despite this treatment, a repeat pituitary MRI in 2024 revealed evidence of iron deposition in the anterior pituitary, which was not reported on the initial scan.
Discussion
Haemochromatosis is a typically an autosomal recessive disorder in which mutations in the *HFE* gene lead to abnormal production of hepcidin, the hormone which regulates iron absorption. Excess iron is deposited in body tissues, which can lead to widespread organ dysfunction. Whilst haemochromatosis can cause diabetes and Addison's disease, the gonadotrophs of the anterior pituitary are disproportionately affected by accumulation of intracellular ferritin due to selective expression of transferrin receptors. Therefore, HH can occur early in the natural history of haemochromatosis, as demonstrated in this Case Study, where the patient had symptoms of androgen deficiency for over 4 years before developing arthritis symptoms due to iron deposition in his joints. Primary testicular dysfunction can also occur due to iron deposition in the testicles. Osteoporosis is prevalent in haemochromatosis due to an increase in the number and size of osteoclasts and the rate of osteoblast apoptosis, so those patients with androgen deficiency are at significantly increased risk.
Question for Consideration
If acquired HH is suspected, should you initially screen for systemic causes for pituitary infiltration (such as haemochromatosis, sarcoidosis)? In this Case Study, infiltration of the pituitary gland was only apparent on the MRI in 2024. This occurred despite receiving regular venesections since 2019, which have so far prevented other systemic complications of haemochromatosis. Why was this the case?

DOI: 10.1530/endoabs.113.WA5.1

## WA5.2

**Immune checkpoint inhibitor–induced hypophysitis: a case report**

Anyat Ali
Sheffield Teaching Hospital NHS Trust, Sheffield, United Kingdom

Background
Immune checkpoint inhibitors (ICIs) such as ipilimumab (CTLA-4 inhibitor) and nivolumab (PD-1 inhibitor) have revolutionised the management of advanced melanoma. However, they are increasingly associated with immune-related adverse events (irAEs), including endocrinopathies. Hypophysitis is a recognised but uncommon complication, particularly with CTLA-4 blockade, and can present with non-specific symptoms that may mimic disease progression or treatment toxicity. Prompt recognition and management are essential to prevent life-threatening complications such as adrenal crisis.
Case Presentation
We report a 58-year-old woman with metastatic melanoma and para-aortic lymphadenopathy, treated with combined ipilimumab and nivolumab. Following her third cycle of therapy, she was admitted with worsening morning headaches, nausea, and a single episode of vomiting. She also described paraesthesia and swelling of her hands and feet. On examination, she was haemodynamically stable with preserved visual fields. Initial investigations revealed **hyponatraemia (Na 123 mmol/l)** and a markedly **low morning cortisol (34 nmol/l)**. Thyroid function tests showed **low free thyroxine (FT4 7.2 pmol/l) with inappropriately low TSH (0.23 mU/l)**, consistent with secondary hypothyroidism. Her thyroid function had been normal one month earlier. The constellation of new endocrine abnormalities in the context of ICI therapy raised the suspicion of **immune-mediated hypophysitis**. MRI of the pituitary demonstrated **diffuse enlargement of the anterior pituitary and infundibulum with homogeneous contrast enhancement**, appearances in keeping with hypophysitis. Pituitary adenoma was considered in the differential but was less likely given the temporal relationship to immunotherapy. The patient was commenced on **hydrocortisone replacement (20 mg three times daily, tapered to a maintenance regimen)**. **Levothyroxine (50 μg daily)** was initiated 48 hours later to avoid precipitating adrenal crisis. A complete pituitary hormonal profile (ACTH, prolactin, LH, FSH, IGF-1, GH) was arranged for further evaluation.
Discussion
This case highlights the importance of maintaining a high index of suspicion for ICI-induced hypophysitis in patients presenting with headache, hyponatraemia, or non-specific constitutional symptoms during immunotherapy. Early diagnosis with biochemical testing and MRI, followed by appropriate corticosteroid replacement, is crucial for preventing adrenal crisis. Thyroid hormone replacement should only be initiated after glucocorticoid therapy is established. Long-term endocrinology follow-up is essential, as many patients require lifelong hormone replacement.
Conclusion
Immune checkpoint inhibitors, while highly effective in advanced melanoma, can precipitate serious endocrine irAEs such as hypophysitis. Our case underscores

the need for **vigilant monitoring, multidisciplinary collaboration, and timely intervention** to optimise both oncological and endocrine outcomes.

DOI: 10.1530/endoabs.113.WA5.2

## WA5.3

**Partial AVP deficiency following transsphenoidal surgery for cushing's disease**

Amy Mach & Rupa Ahluwalia
Norfolk & Norwich University Hospital, Norwich, United Kingdom

Background
Transsphenoidal surgery (TSS) is the standard treatment for Cushing's disease but carries the risk of postoperative complications, including adrenal insufficiency, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and arginine vasopressin (AVP) deficiency. Early identification of these complications is crucial to facilitate prompt management and reduce morbidity.
Case
A 43-year-old woman presented with acute onset vomiting, polydipsia and polyuria. She had undergone TSS for Cushing's disease two weeks prior, requiring two operations. She had recently been reviewed by the endocrinology team and started on hydrocortisone (10 mg morning, 5 mg afternoon, 5 mg evening) for steroid withdrawal symptoms. On presentation, she had experienced two episodes of vomiting and was administered intramuscular hydrocortisone due to suspected adrenal crisis, although this was later thought to be an unlikely cause of her symptoms. Initial blood tests revealed normal sodium of 144 mmol/l (N-133-146 mmol/l), elevated serum osmolality of 307 mOsm/kg (N-275-295 mOsm/kg), and elevated urine osmolality 385 mOsm/kg. A 9 am cortisol level was 370 nmol/l (N > 350 nmol/l). Despite ongoing nausea, her vomiting resolved and there were no signs of meningism. She reported drinking 3–4 litres of fluid per day and had increased urine output, raising concern for AVP deficiency in the context of recent pituitary surgery. She was commenced on intravenous fluids. Over subsequent days, her thirst improved, and fluid balance normalised, supporting a diagnosis of transient AVP deficiency. She was discharged on hydrocortisone and will be followed up in endocrine clinic. Venous thromboembolism (VTE) prophylaxis was extended for a total of three months given her high thrombotic risk post-op for Cushing's disease.
Discussion
This case highlights the importance of vigilant postoperative monitoring in patients with Cushing's disease undergoing TSS. Partial or transient AVP deficiency may resolve without specific treatment. Steroid cover and proactive management of fluid and electrolyte balance are warranted. Furthermore, prolonged VTE prophylaxis is critical in this high-risk group. Clinicians must maintain a high index of suspicion for these complications to ensure timely diagnosis and optimise management.

DOI: 10.1530/endoabs.113.WA5.3

## WA5.4

**A complex case of post-operative adipsic diabetes insipidus and cognitive impairment**

Elaine Butterly, Jenna Cowan, Vincent McAulay, Alison MacEwan & Stewart Ferguson
University Hospital Crosshouse, Kilmarnock, United Kingdom

A 16-year-old female was referred on a routine basis to endocrinology with short stature and primary amenorrhoea. Meanwhile, she presented acutely via ophthalmology with a bitemporal hemianopia. Urgent pituitary MRI imaging showed a 4.5 x 3.8 x 4.5 cm partially cystic suprasellar mass with optic chiasm compression. Initial biochemistry showed hypogonadotrophic hypogonadism (oestradiol 62 pmol/l, LH 1.7 U/l, FSH 4.5 U/l), a borderline low IGF 1 89 ug/l but otherwise intact pituitary function. Urgent trans-sphenoidal debulking surgery was subsequently performed to preserve visual function. Pathology confirmed an adamantinomatous type WHO grade 1 craniopharyngioma. Post-operative recovery was complicated by panhypopituitarism and polyuria. Polyuria was evident day 2 post-operatively and initially treated with IV Desmopressin as sodium began to rise to 148 mmol/l. Biochemistry confirmed a rising serum osmolality (306 mOsm/kg) with inappropriately dilute urine (urine osmolality 70 mOsm/kg). AVP-deficiency (AVP-D) was diagnosed on day 3 due to persistent polyuria and hypernatraemia and regular Desmopressin was commenced. Subsequent post-operative recovery has proven to be challenging, with AVP-D complicated by hyperphagia, cognitive dysfunction and added instability associated with recurrent antibiotic-resistant E. coli urinary infections. Fluid balance remains a concern as by 6 weeks post-op the thirst reflex remained absent confirming the diagnosis of adipsic AVP-D. Regular oral Desmopressin was commenced aiming to control polyuria however oral intake has remained very poor requiring ongoing critical care nursing to ensure sufficient oversight of fluid balance. Despite regular Desmopressin with close biochemical monitoring, fluid balance and weights, the Sodium concentration has fluctuated, with extremes of Na+ 113 mmol/l and Na+ 164 mmol/l in the six weeks post-operatively. Urine output was still up to 3 litre daily on oral Demsopressin 200 micrograms three times daily but was subsequently curtailed by increased oral Desmopressin dosing. However, this was later complicated by the development of hyponatraemia. A management plan utilising the daily fluid balance and weight to estimate the required oral fluid intake has achieved relative stability but challenges remain in terms of attaining sufficient stability to facilitate a safe future discharge from hospital. Adipsic AVP-D presents as a combination of anti-diuretic hormone deficiency and an absent thirst reflex due to hypothalamic osmoreceptor damage, leading to an extremely problematic disorder of water and sodium balance. It presents a significant challenge in the post-operative period and beyond, particularly when complicated by cognitive dysfunction.

DOI: 10.1530/endoabs.113.WA5.4

# Workshop B: Disorders of growth and development

## WB1.1

**A case of partial androgen insensitivity syndrome**

Sushma Burri & Gul Bano
St Georges Hospital, London, United Kingdom

23 yr old male reviewed in endocrine clinic due to Severe Gynecomastia. He was born of the consanguineous parents. His milestones were normal. He had bilateral undescended testes and a very complicated penoscrotal transposition penile urethral meatus. He had bilateral orchidopexy and hypospadias repair by paediatric surgeon at the age of 9. He achieved puberty at 14 yrs and started shaving around 17 yrs. On examination his Height was 179 cm, weight 78.2 kg, with BMI of 24.41 kg/m$^2$. He had normal secondary sexual characteristics. The right testicle was small and left testicle hardly felt. He had gynaecomastia. He had XY karyotype. His blood results showed Testosterone 26.2 nmol/l, FSH 7.7 zzIU/l, and LH 21.4 zzIU/l. He had normal TSH 1.26 mu/l, Cortisol 343 nmol/l, IGF1 40.6 nmol/l, and Prolactin 315 mu/l. His Androstenedione was 4.8 nmol/l, Dihydrotestosterone 1.04 nmol/l, and Pre-stimulated T/DHT ratio 20.01. HCG stimulation test showed post stimulation testosterone 34.6 nmol/l, DHT 1.42 nmol/l, T/DHT ratio $>20$. US urinary tract showed Posterior to the bladder there are some hypoechoic structures which are possibly seminal vesicles, The prostate is not well delineated but appears small and measures ~6 ml, which suggested the possibility of Partial Androgen insensitivity syndrome. He had a genetic analysis and this confirmed the **diagnosis of AR-related androgen insensitivity**, He had breast reduction surgery

DOI: 10.1530/endoabs.113.WB1.1

## WB1.2

**Pubertal and growth delay from chronic non-adherence to levothyroxine**

Amina Al Qaysi & Mike Matheou
OCDEM, Oxford, United Kingdom

Introduction
Untreated primary hypothyroidism during adolescence can cause serious complications including impaired growth, delayed puberty, and pituitary enlargement. When imaging reveals pituitary enlargement, distinguishing between hyperplasia and adenoma is challenging. This case describes a young adult with longstanding untreated hypothyroidism who presented with delayed skeletal maturation, underdeveloped secondary sexual characteristics, and pituitary enlargement, which improved with thyroid hormone replacement.
Clinical Case
A 23-year-old man was referred to endocrinology after a distal radial fracture. Imaging incidentally showed open epiphyses, an unusual finding for his age. He had been diagnosed with primary hypothyroidism at 16 but had inconsistently taken Levothyroxine. He reported fatigue and short stature. Though he declined a detailed physical exam, lack of facial, axillary, and abdominal hair raised concerns for delayed puberty. Laboratory tests showed markedly elevated TSH and low free T4, consistent with poorly managed hypothyroidism. An insulin tolerance test confirmed growth hormone deficiency. Pituitary MRI revealed diffuse enlargement without a discrete mass. To support adherence, he began a once weekly Levothyroxine regimen, later followed by growth hormone therapy. Over several months, he reported improved mood, increased energy, and some height gain. A follow up MRI showed reduced pituitary size, consistent with reversible hyperplasia. Reassessment of his growth hormone axis is planned after stabilizing thyroid function.
Discussion
This case illustrates the consequences of prolonged untreated hypothyroidism in adolescence, including delayed epiphyseal closure, pubertal delay, and pituitary hyperplasia mimicking adenoma. It emphasizes the importance of early diagnosis, treatment adherence, and careful interpretation of pituitary imaging. Ongoing follow-up will guide the need for long-term growth hormone therapy as endocrine function normalizes.

DOI: 10.1530/endoabs.113.WB1.2

## WB2.1

**A journey through a late presentation of hypogonadotropic hypogonadism in an 18 year old male: gonadotropin induced puberty, testicular growth and spontaneous descent**

Wut Yee Win & Ruth Ronneberger
Cambridge University Hospital, Cambridge, United Kingdom

Introduction
Hypogonadotropic hypogonadism(HH) is characterized by low gonadotropin(LH and FSH) secretion, resulting in impaired gonadal function, delayed or absent puberty, and underdeveloped secondary sexual characteristics. It can be congenital or acquired, necessitating careful evaluation and tailored treatment. This case report details the clinical course and management of an 18-year-old male who presented to the adult endocrine service.
Case Presentation
An 18-year-old male was referred for delayed growth, with a height of 1.72 m, weight of 57 kg, and a mid-parental height of 176.50–193.50 cm. Laboratory studies showed undetectable LH, low FSH, and very low testosterone, with normal other anterior pituitary hormones. Physical exam revealed Tanner stage-2, an unpalpable right testis in the inguinal canal, and a left testis measuring 1-2 ml. MRI showed a normal pituitary. Bone age was delayed at 14-years, compared to his chronological age of 18. After discussion with the patient and his family, the decision was made to commence puberty induction treatment with gonadotropins rather than testosterone. A previously scheduled orchidopexy was withheld, and he was started on treatment with FSH. Testicular volumes and penile size increased within the next 2-3 months, and treatment with hCG was added. Over subsequent months, testicular size continued to increase, he progressed to Tanner stage-3, his height reached 180 cm. The right testis descended into the scrotum. Treatment doses was adjusted due to increased oestradiol levels and, mild gynecomastia but they both resolved after reduction of hCG, while pubertal development continued.

Initial visit bloods

| | 06/10/23 | 30/01/24 | 12/04/24 | 07/06/24 | 18/06/24 | 17/07/24 |
|---|---|---|---|---|---|---|
| IGF-1 | **19.8** | **20.7** | | | | **43.0** |
| LH | **1.1(L)** | 1.5 | | | **<0.2** | **<0.2** |
| FSH | 1.9 | 2.1 | 7.5 | | **1.2** | 4.2 |
| Oestradiol | | <78 | | | 137 | **275** |
| Testosterone (Male-Adult) | **1.6** | **0.9** | **3.8** | **37.5** | 17.7 | **40.7** |

Final bloods

| | 07/03/25 | 24/04/25 |
|---|---|---|
| LH | **<0.2** | 2.8 |
| FSH | 1.4 | 6.0 |
| Oestradiol | 144 | 89 |
| Testosterone (Male-Adult) | 8.3 | 9.1 |

| Reference | Range & Units |
|---|---|
| IGF-1 | 15.2-42.0 nmol/l |
| LH | 1.5 -9.3 U/l |
| FSH | 1.4-18.1 U/l |
| Oestradiol | 0-146 pmol/l |
| Testosterone | 7.9-31.3 nmol/l |

Discussion
This case highlights the challenges in managing HH presenting in late adolescence. Thorough evaluation confirmed HH with a normal pituitary. Gonadotropin therapy gradually promoted testicular growth, secondary sexual development, and spontaneous testicular descent.
Conclusion
While male puberty induction treatment traditionally included testosterone treatment, Gonadotropin therapy can increase the chances of future fertility, while still promoting testicular growth, secondary sexual development, and, as shown in our patient, spontaneous testicular descent. Early diagnosis and personalized management are key to optimizing puberty and fertility, with ongoing assessment of testicular function and semen parameters necessary for future reproductive planning.

DOI: 10.1530/endoabs.113.WB2.1

## WB2.2

**Reversal of primary amenorrhea with titrated Mounjaro therapy**

Catherine Cucknell
Torbay and South Devon NHS Foundation Trust, Torquay, United Kingdom

A 21-year-old lady was reviewed for consideration of acceptance into the Tier 3 weight management programme. Past history included PCOS, MAFLD, Hidradenitis suppurativa and T2 DM on Mounjaro. XX's key concern however, was that she was seeking pregnancy and had never had an unstimulated period. XX was accepted into the programme and referred onto our Diabetes clinic for assessment of her endocrinopathies and to maximise her glycaemic

co-morbidities. When seen in the diabetes clinic three months later, on single agent Mounjaro therapy, her HbA1 c had improved from 60 to 35 mmol/mol with weight loss from 119 to 111 kg (7% of body weight). On review of history, she had been referred age 16 to Gynaecology for primary amenorrhea. She had reported going through puberty at the same stage as her peers and it was noted at age 16 she had a C-cup bra and a BMI of 34. Biochemistry identified hyperandrogenism (Testosterone 2.19 nmol/l) but no hirsutism or acne was reported. An USS showed a normal sized uterus and bilateral small ovarian follicles consistent with PCOS however the report stated that this was likely normal for her age. She went on to have 3 months of cyclical norethisterone with withdraw bleeds. She was diagnosed with amenorrhoea secondary to probable anovulatory PCOS. XX wanted these issues reviewed again feeling that despite weight loss she still hadn't had regular cycles which were important to her for achieving motherhood. This was significantly affecting her mental health. On review of old notes oestradiol was consistently $<150$ nmol/l with a non-elevated LH and FSH. Her prolactin and other pituitary axes were intact. Biochemical hyperandrogenism was again present but she reported a Ferriman-Gallway score of 24 (hirsutism). A screen for CAH and cortisol excess were negative. On further review four months later, with further weight loss to 101 kg, (BMI 32.2, 15% weight loss) XX had reported the first spontaneous period. This case report identifies a young lady with amenorrhoea secondary to PCOS or obesity-related hypogonadotropic hypogonadism which resolved on weight loss. Neither obesity-related menstrual irregularities or male testosterone deficiency are identified in NICE guidelines as weight-related health conditions for Mounjaro. Their presence could be considered when identifying the benefit of ongoing titration of Mounjaro/GLP-1 therapy in patients with T2 DM despite achieving euglycemia.

DOI: 10.1530/endoabs.113.WB2.2

## WB3.1

**"Uterine development after pubertal induction in mosaic turner syndrome: re-evaluating apparent müllerian agenesis in hypoestrogenic states."**

Sharmila Ahamed, Waseem Majeed & Sarah Rahim
Salford Royal Hospital, Salford, United Kingdom

Background
Turner syndrome (TS) is classically associated with gonadal dysgenesis, hypergonadotropic hypogonadism, and a hypoplastic uterus. Complete Müllerian agenesis is not a recognised feature of TS. In hypoestrogenic states, the uterus may appear absent on early imaging, posing diagnostic challenges and psychosocial distress for affected individuals.
Case Presentation
A 23-year-old woman with mosaic TS (45,X[5]/46,XX[25]) presented in 2019 with primary amenorrhea, minimal breast development (Tanner stage 2), and sparse pubic hair. Pelvic ultrasound and MRI suggested an absent uterus, cervix, and ovaries. Biochemistry confirmed hypergonadotropic hypogonadism with female-range testosterone, which is against androgen insensitivity syndrome. Bone age was delayed (13 years at chronological age 18). She commenced pubertal induction with estradiol patches, gradually titrated over three years, with the addition of cyclical progesterone. Early continuous progesterone use was complicated by low mood, necessitating regimen modification. She was also commenced on vitamin D and citalopram.
Results
She tolerated hormone therapy well, achieving Tanner progression, regular withdrawal bleeds, and improved psychosocial adjustment. Multidisciplinary monitoring included cardiac MRI/echo (normal thoracic aorta, Tri leaflet aortic valve), audiology (discharged with periodic GP review), and bone health surveillance. Repeat pelvic MRI in July 2025 demonstrated interval development of uterus and cervix ($7 \times 3$ cm, endometrium 10 mm), with small adnexal tissues. This finding strongly suggested that the previously reported Müllerian agenesis was secondary to long-standing estrogen deficiency rather than true agenesis.
Conclusion
This case highlights that apparent "uterine agenesis" in mosaic Turner syndrome may in fact reflect profound hypoestrogenism, with potential for uterine development following prolonged hormone replacement. Clinicians should exercise caution in interpreting an absent uterus on adolescent imaging in hypoestrogenic states and consider re-imaging after pubertal induction. Structured pubertal induction, combined with multidisciplinary monitoring of cardiac, bone, auditory, and psychosocial health, is essential in optimising outcomes for women with Turner mosaicism.

DOI: 10.1530/endoabs.113.WB3.1

## WB4.1

**Primary ovarian insufficiency with severe osteoporosis in adolescence**

Anjana Sasidharan & Chithrabhanu Ballav
Buckinghamshire NHS Foundation Trust, Aylesbury, United Kingdom

Introduction
We present the case of a 16-year-old woman with primary amenorrhoea and severe spinal osteoporosis from Primary Ovarian Insufficiency (POI). POI is a rare cause of primary amenorrhoea diagnosed by elevated gonadotropins on at least two occasions measured 4-6 weeks apart in women with amenorrhoea or oligomenorrhoea under the age of 40
Case report
A 16-year-old girl was referred by her general practitioner for evaluation of primary amenorrhoea. She had no history of galactorrhoea, hirsutism or visual disturbances. She had an unremarkable childhood medical history and no significant family history. Her height was 153.6 cm, weight 42.6 kg (BMI 18.1). Examination revealed delayed secondary sexual characteristics (Tanner stage 2 breasts, sparse axillary hair, Tanner stage 3 pubic hair). Genital examination revealed an intact hymen with a central opening and no evidence of outflow tract obstruction. She had central hypogonadism: FSH 114.1 IU/l, (follicular phase 3.0 - 8.1, luteal phase 1.4 - 5.5, post-menopausal 26 – 133 IU/l) and LH 25.4 IU/l (follicular phase 1.8 - 11.8, luteal phase 0.6 - 14.0, post-menopausal 5.2 - 62.0 IU/l) with low oestradiol $<37$ pmol/l, follicular phase 77 – 922, luteal phase 77 – 1145, post-menopausal $<103$ pmol/l). Thyroid function, prolactin, DHEAS, and testosterone were normal. Transvaginal ultrasound showed a normal uterus and very small ovaries without dominant follicles. Karyotype analysis revealed a 46,XX pattern, and FMR1 mutation was negative. She had no clinical features suggestive of autoimmune disease; cortisol and thyroid antibodies were negative, and ovarian antibody testing is pending. Bone densitometry revealed severe osteoporosis (Z score –4.3 at spine, –2.8 at femur, –2.9 at hip). She was commenced on hormone replacement therapy (HRT) with oestrogen patch and oral progesterone, with counselling regarding benefits and risks, particularly for bone health, and advised vitamin D supplementation alongside dietary and lifestyle optimization. Fertility counselling was provided, with discussion of future assisted reproductive options, including oocyte donation.
Discussion
This case illustrates the presentation of POI in adolescence with primary amenorrhoea and osteoporosis. The manifestation with hypergonadotrophic hypogonadism and normal genetics is consistent with idiopathic POI; autoimmune etiology has been ruled out by negative antibody results. Early hormone replacement therapy with oestrogen patches is vital to optimize bone health, support pubertal development, and reduce long-term cardiovascular risks. Ongoing psychological support and long-term follow up are important to address both medical and emotional aspects of POI.
References
1. Meczekalski B, Niwczyk O, Bala G, Szeliga A. *Managing Early Onset Osteoporosis: The Impact of Premature Ovarian Insufficiency on Bone Health.* J Clin Med. 2023;12(12):4042. doi:10.3390/jcm12124042
2. Pederson, Julia & Kumar, Rajiv & Hillard, Paula & Bachrach, Laura. (2015). Primary ovarian insufficiency in adolescents: a case series. International Journal of Pediatric Endocrinology. 2015. 10.1186/s13633-015-0009-z.

DOI: 10.1530/endoabs.113.WB4.1

## WB5.1

**A case of delayed puberty in the male secondary to hypogonadotrophic hypogonadism and partial growth hormone deficiency**

Andrew Down
Bristol Royal Infirmary, Bristol, United Kingdom

We report the case of a 20 year old male referred to Endocrine clinic with short stature and delayed puberty. He sustained a distal radial fracture, subsequently classified Salter-Harris type 2, following a fall onto his outstretched hand whilst intoxicated. Plain radiographs demonstrated skeletal immaturity with open epiphyseal plates. His height, 162.8 cm, was notably less than his 2 older brothers, and his younger sister. His mother achieved a height of 163 cm and his father 188 cm. He would therefore be estimated to achieve a height of 182 cm, or at least 172 cm. He reported that his libido was fine, and he had no difficulty achieving erections or ejaculation. He had no headache or visual symptoms. He had no personal medical history except for the fracture. There was no history of trauma to the head or testicles. He was not taking any regular medications. Educational attainment had was acceptable, and he is employed as an apprentice data engineer. He had a family history of a brother with bladder exstrophy with no associated genetic abnormalities. On assessment in clinic he was noted to have sparse pubic hair, with a complete absence of coarse hair on the jaw, axillae,

limbs, chest and abdomen. He had bilateral gynaecomastia. Testicles had descended normally into the scrotum and had a volume of 20 mls. He did not have any evident features of Cushing's. Given the presenting complaint and findings of incomplete secondary sexual characteristics, he was investigated for delayed puberty. Hormone testing revealed a low-normal total and free testosterone, with low-normal FSH & LH. Random cortisol was non-reassuring, but a short Synacthen test excluded steroid insufficiency. Thyroid function, IGF-1, prolactin, calcium, renal function & electrolytes and haemoglobin concentration were all normal. Coeliac screen was negative and vitamin D level was mildly low. MRI pituitary demonstrated a normal pituitary gland. Insulin tolerance test demonstrated a peak growth hormone level of 4.4 µg/l suggesting partial growth hormone deficiency. The patient has been referred to clinical genetics for counselling and genetic testing to look for an underlying cause of hypogonadotrophic hypogonadism. He will be reviewed in clinic to discuss hormone replacement therapy.

DOI: 10.1530/endoabs.113.WB5.1

# Workshop C: Disorders of the thyroid gland

## WC1.1

**Assay interference in familial dysalbuminemic hyperthyroxinemia**

Qasim Nazir, Abbas Khalil & Amutha Krishnan
Nobles Hospital, Douglas, Isle of Man, United Kingdom

Familial Dysalbuminemic Hyperthyroxinemia is an autosomal dominant condition that is caused by a mutant albumin molecule with an increased affinity for serum thyroxine (T4). Assay interference occurs because the increased affinity leads to spuriously high T4 readings in many immunoassay methods, despite a normal thyroid status. This creates a misleading biochemical profile that mimics true hyperthyroidism and can be misdiagnosed leading to inappropriate treatment. (Khoo *et al*., 2020) A 68-year-old male presented to his GP in 2020 with a UTI. During routine investigations, a mildly elevated total T4 of 23.7 (NR 12-22 pmol/l) was noted, with a normal TSH 0.87 (NR 0.27-4.2 uIU/ml). Previous T4 and TSH were normal in 2012. Repeat thyroid function tests in 2022 demonstrated a further increase in total T4 to 26.7 pmol/l, with persistently normal TSH. This discordant thyroid function raised concerns for secondary hyperthyroidism, prompting referral to endocrinology. His past medical history included benign prostatic hyperplasia and a tonsillectomy. Family history was not significant of any endocrinology disorders. Given persistent biochemical discrepancies and lack of clinical correlation, advanced thyroid studies were performed. These confirmed a diagnosis of Familial Dysalbuminemic Hyperthyroxinaemia (FDH) via ligand binding assay. FDH is a rare, benign and non-thyrotoxic condition, explaining the patient's asymptomatic status despite abnormal thyroid biochemistry. The effect is assay-dependent, with certain platforms known to over-read in FDH. In 2012 the Abbott Architect Free T4 Assay with the Chemiluminescence method was used in our lab, this assay was changed in 2020 to Roche Cobas Pro Elecsys FT4. Abbott Architect was less susceptible when compared to Roche which might explain the normal thyroid tests in 2012. Immunoassay methods are susceptible to interference from FDH, indicating that it is not only a major cause of discordant thyroid function results, but may also lead to significant misdiagnosis, unnecessary investigations and inappropriate treatment. (Khoo *et al*., 2020)

Reference

Khoo, S., Lyons, G., McGowan, A., Gurnell, M., Oddy, S., Visser, W.E., van den Berg, S., Halsall, D., Taylor, K., Chatterjee, K. and Moran, C. (2020). Familial dysalbuminaemic hyperthyroxinaemia interferes with current free thyroid hormone immunoassay methods. *European Journal of Endocrinology*, [online] 182(6), pp.533–538. doi:https://doi.org/10.1530/eje-19-1021.

DOI: 10.1530/endoabs.113.WC1.1

## WC1.2

**Management challenges of subclinical hypothyroidism**

Shree Lakshmi Padmanabhan
University Hospitals Dorset, Bournemouth, United Kingdom

Background

Subclinical hypothyroidism (SCH) in women planning pregnancy is is associated with adverse maternal and fetal outcomes, particularly when thyroid autoantibodies are present. Several professional societies, recommend earlier intervention in such cases. However, a lack of consistent international guidelines makes clinical decision-making difficult in practice.

Case Presentation

A 28-year-old woman with type 1 diabetes mellitus, well controlled on a hybrid closed-loop insulin pump, underwent routine thyroid function testing at her annual review. Initial results in January 2025 were normal (TSH 0.30 mU/l, FT4 18.8 pmol/l). Six months later, repeat testing revealed TSH 8.9 mU/l and FT4 11.6 pmol/l. The patient had discontinued her contraceptive patch six months earlier while planning pregnancy, though menstruation had not resumed. She denied hypothyroid symptoms such as lethargy, weight gain, or cold intolerance. Follow-up thyroid function three weeks later demonstrated partial improvement (TSH 5.6 mU/l, FT4 12.8 pmol/l). Levothyroxine therapy was initially deferred given the downward trend. Six weeks later, TSH was 4.0 mU/l with stable FT4 at 12.8 pmol/l. Her case generated debate within the consultant group. Some clinicians advocated starting levothyroxine immediately due to her pre-conception status, while others advised awaiting thyroid antibody testing. Antibody results revealed markedly positive thyroid peroxidase antibodies (217 IU/mL) and negative TSH receptor antibodies (1.5 IU/l). Considering these findings, along with her intention to conceive, levothyroxine 50 µg daily was initiated.

Discussion

This case highlights the diagnostic and therapeutic uncertainty of SCH in young women planning pregnancy. The presence of thyroid autoantibodies increases the likelihood of progression to overt hypothyroidism, providing a strong rationale for treatment. Guideline recommendations vary. NICE suggests treating SCH (TSH 4–10 mU/l on two occasions) only if the patient is symptomatic. Whereas, BTA recommends treatment when thyroid antibodies are positive or TSH exceeds 10 mU/l, while emphasizing that even mild TSH elevations in pregnancy or pre-conception should be managed as thyroid failure due to associated risks for both mother and fetus. ATA recommends treatment if TSH $>10$, except in patients with increased Cardiovascular risk. This case underscores the need for individualized decision-making, particularly in antibody-positive but asymptomatic women. It also raises the question of whether treatment would still be appropriate in antibody-negative women with TSH levels above 2.5 mU/l during pre-conception.

Conclusion

Managing subclinical hypothyroidism in women planning pregnancy is rarely straightforward. This case shows how fluctuating thyroid results, positive antibody status, and differing guideline recommendations can make decisions challenging.

DOI: 10.1530/endoabs.113.WC1.2

## WC2.1

**Avoiding misdiagnosis: clinical implications of familial dysalbuminaemic hyperthyroxinaemia**

Abbas Khalil, Qasim Nazir & Amutha Krishnan
Nobles Hospital, Douglas, Isle of Man, United Kingdom

Familial Dysalbuminaemic Hyperthyroxinaemia (FDH) is a benign inherited disorder caused by mutations in the albumin gene that increase the affinity of albumin for thyroxine, leading to elevated total thyroxine (T4) levels with normal free hormone concentrations. This biochemical anomaly can complicate the interpretation of thyroid function tests (TFTs) and, if unrecognised, may result in misdiagnosis and inappropriate treatment. We present a case illustrating the long-term clinical and therapeutic implications of undiagnosed FDH. (Kragh-Hansen *et al*., 2017) An 84 year old woman had been diagnosed with presumed "thyrotoxicosis" in 1983, underwent radioiodine treatment in 1989. Over subsequent decades, she was managed for iatrogenic hypothyroidism with levothyroxine replacement. Her clinical course was marked by substantial fluctuations in TFTs, with T4 levels ranging from 24.4 to 47.6 pmol/l (6.5 – 17.0) and TSH ranging from 0.46 to 100 mU/l (0.34 – 4.94). Notably, there were multiple periods where she was clinically euthyroid despite marked biochemical variation, prompting repeated adjustments in levothyroxine dosing. Patient reported feeling symptomatically well when her TSH was within target range with accompanying high T4 level. These fluctuations led to concerns regarding medication adherence.

| | 21/07/06 | 05/10/12 | 12/03/13 | 20/01/14 | 22/06/15 | 27/10/15 | 18/01/19 | 15/04/20 |
|---|---|---|---|---|---|---|---|---|
| T4 | 27.5 | 16.6 | 27.6 | 13.5 | 67.5 | 31.0 | 55.9 | 33.3 |
| TSH | 0.4 | 56.8 | 2.46 | >100.0 | 0.18 | 33.83 | 0.32 | 19.00 |

In 2020, in view of these marked fluctuations in her TFTs her serum sample was sent to Addeenbrooks hospital which confirmed FDH, finally resolving the long-standing diagnostic uncertainty. The diagnosis was communicated to the patient, with reassurance that FDH is a benign, inherited condition requiring no specific therapy. The patient was discharged from specialist endocrine care, with advice that any future levothyroxine dose adjustments should be guided by clinical assessment and TSH levels. Retrospective review of the patient's initial presentation in the 1980 s suggested that FDH may have contributed to the apparent hyperthyroxinaemia and possible misclassification as thyrotoxicosis, though this could not be confirmed due to destruction of historical records. The case underscores the importance of considering FDH in patients with discordant TFTs—particularly elevated total T4 with non-suppressed TSH—and stable clinical status. Recognition of FDH can prevent unnecessary investigations, inappropriate treatments, and prolonged diagnostic uncertainty. This case highlights the need for increased awareness of rare binding protein abnormalities in the interpretation of thyroid biochemistry. Early use of specialist assays or referral to reference laboratories can facilitate timely diagnosis, reducing the risk of overtreatment and improving patient confidence in their care.

Reference

Kragh-Hansen U, Galliano M, Minchiotti L. *Clinical, Genetic, and Protein Structural Aspects of Familial Dysalbuminaemic Hyperthyroxinaemia and Hypertriiodothyroninemia*. Front Endocrinol (Lausanne). 2017;8:297. doi:10.3389/fendo.2017.00297

DOI: 10.1530/endoabs.113.WC2.1

## WC2.2

**Iatrogenic thyroid dysfunctions: two clinical cases demonstrating the jod-basedow and wolf-chaikoff effects**

Atia Haroon[1], Malagalage Nishadi Saumya Kumari Perera[2] & Ganganatha Govinnage[2]
[1]Grange University Hospital, Aneurin Bevan University Health Board, Cwmbran, South Wales, United Kingdom; [2]Basildon University Hospital, Mid and South Essex NHS Foundation Tust., Basildon, United Kingdom

Background
Excessive iodine exposure can precipitate thyroid dysfunctions through two mechanisms: the Jod-Basedow effect, where failure of inhibition and autoregulation of thyroid gland leads to hyperthyroidism, and the Wolf-Chaikoff effect - a phenomenon in which persistent inhibition of the thyroid gland results in hypothyroidism. Iodinated contrast media and amiodarone are common iatrogenic triggers, and elderly patients and those with underlying thyroid disease are particularly at risk (1–2).
Case 1
An 80-year-old man with ischaemic heart disease, atrial fibrillation, and heart failure presented with diarrhoea and unintentional weight loss. Investigations showed hyperthyroidism (T4 32.3 pmol/l, TSH $<0.01$ mU/l) with negative antibodies and multinodular goitre on ultrasound. Previous results indicated subclinical hyperthyroidism. Three weeks earlier, he had undergone percutaneous coronary intervention with iodinated contrast. He was diagnosed with Jod-Basedow thyrotoxicosis and commenced on carbimazole with improvement on follow-up. It was noteworthy that he did not exhibit any autonomic signs and symptoms of thyrotoxicosis likely due to regular use of bisoprolol for his atrial fibrillation.
Case2
An 89-year-old man with chronic kidney disease and atrial fibrillation on long-term amiodarone was admitted with worsening renal function and bradycardia with an average heart rate of 50 beats per minute. Investigations revealed profound hypothyroidism (TSH 167.6 mU/l, FT4 4.4 pmol/l) with negative autoantibodies and a normal ultrasound scan of the thyroid gland. This was consistent with amiodarone-induced hypothyroidism demonstrating the Wolf-Chaikoff effect. Amiodarone was discontinued and levothyroxine was initiated, leading to euthyroidism during follow-up.
Conclusion
Iodine-induced thyroid dysfunction is an important but under-recognised complication. These two cases demonstrate that susceptible patient groups, including the elderly population and those with chronic kidney disease and underlying thyroid conditions, are at an increased risk of developing overt thyroid dysfunction following iatrogenic iodine exposure. A detailed clinical history, including recent contrast exposure and medication history, with a low threshold for thyroid function testing, is essential to establish a diagnosis. Prompt recognition allows timely treatment and optimisation of outcomes.
References
1. Leung AM, Braverman LE. Consequences of excess iodine. Nat Rev Endocrinol. 2014 Mar;10(3):136-42. doi: 10.1038/nrendo.2013.251. Epub 2013 Dec 17. PMID: 24342882; PMCID: PMC3976240.
2. Seo Young Sohn, Kosuke Inoue, Connie M Rhee, Angela M Leung, Risks of Iodine Excess, *Endocrine Reviews*, 2024;, bnae019, https://doi.org/10.1210/endrev/bnae019
DOI: 10.1530/endoabs.113.WC2.2

## WC2.3

**From subclinical hyperthyroidism to atrial fibrillation: the silent progression of multinodular goitre**

Muhammad Siddique & PuiSan Yap
Aberdeen Royal Infirmary, Aberdeen, United Kingdom

Background
Subclinical hyperthyroidism is characterized by low or suppressed thyroid stimulating hormone (TSH) with normal thyroxine(T4) and normal Triiodothyronine (T3) on thyroid function test (TFT). It has various endogenous and exogenous causes. It may have subtle clinical signs and symptoms. Studies have shown that subclinical hyperthyroidism is associated with increased coronary heart disease mortality, atrial fibrillation, heart failure and fractures. Patients are offered treatment if over 65 years or in those under 65 years old who are symptomatic or with osteoporosis and heart disease.
Case
A 59-year-old female with background history of multinodular goitre and subclinical hyperthyroidism diagnosed in 2010 presented to GP new symptoms of fatigue. In 2010, she was diagnosed with 2 cm nodule in right upper lobe and had two negative fine needle aspiration cytology (FNAC). At that time, her TFTs showed subclinical hyperthyroidism with TSH $<0.10$ mU/l (0.35- 3.30 mU/l), FT3 of 5.3 pmol/l (3.0-7.0 pmol/l) and FT4 of12 pmol/l (10-25 pmol/l). She was discharged from clinic with plan of annual TFTs monitoring. On surveillance, she persistently remained subclinical hyperthyroid and asymptomatic. In 2025, she developed another nodule on same side of her neck which was referred to ear, nose and throat (ENT) for urgent review for suspected cancer. She was evaluated by ENT, and she was for conservative management given unchanged picture over last 15 years. At the same time, there was an incidental finding of atrial fibrillation on her smart watch. The assessment revealed she had persistent subclinical hyperthyroidism on biochemistry testing and ECG showed new atrial fibrillation. She was reviewed by cardiology team and had echocardiogram which showed dilated atria and reduced LVEF of 45%. She was treated with anticoagulation and bisoprolol. On endocrine review, she described that she is getting fatigue over last few months but denied any other specific symptoms of hyperthyroidism or palpitations. She was an ex-smoker, and her mother had thyroidectomy. Thyroid function test showed subclinical hyperthyroidism with suppressed TSH $<0.01$ mU/l (0.35-4.94 mU/l) and normal T3 of 5.5 pmol/l (2.4-6.0 pmol/l) and T4 of 14 pmol/l(8.0- 19.1 pmol/l). Both thyrotropin receptor and thyroid peroxidase antibodies were negative. In the context of long standing suppressed TSH and new atrial fibrillation, she was started on carbimazole.
Discussion points
When should treatment be considered in asymptomatic patients? Can we prevent all potential complications with early interventions? Treatment of choice medication versus low dose radioiodine? Does borderline thyroid function with positive antibodies need treatment?
DOI: 10.1530/endoabs.113.WC2.3

## WC3.1

**When numbers lie: misleading thyroid profile due to heterophile antibody interference in a comorbid inpatient**

Vidya Nair, Sing Sim, Piyumi Wijewickrama, Kade Flowers & Samuel Brown
Royal Sussex County Hospital, Brighton, United Kingdom

Introduction
Thyroid function tests are crucial in diagnosing and managing endocrine disorders, but their reliability can be compromised by analytical interference. Rare but important cause is heterophile antibody interference where endogenous antibodies bind to assay antibodies resulting in abnormal results. This can mimic thyroid disease leading to unnecessary investigations or treatments. Correlating laboratory data with patient's clinical status and working closely with biochemistry colleagues will help in identifying this promptly.
Case report
A 72-year-old gentleman with type 2 diabetes mellitus on insulin and a background of left renal cell carcinoma was admitted with biliary sepsis and an obstructed femoral hernia requiring surgical repair. During admission, routine thyroid function tests performed on the Roche platform showed a markedly elevated free thyroxine (FT4) (70.9 mU/l) and with an inappropriately normal thyroid stimulating hormone (TSH) (4.58 pmol/l). Free triiodothyronine (FT3) was also elevated (9.2 pmol/l). Thyroid antibodies were negative. The patient was asymptomatic and clinically euthyroid, He was receiving unfractionated heparin for venous thromboembolism prophylaxis, raising a suspicion of heparin-induced displacement of T4 from binding proteins. Heparin was withheld for 24 hours but repeat thyroid functions remained unchanged. Given the discordance between biochemical and clinical findings, the case was discussed with biochemists and targeted interference studies were undertaken. Dilution studies demonstrated non-linear FT4 and FT3 values; however, this was also seen in control samples and therefore reflected assay characteristics rather than interference. Polyethylene glycol (PEG) precipitation produced a marked reduction in free hormone concentrations in the patient's sample but not in controls, consistent with the presence of a large protein such as a heterophile antibody. To confirm the finding, samples were tested on the Abbott platform, showing normal results (TSH 3.41 mU/l, FT4 16.2 pmol/l, FT3 3.09 pmol/l). A sample was also sent for assessment of total T4 levels which confirmed calculated FT4 was slightly lower than measured FT4, consistent with displacement. The overall picture confirmed heterophile antibody interference as the key explanation for the abnormal thyroid profile with heparin effect being a possible confounding factor. No thyroid-specific treatment or further investigations were needed.

| Test platform | TSH mU/l | FREE T4 pmol/l | Free T3 pmol/l |
|---|---|---|---|
| Roche | 4.58 | 70.9 | 9.2 |
| Abbot | 3.41 | 16.2 | 3.09 |

Conclusion
This case demonstrates that marked biochemical abnormalities in a euthyroid patient should raise suspicion of assay interference. Heterophile antibody interference can be identified with PEG precipitation and cross-platform testing. Close clinician–laboratory collaboration prevents unnecessary investigations, treatment, and potential patient harm.

DOI: 10.1530/endoabs.113.WC3.1

## WC3.2

**An uncommon explanation of abnormal thyroid function tests: assay interference with macro-TSH**

Christina Triantafyllou & Koteshwara Muralidhara
Kingston Hospital, London, United Kingdom

Case
A 31-year-old female presented to Gynaecology abroad with a three-month-history of secondary amenorrhoea in 2011. Thyroid function checked and TSH was high with normal free T4 (FT4) and free T3 (FT3). She was commenced on Levothyroxine with gradual dose titrations up to a maximum dose of 75 micrograms daily. Despite variations in levels and some response, TSH never normalised, and she stopped Levothyroxine in 2015. She moved to the UK in 2016 and was referred to our Service in 2020 with "abnormal thyroid function" and TSH ranging between 32 and 59 mU/l (normal reference range 0.35-5 mU/l). FT4 and FT3 were normal on serial testing with negative TPO antibodies. Pituitary function was checked with normal cortisol, prolactin and gonadotrophins. Patient was taking no regular medication, except supplements of vitamin C, zinc and occasional use of bone complex. She reported occasional cold intolerance but no other symptoms of thyroid dysfunction. Her mother had normal TSH; her father and brother had never been tested. Her TFTs were repeated and sent to another lab to exclude assay interference; TSH confirmed to be high at 39.9 mU/l in our lab and 17.43 mU/l in external lab. Given she had experienced some response to the raised TSH with Levothyroxine, she was diagnosed with subclinical hypothyroidism, advised to restart Levothyroxine and discharged. She went back to Sweden and returned to the UK in 2024 at 24 weeks of her first pregnancy. She had been tested for interference of macro-TSH and confirmed in Sweden. Her thyroid function tests were repeated with us, and further tests were sent to Addenbrooke's Hospital where interference with macro-TSH was confirmed. TSH on Atellica was 34.16 mU/l with borderline recovery with polyethylene glycol (PEG) precipitation. The best estimate of bioactive TSH was 5.5-16.3 mU/l.
Discussion
Macro-TSH is a rare finding, caused by binding of TSH to other plasma proteins, commonly immunoglobulins, resulting in falsely elevated TSH measurement. The biochemical profile mimics subclinical hypothyroidism and if not identified early, can result in inappropriately high Levothyroxine doses. Due to assay interference, TSH is not a reliable indicator of thyroid status. Clinical judgement and monitoring of FT4 and FT3 is recommended to guide management. Our patient remained clinically and biochemically euthyroid for the duration of her pregnancy and did not require any treatment. As macro-TSH can cross the placenta and interfere with the heel-prick test, further neonatal testing might be indicated.

DOI: 10.1530/endoabs.113.WC3.2

## WC3.3

**Elevated TSH with elevated FT3 and FT4: a diagnostic dilemma**

Andrew Gerges[1] & Suresha Muniyappa[2]
[1]Sheffield Teaching Hospitals NHS Trust, Sheffield, United Kingdom; [2]Doncaster and Bassetlaw Teaching Hospitals NHS Trust, Doncaster, United Kingdom

Introduction
Central hyperthyroidism, characterized by elevated thyroid hormones (FT3 and FT4) and inappropriately normal or elevated TSH, presents a diagnostic challenge. The two primary differential diagnoses are TSH-secreting pituitary adenomas (TSHomas) and resistance to thyroid hormone (RTH). While both conditions can cause similar biochemical abnormalities, they have distinct underlying mechanisms. Differentiating between these conditions requires dynamic testing, imaging, and, in the case of RTH, genetic testing.
Case Report
A 43-year-old male presented with elevated TSH (6.28 mU/l), FT4 (31.7 pmol/l), and FT3 (8.3 pmol/l), consistent with central hyperthyroidism. These findings had remained consistent since 2012, with an FT4 of 29.3 pmol/l. The patient reported no symptoms of hyperthyroidism, including no tremors, palpitations, or significant weight changes. He did mention experiencing headaches twice a week but denied visual disturbances, galactorrhea, or changes in libido. On clinical examination, his heart rate was normal (75 BPM), and his BMI was 29.1. The patient's medical history included atrial fibrillation and asthma, for which he takes Bisoprolol, Atorvastatin, and Ezetimibe. Laboratory tests excluded Dysalbuminemic Hyperthyroxinemia, and thyroid antibodies were negative. Pituitary MRI revealed a 5 mm microadenoma on the right side, with no abnormalities in the pituitary stalk, optic chiasm, or cavernous sinuses. These findings raised suspicion for TSHoma. However, further investigation was needed to clarify the diagnosis. The patient was referred to the pituitary multidisciplinary team (MDT) for further evaluation, which included a complex pituitary scan and TRH stimulation test. Genetic testing was also recommended to rule out RTH, a condition in which tissues, including the pituitary, are resistant to thyroid hormone feedback.
Conclusion
This case presents a diagnostic challenge of elevated TSH with high FT3 and FT4, where the differential diagnosis includes TSHoma and RTH. The TRH stimulation test is crucial in differentiating these conditions, with TSHoma typically showing a blunted or absent TSH response, while RTH may show exaggerated or normal TSH response despite elevated thyroid hormones. Pituitary MRI remains essential for diagnosing TSHoma, while genetic testing is the definitive tool for diagnosing RTH. While the diagnosis is still pending, this case highlights the importance of a thorough diagnostic approach, including dynamic testing, imaging, and genetic analysis to guide appropriate management.

DOI: 10.1530/endoabs.113.WC3.3

## WC4.1

**A challenging case of resistance to thyroid hormone presenting with atrial fibrillation in an elderly woman**

Ahmed Ali[1,2], Salma Elhassan[2] & Bheesham Tarachand[1]
[1]North Tees and Hartlepool NHS Foundation Trust, Stockton-On-Tees, United Kingdom; [2]University of Khartoum, Khartoum, Sudan

Background
Resistance to thyroid hormone (RTH) is a rare disorder, most often caused by pathogenic variants in the *THRB* gene, characterised by elevated circulating thyroid hormones with non-suppressed or elevated thyroid-stimulating hormone (TSH). Clinical presentations range from asymptomatic goitre to mixed features of hypo- and hyperthyroidism, with significant inter-individual variability.
Case Presentation
A 78-year-old Caucasian woman presented with new-onset atrial fibrillation (AF) and fast ventricular response. Initial thyroid function tests revealed elevated free thyroxine (fT4) with normal TSH. She re-presented within one week with recurrent palpitations, gastrointestinal symptoms, and mild weight loss. Repeat investigations confirmed persistently elevated fT4 and free triiodothyronine (fT3) with non-suppressed TSH. Autoimmune thyroid disease was excluded, and radionuclide imaging demonstrated multinodular goitre with retrosternal extension. Despite carbimazole therapy, thyroid hormone levels remained high. Further evaluation ruled out assay interference and TSH-secreting pituitary adenoma (normal alpha subunit, unremarkable pituitary MRI). Genetic testing identified a heterozygous THRB c.959 G>C (p.Arg320 Pro) variant, classified as likely pathogenic, confirming RTH. Carbimazole was discontinued. The patient unfortunately died several weeks later from unrelated causes.
Discussion
This case illustrates a late-onset presentation of genetically confirmed RTH complicated by AF. The coexistence of multinodular goitre and AF initially suggested toxic nodular disease, delaying recognition of RTH. Cardiovascular manifestations are uncommon in RTH, but tissue-specific variability in thyroid hormone receptor expression may explain susceptibility in selected patients.
Conclusion
RTH should be considered in patients with elevated thyroid hormones and non-suppressed TSH after exclusion of secondary causes. Early endocrine involvement and genetic testing are crucial to avoid unnecessary antithyroid therapy and to guide family counselling.

DOI: 10.1530/endoabs.113.WC4.1

## WC4.2

**Macrothyrotropin as a cause of falsely elevated TSH in two clinically euthyroid patients**

Isabelle van Heeswijk[1], Vakkat Muraleedharan[2], Melanie Griffiths[2] & Steve Jones[2]
[1]Queens Hospital Burton, Burton on Trent, United Kingdom; [2]Kings Mill Hospital, Mansfield, United Kingdom

Introduction
MacroTSH or macrothyrotropin is a complex of TSH with IgG, resulting in a molecule with large molecular mass (>150 kDa) but low bioactivity. It can result in falsely elevated TSH levels due to persistence in the circulation, whilst T4 levels remain in normal range and the patient is clinically euthyroid. The clinical and biochemical picture mimics that of subclinical hypothyroidism. Failure to identify macroTSH may result in unnecessary hormone replacement.
Case Description
A 94 year old gentleman with a background of chronic lymphocytic leukaemia, treated with ibrutinib underwent a thyroid function test as part of a screen for weight gain and lethargy. Unexpectedly, as he was clinically euthyroid, the TSH was markedly elevated at 98.0. T4, however, was in the normal range at 14.4. Initially, he was presumed to have subclinical hypothyroidism above the threshold requiring levothyroxine therapy. The possibility of macro-TSH was raised by the clinical chemistry team and a MACROTSH-PEG precipitation study was performed which confirmed the presence of large molecular weight proteins. As the TSH was raised (29 mIU/l) even on the PEG precipitation study, the patient was presumed to have a degree of subclinical hypothyroidism in addition. He was commenced on levothyroxine 25 micrograms once daily. Follow up thyroid function tests demonstrated a decrease in TSH. A second case concerns as a 62 year old female with a background of type 2 diabetes AF and fatty liver, admitted with weakness. TFTs were performed as part of a neuropathy screen. She was clinically euthyroid at presentation. Initial TSH was 23.0 and T4 17.9. PEG precipitation demonstrated 38% recovery (TSH 8.74). The patient was not treated due to the corrected TSH <10 and normal T4. She was diagnosed with a sensory motor axonal polyneuropathy and following a course of prednisolone for vasculitis, TSH fell back to normal range.
Discussion
The polyethylene glycol precipitation method is used in order to remove high molecular weight proteins that could falsely elevate TSH readings. A low post-PEG TSH recovery indicates the presence of high molecular weight molecules interfering with the assay (including macro-TSH or interfering antibodies). This method was utilised in order to differentiate possible macro-TSH from subclinical hypothyroidism in our patients.

DOI: 10.1530/endoabs.113.WC4.2

## WC4.3

Abstract Withdrawn

DOI: 10.1530/endoabs.113.WC4.3

## WC5.1

**Contrasting discordant thyroid function tests in a family with resistance to thyroid hormone β syndrome**

Sarah Chew Sue Mei, Mark Cohen & Bernard Freudenthal
Barnet Hospital, Royal Free London NHS Foundation Trust, London, United Kingdom

A 79-year-old female was referred to our endocrinology service for evaluation of persistently discordant thyroid function tests (TFTs). She had been diagnosed with primary hypothyroidism (no thyroid antibodies were sent) in 2004 and had been treated with levothyroxine since then. On presentation, she was clinically euthyroid and there was no neck swelling. Her weight was 62 kg. TFTs showed elevated free thyroxine (FT4) (29 pmol/l (RR 11.9-21.6)), normal total triiodothyronine (FT3) (4.7 pmol/l (RR 3.1-6.8)), and elevated thyroid stimulating hormone (TSH) (6.44 mU/l (RR 0.3-4.2)), while taking levothyroxine 150 mg daily. When her levothyroxine dosage was reduced to 125 mg daily, she reported symptoms of fatigue, cold intolerance, and weight gain. Her body temperature was 35.8°C. These clinical features of hypothyroidism along with a significant rise in TSH (78 mU/l) and normal FT4 (17.9 pmol/l) prompted an increase of levothyroxine up to 200 mg daily. TFTs on levothyroxine 200 mg daily remained discordant, with elevated FT4 (35.1 pmol/l), normal FT3 (5 pmol/l) and a normalised TSH(1.47 mIU/l). Her hypothyroid symptoms resolved, but she subsequently was diagnosed with atrial fibrillation. Underlying causes of her persistently discordant TFTs were considered. Patient reported full compliance to levothyroxine and there was no concern for malabsorption or accelerated metabolism of thyroxine. Other potential causes of intercurrent illness or concurrent medication were excluded. Laboratory analyses excluded assay artefact and abnormal circulating thyroid hormone binding proteins. During this period of investigation, her 50-year-old daughter reported symptoms of thyrotoxicosis (anxiety, sweating and palpitations), and was found to have elevated FT4 (34.9 pmol/l), elevated FT3 (7.7 pmol/l) and normal range TSH (1.5 mIU/l). MRI Pituitary was normal, and dynamic testing with thyrotropin-releasing hormone (TRH) or T3 could not be performed due to her needle-phobia. Genetic analysis identified a thyroid hormone receptor beta (THRbeta) gene heterozygous mutation c.749 T>Cp.(Ile250 Thr), consistent with Resistance to Thyroid Hormone-beta (RTH-β) syndrome. Considering the index case's need to maintain elevated FT4 levels to achieve a normal TSH level, coupled with the confirmed diagnosis of RTH-β in her daughter (who likely inherited the maternal mutation), a presumptive diagnosis of coexistent RTH-β and primary hypothyroidism was established for the index case. She remains well with long-term levothyroxine therapy, targeted to achieve normal range TSH.
Learning points
(1) The requirement for supraphysiological doses of levothyroxine (above 1.6μg/kg) to normalize TSH in primary hypothyroidism, in conjunction with raised FT4 and/or FT3 concentrations, can suggest underlying, coexistent RTHβ
(2) Elevated FT4 and/or FT3 with non-suppressed (normal) TSH in relatives of an index case may indicate an inherited condition such as RTHβ.
(3) Further research is needed to define the optimal TSH targets for managing hypothyroidism (of other etiologies) with concurrent RTHβ.

DOI: 10.1530/endoabs.113.WC5.1

## WC5.2

**Thyroid hormones on the fence: navigating diagnostic gray zones**

Saadia Saeed, Mohammad Misbah & Simon Holmes
Mid Yorkshire Teaching NHS Trust, Wakefield, United Kingdom

A 30-year-old gentleman presented with non-specific symptoms of tiredness and lethargy persisting over many years. Initial private TFTs in 2021 revealed a normal TSH of 2.29 mIU/l and elevated FT4 at 39.4 pmol/l. Repeat testing by his GP showed similar results (TSH 1.85, FT4 39.3, and free T3 9.3 pmol/l). Due to these abnormal thyroid function results and ongoing symptoms, he was referred to Endocrinology for further assessment. The patient reported no hyperthyroid symptoms such as weight loss, fever, increased sweating, neck pain / swelling, tremor, or palpitations. His medical history was unremarkable, with no medications except for past smoking cessation 10 years prior. Family history included multiple sclerosis in his mother only. On examination, he was euthyroid with no goitre and no Thyroid Eye signs. Given the discordant TFT results and clinical euthyroidism, an alternative assay at Leeds confirmed elevated thyroid hormones (TSH 2.0, FT4 35, FT3 11 pmol/l). The patient led an active lifestyle as a fitness enthusiast, frequenting the gym 4–5 times weekly, and had a physically demanding occupation. He regularly took creatine, multivitamins, and minerals, which were discontinued for 6–8 weeks to exclude assay interference. Repeat TFTs remained unchanged (TSH 1.85, FT4 39.3, FT3 9.3). Subsequently, a thyrotropin-releasing hormone (TRH) stimulation test was performed with the following results:

| Time (minutes) | TSH (mIU/l) | Free T4 ( pmol/l) |
|---|---|---|
| 0 | 1.85 | 40.9 |
| 30 | 20.1 | 44.3 |
| 60 | 13.1 | 41.1 |

The exaggerated rise in TSH following TRH administration strongly suggests a diagnosis of thyroid hormone resistance (THR) rather than a TSH-secreting pituitary adenoma (TSHoma), which typically shows a blunted TSH response. The patient exhibited no clinical signs of pituitary disease, lowering suspicion for TSHoma. Given his euthyroid status and absence of symptoms, no thyroid hormone treatment was initiated. This case exemplifies the diagnostic challenges in thyroid hormone excess with non-suppressed TSH and highlights the utility of the TRH test in differentiating THR from TSHoma
Conclusion
- The TRH test showed a clear, exaggerated TSH rise, which strongly favors THR over TSHoma.
- The lack of pituitary symptoms or clinical suspicion lowers the pre-test probability of TSHoma.
- MRI and alpha-subunit measurement remain options if the clinical or biochemical picture changes or if there is diagnostic uncertainty.
- This approach aligns with a targeted, cost-effective diagnostic strategy minimizing unnecessary tests.
- Will continue clinical and biochemical monitoring to catch any evolution.

DOI: 10.1530/endoabs.113.WC5.2

# Workshop D: Disorders of the adrenal gland

## WD1.1

### Adrenal insufficiency: the critical crossroads!

Namita Bhardwaj[1] & Fahad Arshad[2]
[1]Sheffield Teaching Hospitals, Sheffield, United Kingdom; [2]Sheffield Teaching Hospital, Sheffield, United Kingdom

57 years old male with past history of hypertension, was diagnosed with severe aortic valve regurgitation, dilated aorta and left ventricle while being worked up for cough and exertional shortness of breath. He was a nonsmoker with active lifestyle and no alcohol intake. He was admitted for elective mechanical aortic valve replacement and reimplantation of coronary arteries. On the day of surgery (day 0) his haemoglobin dropped from 157 to 73 g/l post operatively for which he received blood transfusions. On day 5, he underwent a repeat procedure due to chest wall bleeding. This was further complicated by heparin induced thrombocytopenia (HIT) and aortic valve abscess. On day 8 he developed mild hyponatremia and orthostatic hypotension. Hyponatremia work up showed low cortisol levels with investigations summarised below in table. He did not receive any intra-operative steroids or medications that could lower cortisol level.

| TEST | Value (reference range) |
|---|---|
| Na | 127 mmol/l on day 11(133-146) |
| Random Cortisol | 54 mmol/l at 1245 hrs on day 11 |
| TSH | 8.3 mIU/l (0.27-4.2) on day 10<br>1.8 mIU/l on day 29 |
| T4 | 16.2 pmol/l ( 11.9-21.6) |
| ACTH | 272 ng/l on day 10 (7.2-63.3 ) |
| Renin | 0.1 nmol/l /h (0.3-2.2) |
| Aldosterone | < 50 pmol/l ( 0-630) |
| Serum osmolality | 265 mOSM/kg ( 275-295) |
| CT Adrenals (day 12) | Bulky adrenals, no evidence of high attenuation collections, shape distortion or peri-adrenal fluid to strongly suggest acute or large haemorrhage. New changes compared to pre-operative changes |
| Adrenal MDT discussion on day 23 | Images could represent hypertrophy. Planned to repeat adrenal CT in 3 months' time. |

He was clinically diagnosed with **primary adrenal insufficiency on the day of low cortisol presumably secondary to bilateral adrenal haemorrhages.** Hyponatremia and postural hypotension improved within 2 days of starting intravenous hydrocortisone replacement. After being managed for 21 days in cardiac intensive care unit, he clinically improved. Subsequently, he was discharged with oral hydrocortisone replacement and fludrocortisone with discharge advice on sick day rules. As per the MDT discussion, the plan was to repeat his CT adrenals in 3 months' time. During admission he was also managed for atrial fibrillation, upper limb occlusive thrombus and HIT under guidance of haemotology team. At the time of writing up this case, he was due for a repeat CT Adrenals followed by Endocrine clinic appointment. He has been doing well post discharge with no further hyponatremia and no symptoms suggesting orthostatic hypotension.

DOI: 10.1530/endoabs.113.WD1.1

## WD1.2

### Hypercalcaemia as the initial manifestation of addison's disease

Nyein Nge Nge[1,2], Taofeek Ojewuyi[2], Ali Rathore[2], Ayanbola Adepoju[2] & Orlaith Fogarty[2]
[1]Addenbrooke Hospital, Cambridge, United Kingdom; [2]Southend University Hospital, Southend-On-Sea, United Kingdom

Background
Hypercalcemia, serum calcium above the reference range, is common biochemical finding. When symptomatic, it may present with bone pain, renal colic, constipation, abdominal pain, or neuropsychiatric manifestations-depression. Hypercalcemia is broadly classified into **PTH-dependent** and **PTH-independent** causes. PTH-dependent causes include primary hyperparathyroidism, tertiary hyperparathyroidism, and familial hypocalciuric hypercalcemia, while PTH-independent causes are often malignancy, granulomatous diseases (e.g., sarcoidosis, tuberculosis), thiazide use, and less commonly, adrenal insufficiency. The mechanisms underlying hypercalcemia in adrenal insufficiency are not fully understood but are thought to involve increased renal calcium reabsorption and enhanced bone resorption through elevated sclerostin levels. Below is a case of undiagnosed primary adrenal insufficiency presenting with hypercalcemia, hyponatremia, and acute kidney injury.
Clinical Case
A 39-year-old man presented with dizziness, low mood, anorexia, nausea, vomiting, and unintentional weight loss. His past medical history included subclinical hypothyroidism and depression, and was taking sertraline. He was clinically dehydrated, hypotensive with a blood pressure of 93/72 mmHg, and had generalized skin hyperpigmentation. Initial blood tests revealed hyponatremia (Na-126 mmol/l,133–146), hypercalcemia (adjusted calcium 3.05 mmol/l,2.2–2.6), and acute kidney injury with a serum creatinine 143μmol/l (baseline 88). Thyroid studies showed elevated TSH (11.36 mU/l,0.3–5.0) with freeT4 at the lower end of normal(8.9 pmol/l,7.9–16.0). An initial working diagnosis was hypercalcemia-induced dehydration with acute kidney injury. He was commenced on intravenous fluids, and sertraline was discontinued in view of hyponatremia. Further investigations demonstrated suppressed parathyroid hormone (0.3 pmol/l,1.3–9.3), excluding primary hyperparathyroidism. Urine osmolality was 390 mmol/kg with urine sodium of 43 mmol/l. In the context of hypotension, hyponatraemia, and other biochemical abnormalities, adrenal insufficiency was suspected. Morning serum cortisol was <11 nmol/l (185–624), confirming adrenal insufficiency. The patient was commenced on hydrocortisone replacement. Levothyroxine therapy for hypothyroidism was initiated one week later. Both hypercalcemia and hyponatremia resolved with treatment. At follow-up, ACTH was markedly elevated at 1301 ng/l (<50), and adrenal autoantibodies were positive, confirming autoimmune primary adrenal insufficiency. Aldosterone was suppressed(<60 pmol/l,90–700) with normal renin (1.4 nmol/l/hr,0.5–3.5). Curiously, renin was initially normal, an uncommon finding in Addison's disease. The patient was initially managed without fludrocortisone, with close renin monitoring. Fludrocortisone was introduced at third months when renin levels began to rise.
Conclusion
This case highlights Addison's disease can present atypically with PTH-independent hypercalcemia, hyponatremia, hypotension, and acute kidney injury. A high index of suspicion will provide prompt diagnosis in patients with unexplained electrolyte disturbances, especially with systemic features such as weight loss and hyperpigmentation. Early glucocorticoid replacement, prior to thyroid hormone initiation, is essential to prevent adrenal crisis[3]. Renin level may be normal at the initial stage, but mineralocorticoid replacement will always be required. Prompt diagnosis and treatment can fully reverse metabolic abnormalities, including the rare manifestation of hypercalcemia.

DOI: 10.1530/endoabs.113.WD1.2

## WD1.3

### Intersecting axes in non-classical cah: adrenal androgens and obesity-related hypogonadism in adulthood

Saadia Saeed, Emma Ward & Talat Mushtaq
Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

A 25-year-old Caucasian male was reviewed in adult endocrinology in Leeds, with a background of non-classical congenital adrenal hyperplasia (CAH) due to partial 21-hydroxylase deficiency. He initially presented at age 5 with behavioural difficulties and body odour, suggestive of early androgen exposure. Examination revealed normal prepubertal genitalia. Investigations showed elevated 17-hydroxyprogesterone (17 OHP; 10.0 nmol/l) and suboptimal cortisol response on synacthen testing, with peak 17 OHP of 258 nmol/l. Urine steroid profiling and genetic testing confirmed the diagnosis. Hydrocortisone was commenced (8–10 mg/m$^2$/day). By age 11, he showed pubertal advancement (bone age 15.1 years; G4 P4; testes 15 mL). GnRH analogue therapy was offered but declined. By age 13, puberty was nearly complete (G5 P5; testes 20–25 mL) with final height on the 50 th centile. Hydrocortisone was tapered to 6.9 mg/m$^2$/day based on 17 OHP levels. Adolescence was complicated by poor adherence, emotional difficulties, and CAMHS involvement. At 16, synacthen testing showed adequate adrenal reserve (cortisol 243 → 457 nmol/l), and maintenance steroid therapy was discontinued. Hydrocortisone was advised only during illness or stress. During this time, he developed obesity and disordered eating behaviours. At age 25, he re-presented with fatigue, delayed sleep phase, and significant weight gain (BMI 47.5). He had restarted paediatric-dose hydrocortisone via his GP but noted no improvement. Repeat SST confirmed adequate adrenal reserve (cortisol 425 → 713 nmol/l), and steroids were stopped. 17 OHP remained elevated (147 nmol/l), as did androstenedione (14.8 nmol/l). Testosterone was low (6.2 nmol/l; ref 8–30) with low SHBG (17) and preserved gonadotropins (LH 4.5, FSH 2.9), consistent with obesity-induced hypogonadotropic hypogonadism. Estradiol was normal; libido and erectile function were intact. Testicular ultrasound was arranged to exclude TARTs. He is now a university student in a stable relationship and is keen to attend Tier 3 weight management services. He has been referred for sleep studies to exclude OSA.
Discussion
Dynamic interplay between adrenal and gonadal axes in non-classical CAH: Although adrenal androgen excess persisted, testicular output was suppressed by obesity-related hypogonadism. In adulthood:
- Adrenal androgens in partial CAH may only modestly boost testosterone.
- If obesity suppresses HPT axis, testicular loss outweighs adrenal contribution.

- The result is low testosterone despite a condition once associated with excess androgens.

Testes provide ~90–95% of adult male testosterone; adrenal overproduction cannot compensate when HPT axis function is impaired.

Conclusion

This case underscores the importance of holistic, longitudinal care in endocrine conditions with paediatric onset. In non-classical CAH, persistent adrenal androgen production does not guarantee sufficient androgenisation in adulthood if testicular output is compromised. Clinicians must be vigilant for obesity-related secondary hypogonadism, and management should prioritise metabolic health alongside endocrine control.

DOI: 10.1530/endoabs.113.WD1.3

## WD2.1

### Isolated ACTH deficiency: an unusual crisis arising from delayed diagnosis

Saadia Khan
University Hospital of North Durham, Durham, United Kingdom

Background

Isolated ACTH deficiency (IAD) is a rare cause of secondary adrenal insufficiency. Unlike Addison's disease, classical features such as hyperpigmentation and marked electrolyte imbalance are absent, often leading to delayed recognition. Patients typically present with nonspecific symptoms such as fatigue, anorexia, and weight loss, which may progress to adrenal crisis if untreated.

Case Presentation

We report a 75-year-old gentleman with no significant past medical history aside from ischaemic heart disease and osteoarthritis, who experienced progressive decline over several months. He presented initially with fatigue, recurrent chest infections, anorexia, weight loss, and generalized weakness. Despite extensive investigations—including CT thorax/abdomen/pelvis, bronchoscopy, bone marrow biopsy, MRI brain and spine, and PET scanning—no underlying pathology was identified. His course was complicated by refractory hypercalcemia, hyponatremia, and acute kidney injury. Over four months, he deteriorated from being fully independent to bedbound, with severe muscle wasting, unsafe swallow necessitating nasogastric feeding, and recurrent hospital admissions. Neurological causes, including motor neuron disease, were strongly considered, but investigations remained unrevealing. Eventually, endocrinology assessment revealed low cortisol with inappropriately low ACTH, and a short Synacthen test confirmed inadequate cortisol response. Other pituitary hormones were preserved, and MRI pituitary was normal. A diagnosis of isolated ACTH deficiency was made. Hydrocortisone replacement therapy resulted in rapid clinical improvement, with resolution of hypercalcemia and restoration of mobility, strength, and independence within weeks. He remains stable on follow-up.

Discussion

This case highlights the diagnostic challenge of IAD due to its nonspecific presentation and absence of hallmark features of primary adrenal failure. Delay in diagnosis can lead to profound deconditioning and misdirected investigations, even raising consideration of palliative care. Hypercalcemia, though uncommon, may be a clue, occurring in up to 8% of patients with ACTH deficiency. Greater clinical awareness is essential, as many cases are initially overlooked or misattributed to infection, malignancy, or neurodegenerative disease. Early dynamic testing could prevent unnecessary invasive investigations, reduce hospital admissions, and markedly improve patient outcomes. Etiologies of IAD include autoimmune processes, gene mutations, trauma, and iatrogenic causes like drugs or immune checkpoint inhibitors. In this patient, no secondary cause was identified.

Conclusion

Isolated ACTH deficiency, though rare, should be considered in patients with unexplained systemic decline, recurrent hospitalizations, and refractory biochemical abnormalities. Early recognition and prompt glucocorticoid replacement can dramatically alter outcomes—even reversing near-terminal deconditioning. Clinicians should maintain a high index of suspicion to prevent missed diagnoses and avoid unnecessary invasive investigations.

DOI: 10.1530/endoabs.113.WD2.1

## WD2.2

### Adrenal crisis in disguise: integrating biochemical, hormonal, and clinical clues

Matus Kalavsky[1] & Beatrice Ranasinghe[2]
[1]Watford General Hospital, Watford, United Kingdom; [2]King's College Hospital NHS Foundation Trust, London, United Kingdom

Background

Addison's disease affects 100–220 people per million in Western Europe and the United States. Diagnosing Addison's disease in the acute setting is challenging, as symptoms are often non-specific and cortisol levels may be equivocal during acute illness.

Case

A 36-year-old woman with hypothyroidism presented with a 10-day history of diarrhoea, vomiting and fatigue after a recent upper respiratory tract infection. She was tachycardic and normotensive, with dry mucous membranes and reduced skin turgor. There was no evidence of hyperpigmentation, involving buccal mucosa or palmar creases. Bloods revealed severe hyponatraemia (109 mmol/l), hyperkalaemia (6.7 mmol/l) and normoglycaemia. Treatment with IV hydrocortisone and fluid resuscitation with 0.9% NaCl was recommended with close monitoring of sodium due to high risk of overcorrection. However, she has been commenced on 1.8% hypertonic saline (1.8% NaCl) that led to a rise in sodium from 109 mmol/l to 122 mmol/l within 24 hours, requiring dextrose infusion to counteract the rapid correction.

Further investigations:

| | |
|---|---|
| Serum osmolality | 259 mosm/kg |
| Urine osmolality | 153 msom/kg |
| Urine sodium | <20 mmol/l |
| 9 am cortisol | 209 nmol/l |
| TSH and free T4 | Normal |

Short Synacthen test (SST) off steroids showed:

| Time (minutes) | Cortisol (nmol/l) | Adrenocorticotropic hormone (ACTH) (ng/l) |
|---|---|---|
| 0 | 175 | 575 |
| 30 | 180 | |
| 60 | 183 | |

Blunted cortisol response on SST, elevated ACTH (575 ng/l), elevated renin (119.5 mu/l), borderline low aldosterone (103 pmol/l), and positive adrenal cortex antibodies confirmed autoimmune adrenalitis. Following transition to oral hydrocortisone (10 mg twice daily), fludrocortisone (50 mg/day) was initiated. Over six weeks, patient fully recovered, resumed work, and had normalised electrolytes, ACTH, and renin levels. As an active runner, she received personalized education on adjusting steroid doses during training, emergency hydrocortisone use, support resources like the Addison's Disease Self-Help Group, and advice to carry medical alert documentation.

Discussion

This case illustrates the diagnostic difficulty of adrenal insufficiency during systemic stress, where cortisol levels can be misleading. Impaired water clearance despite hypotonicity reflects persistent antidiuretic hormone (ADH) secretion secondary to glucocorticoid deficiency—a subtle but key feature. Initiation of steroids suppresses ADH, potentially causing rapid aquaresis and sodium overcorrection, highlighting the need for careful fluid and electrolyte management in such cases to prevent osmotic demyelination. Fludrocortisone dosing is best guided by renin to optimise sodium and volume status. Hydrocortisone replacement should be personalised based on clinical and biochemical responses to avoid under- or overtreatment.

DOI: 10.1530/endoabs.113.WD2.2

## WD2.3

### Diagnosis and work-up of primary adrenal insufficiency

Rupert Larkin
North Bristol NHS Trust, Bristol, United Kingdom

This case of a young adult patient presenting with autoimmune primary adrenal insufficiency highlights several important diagnostic and management considerations that trainee Endocrinologists should be aware of. This 30-year-old male with no significant past medical history presented to the Emergency Department with a two-week history of dizziness, weight loss and vomiting. Examination revealed hypotension and several hyperpigmented skin patches overlying the spine. Bloods revealed severe hypoosmolar hyponatraemia with a serum sodium of 117 mmol/l (ref 133 – 146 mmol/l) and serum osmolality 242 mOsmol/Kg (ref 275-295 mOsmol/Kg). A random serum cortisol was 84 nmol/l, prompting the completion of a Short Synacthen Test (SST) which demonstrated a sub-optimal adrenal response (Table 1).

**Table 1** Short Synacthen Test

| Interval (mins) | Cortisol (nmol/l) |
|---|---|
| 0 | 173 |
| 30 | 172 |
| 60 | 155 (normal cut off >450 nmol/l) |

A provisional diagnosis of primary adrenal insufficiency was made, and the patient was commenced on corticosteroid and mineralocorticoid replacement with hydrocortisone 10/5/5 mg and fludrocortisone 100 micrograms daily respectively. He received education on adrenal insufficiency, including sick day steroid rules and teaching on how to administer an emergency intramuscular hydrocortisone injection. This patient had undergone a healthy childhood with no intellectual delay or behavioural issues, however for completeness he was screened for adrenoleukodystrophy via plasma very long chain fatty acids. The result was normal. Adrenal cortex antibodies subsequently returned positive, thereby confirming a diagnosis of autoimmune primary adrenal insufficiency (PAI) Given the association between autoimmune PAI and other autoimmune endocrinopathies, the patient also underwent baseline screening for Coeliac disease, Type 1 Diabetes Mellitus and autoimmune thyroid disease. This screening was negative but will need to be repeated at regular intervals as part of long term follow up. Two months after originally presenting he was seen in the Endocrinology clinic where he reported significantly improved wellbeing and energy levels. Examination revealed ongoing hyperpigmented patches overlying the spine which the patient felt were unchanged. Clinic bloods demonstrated an elevated plasma renin of 321 mIU/l (ref 3.4-56 mIU/l), suggesting inadequate mineralocorticoid replacement, and prompting an increase to his fludrocortisone dose.

DOI: 10.1530/endoabs.113.WD2.3

## WD2.4

### Optimising glucocorticoid therapy in congenital adrenal hyperplasia: balancing acth suppression and long-term steroid-related complications

Magdalin Jerrahrd, Yi Yi Aung & Sherif Ghieth
University Hospitals Plymouth Trust, Department of Endocrinology and Diabetes, Plymouth, United Kingdom

We report the management of a 49-year-old woman with classic congenital adrenal hyperplasia (CAH) with background of multiple sclerosis. She was treated for many years with twice-daily hydrocortisone and fludrocortisone. Despite good adherence, she experienced persistent biochemical hyperandrogenism (elevated testosterone, ACTH and 17-hydroxyprogesterone), hirsutism, menstrual disturbance, and periods of fatigue. Attempts to increase hydrocortisone to three daily doses achieved partial biochemical control but led to adverse effects, including recurrent episodes of raised intraocular pressure. To improve disease control while minimising side effects, therapy was switched to prednisolone, initially given as a split dose (4 mg morning, 1 mg evening). This regimen resulted in significant biochemical improvement, with normalisation of testosterone, androstenedione, and ACTH levels, along with resumption of menstrual periods and reduction in hirsutism. Bone density remained normal on serial DEXA scans. However, occasional lapses in adherence to the evening dose were associated with biochemical relapse, highlighting the importance of dose timing and compliance. Clinical discussions also considered lifestyle factors, working hours, and symptom control when individualising her regimen. This case highlights the importance of fine-tuning glucocorticoid therapy in CAH. Splitting prednisolone dosing achieved a balance between androgen suppression and avoidance of steroid-related complications, with meaningful improvements in clinical and biochemical outcomes. Individualised treatment, patient education on compliance, and regular biochemical monitoring are essential for long-term optimisation of therapy.

DOI: 10.1530/endoabs.113.WD2.4

## WD3.1

### Co-presentation of graves' disease and addisons disease with addisonian crisis

Maimoona Nawaz & Akheel Syed
Salford Royal Hospital, Manchester, United Kingdom

Introduction
Primary adrenal insufficiency and Graves' disease both have an autoimmune aetiology with an incidence of 0.44 and 20 to 50 per 100,000 cases respectively [1, 2]. An acute presentation with both conditions at the same time is rare We present a case of a male patient who presented to hospital with a recent diagnosis of Graves thyrotoxicosis who was found to be in adrenal crisis.
Case
A 37-year-old man presented to the emergency department with nausea, vomiting and hypotension. His GP had diagnosed hyperthyroidism two weeks previously and commenced carbimazole pending endocrinology review. His heart rate was 111 beats/min, blood pressure 82/48 mmHg, respiratory rate 28 breaths/min, oxygen saturation 97% on air and temperature 36.6 °C. Tanned skin with dark palmar creases were noted. He had tremor on outstretching his hands. Blood tests revealed low cortisol, hyponatraemia, and hyperthyroidism (see Table). Addisonian crisis was diagnosed, and he was commenced on intravenous hydrocortisone. A short Synacthen® test confirmed hypoadrenalism. Once stable, he was commenced on oral hydrocortisone and fludrocortisone.
Discussion
Simultaneous presentation with Addison's disease and Graves' disease is rare. In thyrotoxicosis without adrenal insufficiency, both cortisol production and degradation are accelerated with circulating levels remaining normal. In hyperthyroidism and adrenal insufficiency, however, the ability to increase the synthesis of cortisol is impaired, leading to decreased levels. The loss of mineralocorticoid activity in primary adrenal insufficiency could also contribute to adrenal crisis in hyperthyroidism. Patients with Addison's disease have a 50% risk of developing a second autoimmune disease during their lifetime, such as hypothyroidism (range 43–44%), vitiligo (9–10%), vitamin B12 deficiency (7–9%), type 1 diabetes (5–6%), coeliac disease (3–6%) and hyperthyroidism (4–5%).
Conclusion
It is rare for primary adrenal insufficiency to present simultaneously with another endocrine emergency. It should be suspected in patients who present to the hospital with hypotension, abdominal pain and vomiting. Treatment for adrenal crisis with glucocorticoids should not be delayed pending confirmatory investigations as it can be lifesaving.

**Table**

| Test | Value | Reference range |
|---|---|---|
| *On presentation* | | |
| Sodium, mmol/l | **126** | 133 – 146 |
| Potassium, mmol/l | 5.0 | 3.5 – 5.3 |
| Calcium, mmol/l | **3.05** | 2.2 – 2.6 |
| Urea, mmol/l | **7.9** | 2.5 – 7.8 |
| Creatinine, μmol/l | 97 | 62 – 115 |
| Thyroid stimulating hormone (TSH), mU/l | **0.02** | 0.35 – 5.50 |
| Free thyroxine, pmol/l | **24.8** | 10.0 – 20.0 |
| Free triiodothyronine, pmol/l | **9.4** | 3.5 – 6.5 |
| Cortisol, nmol/l | **19** | 200 – 500 |
| *Further investigations* | | |
| Thyroid peroxidase antibody, IU/mL | **81** | 0 – 35 |
| TSH receptor antibody, U/l | **2.0** | 0.0 – 0.4 |
| Adrenocorticotropic hormone, ng/l | **437** | 0 – 46 |
| Anti-adrenal cortex antibody | **Positive** | |
| *Short Synacthen® Test* | | |
| Basal Cortisol, nmol/l | **42** | |
| 30-min Cortisol, nmol/l | **41** | |
| 60-min Cortisol, nmol/l | **33** | |

DOI: 10.1530/endoabs.113.WD3.1

## WD3.2

### A challenging case of primary adrenal insufficiency with multiple autoimmune conditions

Laura Ryan[1] & Antoinette Tuthill[1,2]
[1]Cork University Hospital, Cork, Ireland; [2]University College Cork, Cork, Ireland

We present the case of a 38 yo female with primary adrenal insufficiency and multiple autoimmune conditions. She initially presented to the medical assessment unit in late 2017 with a two week history of fatigue. She was noted to be hypotensive, hyponatraemic at 130 mmol/l and a random cortisol returned at 82 nmol/l. Short synacthen testing confirmed adrenal insufficiency with a 0 minute cortisol of 74 nmol/l and 60 minute cortisol of 70 nmol/l. ACTH was elevated at 212.6 pmol/l and 21-hydroxylase antibodies were positive. She was commenced on hydrocortisone and fludrocortisone replacement with doses adjusted based on symptoms, cortisol day curve levels and renin levels respectively. She had several admissions due to viral illnesses requiring stress dose steroids and had difficulty reducing the hydrocortisone dose due to symptoms so is maintained on hydrocortisone 15 mg mane, 10 mg midi and 5 mg tarde as per patient preference. At the time of presentation LFTs were deranged however a non-invasive liver screen was unremarkable. Anti-TTG and anti-endomysial antibodies were mildly raised so she proceeded to an OGD; histology confirmed coeliac disease and a gluten free diet was recommended. Despite adherence to the diet she had a persistently elevated ALT and IgG. Repeat antibody testing returned a positive ANA and anti-smooth muscle antibody. A liver biopsy confirmed a diagnosis of autoimmune hepatitis. Following a period of monitoring she was commenced on budesonide and subsequently azathioprine with resultant improvement in LFTs. Six months after being diagnosed with adrenal insufficiency she reported amenorrhoea and on investigation was noted to have an oestradiol level of $<37$ pmol/l with LH 19.8 IU/l and FSH 15.1 IU/l, with

the same pattern on repeat testing, consistent with premature ovarian insufficiency and hormone replacement therapy was commenced. She desired a pregnancy and underwent IVF with a successful pregnancy on her 4th cycle and then had a subsequent pregnancy with a spontaneous conception. Her case has been challenging to manage due to multiple new diagnoses of autoimmune conditions, admissions with crises, the use of budesonide with supraphysiological doses of hydrocortisone and navigating IVF and pregnancy with these.

DOI: 10.1530/endoabs.113.WD3.2

## WD3.3

Abstract Withdrawn

DOI: 10.1530/endoabs.113.WD3.3

## WD4.1

**Unmasking adrenal suppression: a case of iatrogenic adrenal insufficiency**

Shamnas Abdul Aziz, Kavish Khatib, Mahender Yadagiri, Auditi Naziat & Vladimir Vaks
Great Western Hospital, Swindon, United Kingdom

Background
Adrenal suppression from prolonged corticosteroid exposure can mask or delay the diagnosis of adrenal insufficiency (AI). Establishing adrenal reserve is challenging when dynamic testing yields equivocal results, while clinical features remain non-specific. This case highlights the diagnostic and management dilemmas in iatrogenic secondary AI.
Case Summary
A 55-year-old man with asthma and chronic rhinosinusitis, treated for many years with high-dose inhaled and intermittent oral corticosteroids, presented with persistent fatigue, myalgia, and low blood pressure. His past medical history included multiple musculoskeletal injuries, high BMI(34 kg/m$^2$), B12 deficiency and dermatological problems, further complicating symptom interpretation. Both initial and the following two repeat short synacthen tests (SST) between 2022-2023 were flat cortisol responses. Although the repeat SST from 2024 showed an appropriate response, we performed insulin tolerance test as he was still symptomatic and this confirmed secondary AI. Pituitary MRI and extended pituitary profile were unremarkable. Autoimmune and paraneoplastic screens were negative. Hydrocortisone replacement (10/5/5 mg) was commenced, later changed to prednisolone for practicality. Despite adherence, the patient reported ongoing disabling fatigue, post-exertional myalgia, and mood disturbance. Clinicians faced a dilemma: whether symptoms reflected under-replacement or were multifactorial, given co-morbidities and psychosocial burden. Dose escalation was considered but tempered by the risk of over-replacement, particularly in the context of obesity, dyslipidaemia, and a strong family history of malignancy and autoimmune disease. Multispecialty review excluded alternative unifying pathology.
Discussion
This case illustrates the inherent challenges in diagnosing and managing secondary adrenal insufficiency caused by long-term steroid use. Dynamic testing may yield variable or inconclusive results, necessitating repetition to unmask adrenal suppression with confidence. Clinical assessment is complicated by the non-specific nature of adrenal insufficiency symptoms, which frequently overlap with other chronic conditions such as asthma, chronic pain, or mood disorders. Even once the diagnosis is established, treatment decisions are complex: while under-replacement risks persistent morbidity, over-replacement increases cardiometabolic and bone-related complications. A tailored approach that balances these competing risks is essential, supported by patient education, reinforcement of sick-day rules, and structured monitoring of quality of life.
Conclusion
This case underscores the complexity of managing iatrogenic adrenal insufficiency: diagnostic tests may be ambiguous, symptoms are often multifactorial, and treatment requires balancing safety with efficacy. Recognising steroid-induced adrenal suppression early, using repeat dynamic testing where necessary, and adopting an individualised, multidisciplinary approach is critical to improving outcomes in this increasingly common endocrine problem.

DOI: 10.1530/endoabs.113.WD4.1

## WD4.2

**"Beyond initial fatigue: long-term physical and psychological management in primary addison's disease"**

Shivani Shivaprasad
University Hospital of North Durham, Durham, United Kingdom

Background
Primary adrenal insufficiency (Addison's disease) is rare but potentially life-threatening if unrecognized. Typical features include fatigue, nausea, weight loss, hyponatraemia, hyperkalaemia, and grey-slate hyperpigmentation. Management is lifelong, requiring individualized glucocorticoid and mineralocorticoid replacement, ongoing monitoring for psychological stress, and vigilance for long-term steroid-related complications. Early recognition in routine clinical practice is crucial to prevent adrenal crises and optimize quality of life as often patients present with nonspecific symptoms such as fatigue, weight loss, and gastrointestinal upset. Diagnostic delay is common, and missed opportunities can worsen morbidity.
Case
A 41-year-old man presented with two weeks of extreme fatigue, nausea, vomiting, and a 1.5-stone weight loss. Initially, he had presented to the emergency department but was discharged, attributing symptoms to gastrointestinal upset. He presented again severely unwell. Examination revealed grey-slate hyperpigmentation, borderline low BP, and tachycardia. Laboratory evaluation showed hyponatraemia (Na 129 mmol/l) and hyperkalaemia (K 5.4 mmol/l), prompting a 9 AM cortisol of 224 nmol/l. Inadequate response to Short Synacthen testing (baseline 230, 30 min 218, 60 min 192 nmol/l) confirmed primary adrenal insufficiency with markedly elevated ACTH (927 ng/l). Adrenal antibodies were negative. He was initially treated with IV hydrocortisone and fluids, transitioned to oral hydrocortisone 20–10–10 mg daily with fludrocortisone 100 mg, and educated on sick-day rules and emergency steroid use. First outpatient review showed normalized electrolytes and improved appetite, prompting taper to 10–5–5 mg daily and continued fludrocortisone 100 mg daily. At the second follow-up, despite normalized electrolytes, he reported ongoing profound fatigue and psychological distress, impairing daily functioning and family life. He was unable to push a shopping trolley, shower without resting for the entire day, or perform work duties, relying heavily on his wife as carer. Severe brain fog, memory difficulties, erectile dysfunction, and disturbed family dynamics highlighted the substantial psychosocial burden of lifelong adrenal insufficiency. Due to ongoing distress and functional impairment, hydrocortisone was increased to four daily doses (12.5–7.5–5–2.5 mg) and fludrocortisone to 150 mg daily, resulting in symptomatic improvement. Discussions addressed long-term risks of chronic glucocorticoid therapy, including metabolic, cardiovascular, and musculoskeletal complications, emphasizing the need for ongoing multidisciplinary care and regular reassessment.
Conclusion
Management of Addison's disease is dynamic and lifelong. Biochemical stability alone is insufficient; therapy should be individualized according to symptoms, functional capacity, and psychosocial impact. Regular monitoring, patient education, and early recognition of physiological and psychological challenges are essential to prevent adrenal crises and optimize quality of life. Referral can be made to the Addison's Disease Self-Help Group UK, where practical advice, support, and shared experiences are offered, helping patients cope long-term and enhancing overall quality of life.

DOI: 10.1530/endoabs.113.WD4.2

## WD4.3

**Congenital adrenal hyperplasia and infertility in men**

Hatem Eid
Rashed Centre for Diabetes and Research, Ajman, UAE

A 29-year-old male presented with primary infertility, with no identifiable wife factor. He had premature puberty and a family history of infertility (sister). He maintained normal libido and erectile function, with regular sexual activity. He noted progressive testicular enlargement. Physical examination revealed normal vital signs and secondary sexual characteristics, with a BMI of 30. No gynecomastia or Cushingoid features were observed. Testicular assessment showed bilaterally enlarged, firm testes with mildly tender bilateral palpable masses. Initial hormonal evaluation demonstrated undetectable FSH and LH, elevated total testosterone 51 nmol/l (N 8.33- 30.30.1 nmol/l), and increased estradiol (275 pmol/l, (N.40-162 pmol/l), ACTH was 42.8 pg/mL (N, 4.7 to 48.8 pg/mL), Semen analysis confirmed azoospermia.
**Differential diagnoses** included
- exogenous testosterone or anabolic steroid use,
- testosterone-secreting tumors,

- congenital adrenal hyperplasia (CAH),
- androgen resistance syndromes.

**Required Work up**
Total testosterone.
LH & FSH.
androstenedione.
17-OH progesterone.
Morning Cortisol
US scrotum
CT adrenal

**Further hormonal workup revealed:**
- Elevated 17-hydroxyprogesterone 615 nmol/l (N 1.12- 7.0 nmol) and androstenedione >35 nmol/l (N. 2.1-10.0 nmol/l).
- Persistently undetectable LH and FSH
- Low morning cortisol 40 nmol/l (N.200 – 650 nmol/l)
- Elevated aldosterone1010 pmol/l (N. 128-650 pmol/l) and renin levels >35 nmol/l (N. 2-10 nmol/l)
- normal HbA1 c 5.1% (4-5.9%)

**Imaging studies:**
- **Testicular ultrasound** showed bilateral enlargement with heterogeneous echotexture and echogenic masses predominantly in the rete testis, suggestive of testicular adrenal rest tumors (TART).
- **CT imaging** revealed mild bilateral adrenal enlargement without discrete lesions.

**Diagnosis**: Congenital adrenal hyperplasia.
**Treatment** initiated: Hydrocortisone (20/20/5) and nighttime dexamethasone (1 mg).
**Follow-up at three months** showed minimal biochemical improvement despite good compliance by the patient. Testosterone remained elevated >35 nmol/l (N. 8.33-30 nmol/l), minimal reduction of 17-OH progesterone 510.40 nmol/l (N 1.12-7.2 nmol/l) and androstenedione levels persisted above normal > 35 nmol/l (N 2.1-10.8 nmol/l), Aldosterone reduced by 50% to normal 550 pmol/l (N.128-650 pmol/l), and azoospermia continued. Testicular findings remained unchanged.
**Follow-up at six months** showed worsening of 17 OH progesterone to 660 nmol/l (N. 2-7 nmol/l), Testosterone remain elevated > 35 nmol/l (N 8-30 nmol/l) as well Androstenedione >35 nmol/l (N. 2.1-10.0 nmol/l).possible steroid side effect as worsening HbA1 c to 6.1(N 4-5.9%).and patient complaint of weight gain.

**Discussion Points:**
- What explains the elevation of renin and aldosterone?
- Why is there inadequate suppression of 17-OH progesterone and androstenedione?
- Could 11β-hydroxylase deficiency be contributing?
- Would genetic testing alter management?
- Is there a role for adrenalectomy?
- Should we measure blood Dexamethasone level, to confirm compliance
- Shall we involve urology for microscopic testicular sperm extraction (microTESES).

DOI: 10.1530/endoabs.113.WD4.3

## WD4.4

### Management of non-classical congenital adrenal hyperplasia across the life course

Natasha Sawhney & Susan McGeoch
NHS Grampian, Aberdeen, United Kingdom

Non-classical congenital adrenal hyperplasia (NCCAH) tends to present in adulthood, is more common than classical CAH and is usually associated with a milder presentation. Patients are not usually steroid dependent as the partial enzymatic defects are overcome by elevation in ACTH. Clinical features of hyperandrogenism and metabolic complications overlap with polycystic ovary syndrome (PCOS). Treatment requirements can vary across the lifespan as detailed in the case presented here. At 36 years old, a female patient received a diagnosis of NCCAH following several years of investigations for hirsutism, irregular periods and significant weight gain in her early 30 s. Initial investigations showed a raised testosterone at 3.4 nmol/l (0.5-2.6) and raised 17 OHP (earliest available level 4 years after diagnosis of 13 nmol/l (0-6). Her BMI was 43.2. Genetic testing later in life confirmed pathogenic variants in the CYP21 A2 gene, which results in 21-hydroxylase deficiency. Her short synacthen test (SST) was normal, with a basal cortisol of 315 nmol/l rising to a peak of 500 nmol/l. Dexamethasone was commenced at a low dose of 0.25 mg per night which successfully treated her hirsutism (this was prior to the CaHASE study published in 2010). After nine years of treatment, the patient developed hypertension and complained of difficulty losing weight; BMI was 46.9. Testosterone was undetectable at <0.5 nmol/l and 17 OHP was low-normal at 1.5 nmol/l. She gradually reduced the frequency of dexamethasone and stopped this in her late 40 s. There was a break in treatment until the age of 54, when she complained of excessive fatigue and ongoing difficulty losing weight; BMI was 52.8 and Epworth score was 14. 17 OHP was raised at 23.8 nmol/l, Androstenedione was raised at 3.5 nmol/l (0-3.0) and testosterone was normal at 1.2 nmol/l. At 56 years old her SST showed a suboptimal cortisol response, rising from 237 to 334 nmol/l, and she commenced hydrocortisone. At the age of 58 she commenced HRT to manage symptoms of night sweats, fatigue and reduced libido. Testosterone, 17 OHP and androstenedione were within the normal range, suggesting over-replacement with hydrocortisone. She has been diagnosed with Type 2 diabetes (HbA1 c 50 mmol/mol) and recently commenced Tirzepatide to facilitate weight loss. Ongoing reduction in hydrocortisone dose is currently being attempted. Optimal management of cases with NCCAH remains to be elucidated and an individualised approach is recommended. Temporary treatment with steroids can be effective at managing hyperandrogenism or cortisol deficiency, but must be balanced against the pre-existing increased risk of metabolic complications.

DOI: 10.1530/endoabs.113.WD4.4

## WD5.1

### Successful slow weaning of long-term prednisolone in a patient with still's disease: clinical progress and ongoing management

Irfan Iqbal Khan, Abdulla Jadallah & Nitin Shekar
Darlington Memorial Hospital, Darlington, United Kingdom

Background
Long-term glucocorticoid therapy can lead to adrenal suppression, making steroid tapering difficult and increasing the risk of adrenal insufficiency. A cautious and individualized approach is often required, particularly in patients who have previously failed standard tapering regimens.
Case Presentation
We describe a 45-year-old female with Still's disease in remission who had been on long-term prednisolone therapy for over 13 years. The patient was hesitant to attempt further steroid reduction after unsuccessful tapering attempts, confirmed by a short synacthen test (SST) in December 2024 showing adrenal suppression (baseline cortisol 160 nmol/l; 30-minute cortisol 232 nmol/l). She also expressed concern about experiencing fatigue or instability, as her role as a counsellor requires full mental alertness and emotional stability. An individualized tapering plan using Meeran's protocol was implemented to allow gradual adrenal recovery. Over two months, she successfully reduced her dose from 3 mg daily to 2 mg on alternate days and 1 mg on the off days. The patient tolerated this regimen well, reporting no symptoms of adrenal insufficiency or postural hypotension. Blood pressure remained within normal limits. A follow-up SST showed marked improvement (baseline cortisol 340 nmol/l; 30-minute cortisol 593 nmol/l). She remains clinically stable, adheres to sick day rules, and continues regular endocrine follow-up.
Conclusion
This case illustrates the value of a slow, patient-centred steroid tapering approach supported by clear education and multidisciplinary monitoring. The successful use of Meeran's protocol demonstrates that individualized tapering regimens can safely restore adrenal function and improve patient confidence during long-term glucocorticoid withdrawal.

DOI: 10.1530/endoabs.113.WD5.1

## WD5.2

### Management of immunotherapy-induced adrenal insufficiency in an elderly gentleman with a background of metastatic melanoma

James Wilkinson & Karim Meeran
Charing Cross Hospital, Imperial College Healthcare NHS Trust, London, United Kingdom

Case presentation
This is an 82 year old gentleman who was initially referred to the endocrinology clinic from the oncology team with symptoms of fatigue and postural dizziness with serially low cortisols. His past medical history was significant for metastatic melanoma which had been first diagnosed in June 2024. He underwent treatment with a wide-local excision in August 2024 and was subsequently started on a 12-month course of pembrolizumab from November 2024 onwards. He did not have any other significant medical issues. He remained physically fit and active and regularly cycled around his home city. He had a transient hyperthyroid episode in December 2024 (TSH <0.01 mU/l free T3 12.9 pmol/l free T4 25.5 pmol/l) and

he subsequently developed primary hypothyroidism within one month of the initial thyroid function test derangement. He started levothyroxine 75 mg once daily and his TSH subsequently normalised on this dose. In March 2024, he had a 9 am cortisol reading of 64 nmol/l along with multiple low random cortisol levels (81, 86 nmol/l). He was initiated on prednisolone 3 mg once daily for steroid replacement. He was seen by the endocrine nurse for education on emergency hydrocortisone injections and steroid sick day rules. A short synacthen test was carried out in September 2025 and this showed an absent response (cortisol 30 mins 33 nmol/l; 60 mins 40 nmol/l; baseline ACTH $<5$ ng/l). His eight-hour prednisolone level was 40 ug/l. He had a brief admission to the oncology team with symptoms of general malaise and a large postural drop that corrected with fluids. His investigations did not suggest the presence of any infection. His oncology team doubled his steroids to 6 mg once daily. The patient was keen to remain on the higher dose but we negotiated a compromise of prednisolone 4 mg once daily with the patient in view of his severe fatigue. He had a previous renin level of 0.2 nmol/l/h. We started a small dose of fludrocortisone as an inpatient. He improved clinically after several days and was discharged home. He continues immunotherapy in the outpatient setting with routine endocrinology follow-up.

Discussion points

What are the diagnostic features of immunotherapy-induced adrenal insufficiency? How does immunotherapy affect different parts of the HPA axis? What are the pros and cons of using prednisolone instead of hydrocortisone as steroid replacement? How do you determine whether a patient is receiving adequate steroid replacement? How can renin be used to guide mineralocorticoid replacement in adrenal insufficiency?

DOI: 10.1530/endoabs.113.WD5.2

## WD5.3

**Steroid-responsive testicular masses in untreated 3β-HSD deficiency: a case of misdiagnosed malignancy**

Balqees Al-Radhi & Kerri Devine
Royal Victoria Infirmary, Newcastle Upon Tyne, United Kingdom

Background

3β-hydroxysteroid dehydrogenase (3β-HSD) deficiency is an exceptionally rare ($<1$ in 1,000,000) form of congenital adrenal hyperplasia (CAH), caused by pathogenic variants in *HSD3 B2*. It disrupts adrenal and gonadal steroidogenesis, leading to impaired cortisol and aldosterone synthesis and accumulation of steroid precursors. Clinical presentation in 46, XY infants includes ambiguous genitalia, hypospadias, and cryptorchidism, with or without salt-wasting crises. Diagnosis requires comprehensive hormonal profiling, ideally during ACTH stimulation, demonstrating elevated 17-hydroxypregnenolone, pregnenolone, and DHEA with relatively low 17-OHP, androstenedione, and cortisol). Genetic confirmation is recommended by Endocrine Society guidelines. Lifelong endocrine follow-up is essential to reduce morbidity, prevent adrenal crises, and monitor for testicular adrenal rest tumours (TARTs), a recognised complication that may mimic malignancy.

Case

We describe a male patient with neonatal presentation (ambiguous genitalia, cryptorchidism, hypospadias) and urinary steroid profiling consistent with 3β-HSD deficiency, who had no long-term endocrine follow-up. He re-presented in adulthood with infertility and primary hypogonadism. Bilateral hyper vascular testicular lesions were detected on ultrasound, raising suspicion of malignancy. Past history included an ITU admission with sepsis in 2015, consistent with unrecognised adrenal crisis. On initiation of oral dexamethasone (0.5 mg nocte), follow-up ultrasound demonstrated reduction in lesion size, strongly suggesting TARTs. Fertility evaluation is ongoing including genetic testing for partner screening.

Discussion

This case illustrates the consequences of untreated 3β-HSD deficiency extending into adulthood. Endocrine Society and UK guidance highlight the importance of accurate biochemical diagnosis, genetic confirmation, and structured transition to adult services. In males with CAH, periodic testicular ultrasound is recommended to screen for TARTs. Differentiating TARTs from testicular cancer is critical; regression with glucocorticoid therapy supports the diagnosis of TARTs and can prevent unnecessary orchidectomy. Early and adequate hormone replacement is vital not only to prevent adrenal crisis but also to improve fertility potential by reducing intratesticular mass effect. This case reinforces that CAH variants other than 21-hydroxylase deficiency require the same principles of lifelong multidisciplinary endocrine care, including reproductive and genetic counselling.

Conclusion

Untreated 3β-HSD deficiency is extremely rare in adulthood. Recognition of this condition, adherence to guideline-based diagnostic pathways, and appropriate long-term management are essential. Glucocorticoid therapy can induce regression of TARTs, avoid unnecessary surgery, and optimise fertility prospects. This case underscores the importance of ongoing surveillance and tailored endocrine care for all CAH variants.

DOI: 10.1530/endoabs.113.WD5.3

# Workshop E: Disorders of the gonads

## WE1.1

### Testosterone therapy in borderline hypogonadism and depression: a case of diagnostic ambiguity, therapeutic entrapment, and iatrogenic erythrocytosis

Idowu Olaogun
Bristol Royal Infirmary, Bristol, United Kingdom

Background
Testosterone replacement therapy (TRT) is a well-established intervention for confirmed male hypogonadism. Within the NHS and other regulated healthcare systems, prescribing is guided by stringent biochemical and clinical criteria, ensuring that treatment is reserved for individuals with unequivocal androgen deficiency and symptomatic burden. This evidence-based framework promotes safety, therapeutic efficacy, and long-term monitoring. In contrast, private prescribing pathways may lack standardised thresholds and oversight, allowing initiation of TRT in patients with borderline biochemical profiles or non-specific symptoms. While this may offer perceived flexibility, it carries significant risks—including inappropriate treatment, adverse effects such as erythrocytosis, and psychological dependence.
Case Presentation
A 43-year-old man was referred to the endocrine clinic with longstanding depressive symptoms, reportedly familial following maternal suicide. His mood and energy levels deteriorated significantly during the COVID-19 pandemic. Initial biochemical evaluation revealed borderline gonadotropin levels (FSH 1.3 IU/l, LH 2.4 IU/l) and low-normal total testosterone (6.8–7.8 nmol/l), with SHBG of 42 nmol/l and calculated free testosterone of 0.22 nmol/l. He reported infrequent morning erections and was not sexually active, limiting assessment of libido. Hematocrit was elevated at 51%, with normal thyroid function (TSH 2.5 mIU/l, FT4 16 pmol/l) and prolactin (345 mIU/l). Bone mineral density and hemoglobin were within normal limits. Despite not meeting NHS criteria for TRT, he initiated therapy via a private clinic, with dose escalation over two years. He reported marginal improvement in energy but no significant mood benefit. His antidepressant dosage increased during this period. Multiple attempts to discontinue TRT were unsuccessful due to disabling fatigue and mood deterioration. He now presents with persistent erythrocytosis and psychological dependence on exogenous testosterone.
Discussion
This case highlights the diagnostic ambiguity and therapeutic complexity of managing borderline androgen deficiency in the context of primary affective disorder. The patient's expectation that TRT would resolve depressive symptoms was unmet, and withdrawal proved destabilising. The development of erythrocytosis underscores the risks of long-term TRT without clear biochemical indication. This case reinforces the importance of multidisciplinary assessment and cautious prescribing, particularly outside established guidelines, and raises important questions about the role of testosterone in mood regulation and the limitations of private practice in managing endocrine-psychiatric overlap.

DOI: 10.1530/endoabs.113.WE1.1

## WE1.2

### Primary ovarian insufficiency presenting as primary amenorrhea in an adolescent

Beenish Masood[1] & Bernard Khoo[1,2]
[1]Royal Free Hospital, London, United Kingdom; [2]University College London, London, United Kingdom

An 18-year-old university student presented with primary amenorrhoea and delayed pubertal development. She reported never having menstruated. Adrenarche occurred between the ages of 12 and 14, with a growth spurt and development of axillary and pubic hair, but breast development remained minimal. On examination, she had Tanner stage 2 breasts and Tanner stage 3 pubic hair, with a wider carrying angle but otherwise normal stature. Investigations showed markedly elevated gonadotrophins (FSH 122 U/l, LH 57.6 U/l) and very low oestradiol (<44 pmol/l), consistent with primary ovarian insufficiency (POI). Prolactin was mildly raised once but normal on repeat testing. MRI pelvis (2023) demonstrated a small uterus (30 × 17 mm) with non-visualisation of the ovaries. Pelvic ultrasound revealed a thin endometrium (2.3 mm) and quiescent ovaries of normal size. Bone age at 17 years corresponded to 14 years. Karyotype confirmed a 46,XX female complement, excluding Turner syndrome, and fragile X testing was negative with no expansion of FMR1 gene. Her autoimmune screen was positive only for gastric parietal cell antibodies. Parathyroid hormone was mildly elevated at 7.4 pmol/l, attributed to vitamin D deficiency. Anti-Müllerian hormone was <0.2 pmol/l. Bone mineral density assessment confirmed reduced bone mass: lumbar spine BMD 0.617 g/cm$^2$ (Z-score –4.8), total hip BMD 0.718 g/cm$^2$ (Z-score –1.9). These results indicated osteoporosis at the lumbar spine and osteopenia at the hip, concerning for her age. The working diagnosis was primary ovarian insufficiency with hypergonadotropic hypogonadism, most likely idiopathic. Management included vitamin D supplementation (oral spray 3000 IU daily), dietary optimisation for bone health, and initiation of hormone replacement therapy (HRT). She was commenced on transdermal oestradiol (Oestrogel 2.25 mg OD) and cyclical progesterone (Utrogestan 200 mg nocte, days 15–26 monthly) to induce menstruation, maintain bone density, and support secondary sexual development. A transdermal route was chosen over oral to reduce the risk of venous thromboembolism. She was counselled that natural conception is unlikely due to anovulation but that pregnancy with assisted fertility and donor oocytes is possible. Since starting HRT, she has reported monthly withdrawal bleeds, a small increase in breast size, and an improvement in overall well-being.

DOI: 10.1530/endoabs.113.WE1.2

## WE2.1

### Impact of misdiagnosis in hypogonadism: a case of prolonged testosterone therapy and axis recovery"

Lida Amer & Alexander Lewis
Manchester Royal Infirmary, Manchester, United Kingdom

Background
Testosterone replacement therapy (TRT) is prescribed for hypogonadotrophic hypogonadism, but inappropriate initiation has major implications for fertility. Discontinuation of TRT is associated with variable recovery times for the hypothalamic–pituitary–gonadal axis and spermatogenesis, typically 6–18 months in published series. Shift work may further alter circadian testosterone rhythms and complicate interpretation.
Case
A 33-year-old male was referred for reassessment of a historical diagnosis of hypogonadotrophic hypogonadism. He had been on long-term TRT with Nebido injections for 8 years. His main concern was fertility. Semen analysis revealed azoospermia, and gonadotrophins were suppressed (FSH <0.3 IU/l, LH <0.1 IU/l). Trough serum testosterone on treatment was normal, with low SHBG.
Investigations
TRT was withdrawn to reassess endogenous pituitary–gonadal function. Over the following 6 months, pituitary hormones normalised, serum testosterone reached 10.4 nmol/l, and calculated free testosterone was reassuring despite low SHBG. The role of shift work in lowering testosterone was discussed, and daytime working was encouraged to support recovery.
Outcome
Hypogonadism resolved within 6 months, with spontaneous partner pregnancy reported. This recovery period is at the shorter end of the expected global range (6–18 months; WHO Task Force, 1990; Liu *et al*., *J Clin Endocrinol Metab*, 2006). Fertility was restored without the need for gonadotrophin induction therapy.
Conclusion
This case highlights recovery of the hypothalamic–pituitary–gonadal axis after prolonged TRT use, the risk of azoospermia from unnecessary therapy, and the impact of circadian disruption from shift work. It underscores the importance of critically re-evaluating historical diagnoses of hypogonadism and providing tailored management for men seeking fertility.

1. Diagnosis and Type of Hypogonadism: It is critical to establish the diagnosis and type of hypogonadism using a combination of clinical history, physical examination, and biochemical tests. This helps in determining whether the condition is primary (testicular) or secondary (pituitary or hypothalamic) hypogonadism.
2. Recovery of spermatogenesis after discontinuing TRT varies; published studies suggest 6–18 months, though some men may take up to 24 months.
3. Calculated Free Testosterone in Low SHBG:
    1. When SHBG (sex hormone-binding globulin) is low, the calculation of free testosterone becomes essential for an accurate assessment of testosterone status. This helps to better understand the bioavailable testosterone in the body.
    2. However, there is ongoing uncertainty in the medical community about reference ranges and their correlation with symptoms. This is an area that needs further research to clarify.
4. Shift work can alter circadian testosterone secretion and should be considered in interpretation and management.

DOI: 10.1530/endoabs.113.WE2.1

## WE2.2

**Late presentation of primary amenorrhoea – a diagnostic work-up**

Rishi Iyer, Gayathri Bhaskaran, Sulmaaz Qamar & Eleni Armeni
Royal Free Hospital, London, United Kingdom

Case
A 25-year-old female presented with primary amenorrhoea and a complex history. Puberty and breast development began age 11, but she did not have menarche. At age 15 she was investigated by gynaecology, and diagnosed with having polycystic ovaries, but was told she did not have PCOS. She also had a history of anxiety and anorexia nervosa from ages 15 to 20, during which, at times, she consumed less than 1200 kcal/day and her BMI dropped to 17 kg/m$^2$. She was managed for anxiety from age 15 to 20. From age 19 to 22 she used a contraceptive implant in the arm. On presentation, she was at a healthy weight (62 kg, BMI 23.9 kg/m$^2$), no longer had an eating disorder, had a Tanner Stage 4/5 and had a normal Ferriman-Gallwey score. Initial workup showed normal gonadotropin levels (FSH 7.2 IU/l, LH 17.2 IU/l) and oestradiol (230 pmol/l), which did not suggest primary ovarian insufficiency or ongoing hypogonadotropic hypogonadism. Her progesterone level was 0.5 nmol/l, and testosterone was 2.1 nmol/l, with an AMH of 65.9 pmol/l. Ultrasound confirmed polycystic ovaries (>20 follicles per ovary) with an endometrial thickness of 7.4 mm. A DXA scan showed her bone density was within the expected range for her age, with Z-scores of -0.5 (lumbar spine) and -1.8 (femoral neck). Adrenal cortex antibodies were negative, and anti-Tg was 30 IU/mL. Genomic analysis ruled out FMR1 gene expansion and karyotyping was normal. A progesterone withdrawal test was administered to assess endometrial and ovarian function, resulting in a seven-day bleed. The positive response indicated a functional hypothalamic-pituitary-gonadal axis and a receptive endometrial lining.
Discussion
The aetiology of her amenorrhoea is likely multifactorial. A positive progesterone challenge, together with the presence of polycystic ovaries and amenorrhoea/anovulation, fulfils the Rotterdam criteria for PCOS. At the same time, her history is also consistent with hypothalamic amenorrhoea related to her eating disorder. It is likely that dysregulated hypothalamic–pituitary–ovarian signalling and asynchronous FSH/lH secretion in PCOS contributed to anovulation, which was further compounded by hypothalamic suppression. The positive response to the progesterone challenge and her preserved bone mineral density suggest a favourable prognosis.

DOI: 10.1530/endoabs.113.WE2.2

## WE3.1

**From supplements to suppression: lessons from two cases in a general endocrine clinic**

Tun Tun[1] & Aye Chan Maung[2]
[1]Horton General Hospital, Oxford University Hospitals NHS Foundation Trust, Banbury, United Kingdom; [2]Great Western Hospitals NHS Foundation Trust, Swindon, United Kingdom

Background
The widespread use of anabolic steroids and contaminated supplements poses a growing challenge in endocrine practice, often leading to hypogonadism, mood disturbances, and impaired quality of life. We present two cases of androgen-related hypogonadism, highlighting the diagnostic complexities and lifestyle factors contributing to these presentations.
Case 1
A 51-year-old man presented to the endocrine clinic with fatigue, "brain fog," and low mood. He reported self-administering intramuscular testosterone enanthate (0.5–2 ml weekly) intermittently for nearly 15 years to enhance muscle growth and recovery after gym training. His testosterone concentrations during supplementation reached as high as 72 nmol/l. While on exogenous testosterone, his hemoglobin was 180 g/l, and he donated blood every four months to manage polycythemia. Eleven months after discontinuing injections, his testosterone levels ranged between 6.2–6.5 nmol/l. Despite preserved libido, erectile function, and secondary sexual characteristics, he described persistent fatigue and low mood, suggestive of androgen withdrawal and suppression of the hypothalamic–pituitary–testicular axis.
Case 2
A 34-year-old man presented with reduced libido, persistent fatigue, and low mood, which had strained his marital relationship. His background included long-term shift work in a chocolate factory and prior engagement in intensive gym training. Four years earlier, a routine GP blood test showed an elevated testosterone of 34.3 nmol/l, with hemoglobin 178 g/l and hematocrit 55.4%. He later reported taking protein supplements for over a decade, which were likely adulterated with exogenous testosterone—a recognized issue with some commercial preparations. Following discontinuation of supplements, serial investigations revealed borderline-low testosterone (8.0–8.2 nmol/l) with normal gonadotrophins.
Discussion
These cases highlight the spectrum of hypogonadism associated with exogenous androgen exposure, whether deliberate or inadvertent. Case 1 demonstrates long-term anabolic steroid use leading to biochemical and symptomatic hypogonadism, while Case 2 underscores the risk of hidden androgen adulteration in dietary supplements. Both patients experienced significant impairment in quality of life, despite relatively modest biochemical abnormalities, reflecting a relative deficiency state after prior exposure to supra-physiological testosterone levels.
Conclusion
Clinicians should maintain a high index of suspicion for exogenous androgen exposure in patients presenting with unexplained hypogonadal symptoms, particularly in those with a history of bodybuilding, supplement use, or performance-enhancing drug exposure.

DOI: 10.1530/endoabs.113.WE3.1

## WE4.1

**Challenges in diagnosing male hypogonadism: a case series highlighting risks of unregulated testosterone therapy**

Afnan Hassan, Lida Amer & Alexander Lewis
Manchester University NHS Foundation Trust, Manchester, United Kingdom

Background
Commercial "testosterone optimisation" services and online supplement providers increasingly market treatment for young men presenting with non-specific symptoms, often without adequate diagnostic work-up. Unregulated testosterone or "booster" supplements can suppress the hypothalamic–pituitary–gonadal (HPG) axis, mimicking hypogonadotropic hypogonadism. Misdiagnosis may expose patients to unnecessary treatments, fertility impairment, and complications including erythrocytosis, testicular atrophy, and metabolic consequences. This case series illustrates these risks and emphasises the importance of specialist assessment in centres with full diagnostic capability.
Case Series
A 35-year-old man presented with progressive reduced libido and energy. He'd sought private hCG therapy due to long NHS waiting times. Baseline testing revealed low testosterone with inappropriately low gonadotrophins, while other pituitary hormones were normal. Given obesity, normal prior fertility, and absence of pituitary pathology, functional hypogonadotrophic hypogonadism was diagnosed. hCG was discontinued, lifestyle modification implemented, and pituitary MRI was normal. Follow-up demonstrated normalisation of hormones with symptomatic improvement, illustrating recovery of HPG function without long-term hormonal therapy. A 33-year-old man with a historical diagnosis of hypogonadotrophic hypogonadism had received Nebido for eight years. He had azoospermia. Therapy withdrawal demonstrated recovery of gonadotrophins and testosterone within six months, leading to fertility restoration with spontaneous partner pregnancy. Circadian disruption from shiftwork contributed to reduced testosterone and was addressed in management. A 27-year-old man with long-standing gynecomastia, fatigue, and poor sleep was referred for raised prolactin. Cannulated sampling showed mild stress-related hyperprolactinaemia, with suppressed gonadotrophins but normal testosterone. He reported use of over-the-counter testosterone boosters. Following discontinuation, gonadotrophins and prolactin normalised. Persistent symptoms were attributed to mild REM- and positional-predominant sleep-disordered breathing, managed with CPAP and sleep hygiene. A 35-year-old man accessed private testosterone and hCG therapy for presumed hypogonadism without full evaluation. After 18 months, he developed testicular atrophy and erythrocytosis requiring venesection. Other pituitary hormones were normal on assessment. All therapy was ceased, and serial monitoring demonstrated recovery of gonadotrophins and testosterone, with normalisation of haematologic parameters.
Discussion and Learning Points
These cases demonstrate how misdiagnosis or unregulated treatments can suppress gonadotrophins, mimic central hypogonadism, and threaten fertility while causing haematologic and metabolic complications. Recovery of the HPG axis is possible but requires structured monitoring and careful counselling. Hypogonadism should be assessed only in specialist centres with validated investigations. Persistent fatigue with normal gonadal function warrants evaluation for alternative causes. Clinicians must educate patients on the risks of private or unregulated therapy and ensure safe, evidence-based management.

DOI: 10.1530/endoabs.113.WE4.1

## WE5.1

### Diagnostic challenges in male anabolic-androgenic steroid use

Florika Radia & Channa Jayasena
St Marys Hospital, London, United Kingdom

A 31-year-old male presented with persistent loss of libido and erectile dysfunction. His symptoms were investigated 3 years prior where his blood results revealed Hb 169 g/l (130-168) HCT 0.544 L/l (0.39 – 0.500) FSH < 0.1 unit/l (1.7-8.0) LH < 0.1 unit/l (2-12) cortisol 247 nmol/l (160-550) prolactin 139 milliunit/l (60-300) TSH 0.98 milliunit/l (0.30-4.20) SHBG 33 nmol/l (15-55) testosterone 14.1 nmol/l (10.0-30.0) oestrodiol 126 pmol/l (<190) and free testosterone 0.292 nmol/l. He had undergone normal puberty, had intact sense of smell, and had a muscular appearance with normal hair distribution His past medical history revealed use of anabolic-androgenic steroids (AAS) including Trenbolone at the age of 18 to enhance body image for a few months. He is currently prescribed Testosterone Enantate 75 mg which was initiated at another clinic. Whilst this normalised his testosterone it did not completely alleviate his symptoms. He reported relationship breakdown and lack of confidence related to persistent symptoms. This case illustrates the diagnostic challenges encountered in AAS use. This patient's suppressed gonadotrophins were consistent with exogenous testosterone or synthetic derivative administration. However, it is important to recognise that some patients misuse drugs that increase endogenous testosterone production e.g. aromatase inhibitors which can present with raised gonadotrophins. Awareness of these differing biochemical profiles is essential to avoid misinterpretation and ensure accurate diagnosis and management.

DOI: 10.1530/endoabs.113.WE5.1

## WE5.2

### Fluctuating severe hyperandrogenism of uncertain origin in a perimenopausal female

Kyi Pyar Than Yu & Probal Moulik
Royal Shrewsbury Hospital, Shrewsbury, United Kingdom

Background
Hyperandrogenism in women presents with diverse clinical manifestations, ranging from mild hirsutism to overt virilization. Establishing the underlying cause is crucial, but diagnostic challenges arise when hormonal levels fluctuate, and imaging is inconclusive. This case highlights the complexity of evaluating unexplained hyperandrogenism in a middle-aged woman.
Case Presentation
A 48-year-old woman was referred to the endocrine clinic with a one-year history of worsening hirsutism and mild virilization, on a six-year background of these virilization symptoms. Current medications included hormone replacement therapy with estradiol and progesterone, taken for the past four years, and a prior short course of Testogel replacement for six to eight months in 2022. On physical examination, she weighed 68.2 kg with a BMI of 24.2 kg/m$^2$. She had androgenic alopecia, clitoromegaly, and voice deepening.
Investigations
The hormonal profile showed elevated serum testosterone at 4.8 nmol/l (reference range 0–1.8). Gonadotropin levels were within the normal range (LH 5.6 IU/l [4-14] , FSH 7.6 IU/l [3-13]). DHEAS, androstenedione, 17-hydroxyprogesterone, and prolactin levels were all normal. Cortisol appropriately suppressed to 26 nmol/l following an overnight dexamethasone suppression test. Interestingly, her testosterone levels were not consistently elevated; they peaked at 9 nmol/l in 2024 but later normalized spontaneously to 1.2 nmol/l in 2025. A 24-hour urinary steroid profile has been requested and is currently pending. Imaging investigations, including transvaginal ultrasound, pelvic MRI, and dedicated adrenal MRI, were unremarkable, with no evidence of ovarian or adrenal pathology.
Management and outcome
Given the normalization of testosterone without intervention and the absence of identifiable ovarian or adrenal tumors, a conservative management approach was adopted. The plan was to continue close follow-up with serial hormonal monitoring and reassessment should androgen levels rise again.
Conclusion
This case highlights the diagnostic challenge of fluctuating hyperandrogenism in women. A transient elevation of testosterone with spontaneous normalization suggests either prior exogenous exposure or intermittent endogenous androgen secretion. In the absence of persistent biochemical or imaging abnormalities, continued surveillance with serial hormonal monitoring represents the most appropriate management approach.

DOI: 10.1530/endoabs.113.WE5.2

# Workshop F: Disorders of the parathyroid glands, calcium metabolism and bone

## WF1.1

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

Muhammad Tahir Younas[1] & Jane Dale[2]
[1]Royal Shrewsbury Hospital, Shrewsbury, United Kingdom; [2]Russells Hall Hospital, Dudley, United Kingdom

Background
X-linked hypophosphatemia (XLH) is a rare hereditary disorder characterised by defective bone and dental mineralisation causing rickets impaired growth, nephrocalcinosis and hyperparathyroidism. It is driven by elevated fibroblast growth factor 23 (FGF23) and consequent hypophosphatemia. Standard management typically involves high doses of oral phosphate salts and active vitamin D analogues. New therapeutic options are emerging, such as Burosumab which is a monoclonal antibody that blocks fibroblast growth factor 23 (FGF23), which leads to increased renal phosphate reabsorption, and increased serum phosphate and 1,25-dihydroxyvitamin D (calcitriol) levels, improving bone mineralisation and quality of life.
Case Report
We describe an unusual case of a 44 year-old man with XLH complicated by tertiary hyperparathyroidism (TH), despite ongoing phosphate and vitamin D replacement. While secondary hyperparathyroidism is a recognised treatment-related complication, progression to irreversible TH is rarely reported. In 2019, he developed hyperparathyroidism and parathyroid imaging (MIBI scan and 4 D CT) demonstrated diffuse parathyroid hyperplasia. He underwent a total parathyroidectomy, which initially normalised calcium levels. Histology confirmed hyperplasia of all four glands. However, in 2022, the patient again developed progressive hypercalcemia and elevated parathyroid hormone (PTH) levels, despite normal phosphate and Vitamin D levels. Repeat MIBI scanning revealed a 12 mm hyperplastic parathyroid nodule in the soft tissues of the neck. Current management considerations include surgical re-exploration, combined with Burosumab and cinacalcet (a calcimimetic) to prevent further recurrence.
Conclusion
This case highlights the challenges of managing refractory tertiary hyperparathyroidism in XLH and the need for alternative therapeutic strategies. Further research is required to establish whether surgical intervention or targeted medical therapy—such as Burosumab, with or without calcimimetics—should be prioritised in this complex clinical setting.
Keywords
Burosumab, calcitriol, fibroblast growth factor 23, hypophosphatemia, tertiary hyperparathyroidism, X-linked hypophosphatemic rickets

DOI: 10.1530/endoabs.113.WF1.1

## WF1.2

### Selecting anabolic therapy in osteoporosis with fragility fractures

Audrey MacDougall, Alexander Comninos, Jeremy Cox, Preeshila Behary & Jacques Abella
St Mary's Hospital, London, United Kingdom

A 77 year-old lady with a past medical history significant for endometrial cancer previously treated with chemotherapy and radiotherapy attended metabolic bone clinic for management of severe osteoporosis of the lumbar spine with previous fragility fractures. She had fallen from standing height within the last year and sustained compression fractures of the lumbar spine at L1 and L4. A DEXA conducted post-fall revealed mean T-scores of -3.6 for the lumbar spine, - 2.1 for the total hips and -2.6 for the femoral necks. Routine blood tests were largely unremarkable- bone profile was in normal range and the patient was vitamin D replete. P1 NP was noted to be slightly raised at 61.3 ug/l, potentially reflecting recent fracture. Risk factors for low bone mineral density identified were being postmenopausal, history of endometrial cancer treated with chemotherapy, and previous fragility fractures. Calculations using FRAX indicated ten-year fracture probabilities of 24% for major osteoporotic and 8.1% for hip fractures, and with NOGG guidelines thus recommending treatment. Treatment options considered included bisphosphonates, denosumab, abaloparitide and romosozumab. Abaloparitide was contraindicated due to previous radiotherapy exposure. The patient met the NOGG criteria for starting romosozumab (severe osteoporosis with fragility fractures within the past 24 months with T score $<$-3.5). In counselling the patient on this medication, a possible increase in cardiovascular risk was discussed (~1% increased risk for heart attack and stroke). The patient's QRISK3 score was calculated, which indicated a risk of heart attack or stroke similar to what would otherwise be expected for her age (absolute 10-year risk of heart attack or stroke 19.7%, relative risk 1.0). She was encouraged to maintain good calcium intake, including regular calcium and vitamin D supplementation, as well as good dental hygiene, with a plan to commence anti-resorptive therapy on completion of the one-year course of romosozumab. The patient was referred to our specialist nursing team for commencement of romosozumab, with a plan to review her again in clinic in 4 months with repeat blood and urine tests for bone turnover markers.

DOI: 10.1530/endoabs.113.WF1.2

## WF2.1

### A journey to diagnosis: oncogenic osteomalacia presenting with recurrent fragility fractures

Mohammed Shamsaldeen, Maria Omer & Rahul Yadav
Warrington Hospital, Warrington, United Kingdom

Background
Oncogenic osteomalacia is a rare, acquired disorder caused by phosphaturic mesenchymal tumours that secrete excess fibroblast growth factor 23 (FGF23), leading to renal phosphate wasting, hypophosphatemia, and defective bone mineralisation. Diagnosis is often delayed due to non-specific symptoms and overlap with osteoporosis.
Case Presentation
A 60-year-old man with asthma and hiatus hernia initially presented in 2019 with progressive right hip and chest wall pain. Blood tests showed persistent hypophosphatemia, low calcium, normal vitamin D, mildly raised alkaline phosphatase, and elevated PTH. He was diagnosed with secondary hyperparathyroidism and treated with calcium and phosphate supplements. Over the next two years, he developed persistent pain requiring hospital admissions and sustained multiple atraumatic fractures. DEXA scanning confirmed osteoporosis, and alendronate was started. Despite treatment, hypophosphatemia persisted, prompting further endocrine review. Followed by rheumatology team for possible seronegative inflammatory spondylarthritis, but analgesics and Trail of disease-modifying therapy failed to improve symptoms. A decline in renal function was noted, suspected to be analgesia-related interstitial nephritis, and Fanconi syndrome was excluded. In March 2022, endocrine review revealed elevated 24-hour urinary phosphate excretion, high serum FGF23, hypocalciuric, and elevated P1 NP, raising suspicion of oncogenic osteomalacia.He underwent a bone scan which revealed which showed multiple areas of increase uptake. This, along with high FGF23, prompt a referral to Sarcoma MDT to look for oncogenic osteomalacia from mesenchymal tumour with the outcome being that 'no evidence of tumour' and they advised a review by metabolic bone clinic. In September 2023, he was reviewed by metabolic bone clinic, PET/CT was arranged and identified intense uptake in the proximal right humerus. MRI confirmed a 34 x21 x18 mm marrow-replacing lesion, and subsequent CT-guided biopsy confirmed aphosphaturic mesenchymal tumour. Genetic testing for PHEX mutations was conducted to exclude X-linked hypophosphatemia. Outcome and follow-up In October 2024, the tumour was surgically resected. Post-operatively, the patient reported significant improvement in mobility and pain reduction. Planned for repeat DEXA scanning to monitor bone recovery and tapering of Phosphate and calcitriol therapy under endocrine supervision.
Conclusion
Oncogenic osteomalacia, although rare, should be considered in adults with persistent hypophosphatemia, renal phosphate wasting, and multiple atraumatic fractures, particularly when elevated FGF23 is present. Tumour localisation often requires dedicated imaging and a multidisciplinary approach. Early identification and resection of the underlying tumour are crucial to reversing metabolic bone disease, improving bone health, and preventing further fractures.

DOI: 10.1530/endoabs.113.WF2.1

## WF2.2

### Hungry bone syndrome following delayed parathyroidectomy in a young male with symptomatic primary hyperparathyroidism and obstructive urolithiasis

Kiran Rathi, Saara Abdinor & Amy Morrison
University Hospitals of Leicester, Leicester, United Kingdom

Background
Hungry Bone Syndrome (HBS) is a rare but serious complication following parathyroidectomy for primary hyperparathyroidism (PHPT), particularly in

patients with long-standing disease and significant skeletal involvement. This case highlights the clinical challenges in managing advanced PHPT complicated by obstructive nephrolithiasis and the postoperative metabolic derangements of HBS.

Case Presentation

A 27-year-old male with a history of acute pancreatitis and prior appendectomy presented to the Emergency Department with fever, right flank pain, and visible hematuria. Imaging revealed a 4×3 mm obstructing right proximal ureteric stone with hydronephrosis. Biochemical evaluation showed severe hypercalcemia (adjusted calcium 3.14 mmol/l), elevated PTH (48.85 pmol/l), low vitamin D (17 nmol/l), and high ALP (367 U/l), suggestive of metabolic bone disease secondary to PHPT. The patient had been diagnosed with PHPT abroad and was awaiting specialist review in the UK. He underwent urological management with stenting and nephrostomy due to recurrent obstruction. Parathyroid imaging revealed a large left inferior parathyroid adenoma (3.1 × 2.2 cm) confirmed on SPECT-CT. Two months post initial presentation, he underwent successful parathyroidectomy. Two days postoperatively, he developed symptomatic hypocalcemia, with a normal adjusted calcium of 2.17 mmol/l, persistent elevation in ALP, and a transiently suppressed PTH (1.07 pmol/l), with low vitamin D (21) consistent with Hungry Bone Syndrome. He was commenced on Colecalciferol, with repeat calcium check after 24 hours indicating this was starting to increase and PTH later normalized to 7.52 pmol/l.

Conclusion

This case illustrates the importance of early recognition and multidisciplinary management of PHPT, particularly in younger patients presenting with renal complications. Timely parathyroidectomy is essential to prevent end-organ damage. Postoperative monitoring for HBS is critical, especially in patients with severe bone disease, high ALP, and vitamin D deficiency pre-operatively.

DOI: 10.1530/endoabs.113.WF2.2

## WF3.1

**Fibrous dysplasia should be considered a differential in asymptomatic, isolated rise in ALP**

Aeysha Harvey
University Hospitals Southampton, Southampton, United Kingdom

Introduction

Fibrous dysplasia is a rare non hereditary genetic disorder in which normal bone marrow is replaced with expansile fibro-osseous lesions, resulting in pain, reduction in bone strength and fractures. It can manifest as monostatic (single bone) or polyostotic (multiple bones) disease with the craniofacial skeleton, long bones and ribs commonly being affected. Extra skeletal features such as skin hyperpigmentation and hyper functioning endocrinopathies may be present if associated with McCune-Alright syndrome, originating from a mutation in the GNAS gene.

Clinical Case

A 62 year old gentleman was referred to Hepatology in 2017 with an isolated rise in alkaline phosphatase (ALP) of 233 U/l (30-130 U/l) for the preceding 4 years. He was asymptomatic but noted to have bilateral hearing aids. He was extensively investigated with a full liver screen, ultrasound and MRCP which were all normal. He was subsequently seen by Rheumatology 7 years later with a persisting rise in ALP, now 356 U/l (30-130 U/l) but with no symptoms suggestive of Paget's disease. Calcium, vitamin D, phosphate, magnesium and renal function were within the normal range. A nuclear medicine bone scan showed extensive heterogenous marked uptake in the skull and mild uptake in L1. As his presentation was not typical for Paget's disease a CT head and skull base was performed which showed very extensive bony 'ground glass' change throughout the majority of this skull base and occipital, most characteristic for extensive, but slightly atypical, fibrous dysplasia with radiological involvement of the optic canals bilaterally. On examination he had no relevant cutaneous changes, no changes in face shape, normal thyroid and testicular ultrasound and no evidence of hyperfunctioning endocrinopathy. Current management strategies focus primarily on symptom control and although bone therapy has not yet been initiated he is keeping a symptom diary.

Conclusion

Fibrous dysplasia should be on the list of differentials for cases that appear as an asymptomatic rise in ALP. Presence of ground glass changes and location of lesions (fibrous dysplasia has a predilection for long bones) may be features that favour fibrous dysplasia. This case demonstrates the importance of implementing a multisciplinary approach to management and the often prolonged diagnostic journey these patients encounter.

DOI: 10.1530/endoabs.113.WF3.1

## WF3.2

**Starved bones: malnutrition, type 3c diabetes, and the perfect storm for osteoporosis**

Mariyam Shazra & Smriti Gaur
Norfolk and Norwich University Hospital NHS Foundation Trust, Norwich, United Kingdom

Introduction

Osteoporosis is a known complication of diabetes. Both type 1 and type 2 increase fracture risk, but type 3 c (pancreatogenic) diabetes can result in even more severe bone disease due to nutritional and metabolic challenges. Here, we present a case of a 44-year-old man with type 3 c diabetes and multiple comorbidities who developed severe osteoporosis, emphasising the importance of a multidisciplinary approach.

Case Presentation

A 44-year-old man with a history of reactivated tuberculosis was referred after a right proximal femoral fracture. His tuberculosis treatment caused chronic pancreatitis, leading to type 3 c diabetes requiring insulin and complicated by gastroparesis. Due to severe malnutrition (BMI 14 kg/m$^2$), he was initiated on total parenteral nutrition two years ago. He also had long-standing suboptimal glycaemic control, a history of bowel surgery for Familial adenomatous polyposis, ankylosing spondylitis, past cannabis use, and a family history of osteoporosis. He was bedbound in a nursing home and required a stretcher for hospital visits. In 2017, his bone density scan confirmed osteoporosis (lumbar spine T-score -3.2), but no treatment was started. Calcium and renal function were satisfactory, but vitamin D was low (34 nmol/l;N-50-120 nmol/l), and ALP remained persistently elevated (394 U/l;N- 30-130 U/l). Because he could not tolerate oral bisphosphonates and preferred to avoid frequent injections due to the injection burden, annual zoledronate infusions were commenced. His vitamin D level was optimised, and his diabetes management was escalated with support from the community diabetes facilitator team.

Discussion

This case highlights the cumulative effects of multiple factors—type 3 c diabetes, malnutrition and malabsorption, low BMI, and immobility on bone health. The loss of insulin's anabolic effects also contributes to higher fracture risk. Therefore, early screening and assessment in the metabolic bone clinics, and integrated multidisciplinary management, including gastroenterology, nutritional service, and diabetologists, are essential for improving outcomes in this high-risk population. Notably, there are currently no specific national guidelines for early evaluation of bone health in people living with diabetes.

Reference

Tomasiuk JM, Nowakowska-Płaza A, Wisłowska M, Głuszko P. Osteoporosis and diabetes - possible links and diagnostic difficulties. Reumatologia. 2023;61(4):294-304. doi: 10.5114/reum/170048. Epub 2023 Sep 3. PMID: 37745139; PMCID: PMC10515121.

DOI: 10.1530/endoabs.113.WF3.2

## WF4.1

**To treat or not to treat: bone health decisions post-parathyroidectomy**

Evgenia Foteinopoulou
Edinburgh Centre for Endocrinology and Diabetes, Edinburgh, United Kingdom

Primary hyperparathyroidism (PHPT) is associated with reduced bone mineral density (BMD), particularly at cortical sites. Parathyroidectomy is the definitive treatment and may result in partial recovery of bone mass. Aa 74-year-old female diagnosed with PHPT underwent successful parathyroidectomy. Pre-operative dual-energy X-ray absorptiometry (DEXA) demonstrated osteoporosis with T-scores of –2.8 at the lumbar spine, –2.5 at the left femoral neck and hip, and –4.6 at the left forearm. The multidisciplinary consensus was to monitor her bone density post-operatively without immediate pharmacological osteoporosis therapy, with reassessment at 2 years. Repeat DEXA in 2025 showed improvement: lumbar spine T-score –2.4, femoral neck and hip T-score –2.3, and forearm T-score –4.5. The forearm measurement remained stable but was not considered clinically significant, as treatment decisions were not based on forearm BMD. This case highlights the potential for improvement in BMD at trabecular and mixed skeletal sites following curative parathyroidectomy in PHPT, supporting a conservative approach with re-evaluation before initiating additional osteoporosis therapy.

Questions

1. After curative parathyroidectomy in PHPT with osteoporosis, should bone-specific therapy be started immediately or delayed until reassessment?
2. What is the optimal timing for repeat DEXA after curative parathyroidectomy?

3. What is the recommended calcium/vitamin D supplementation strategy post-parathyroidectomy in older patients with osteoporosis?

DOI: 10.1530/endoabs.113.WF4.1

## WF5.1

### Severe hypercalcaemic crisis and high bone turnover in primary hyperparathyroidism: the role of early parathyroidectomy and the challenge of hungry bone syndrome

Karishma Davi
University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

Introduction

Severe hypercalcaemic crisis is a recognized and potentially life threatening presentation of Primary Hyperparathyroidism. Marked bone turnover suggested by elevated ALP predisposes to Hungry Bone Syndrome following parathyroidectomy. This case highlights severe symptomatic hypercalcaemic crisis due to a parathyroid adenoma, with marked skeletal and renal involvement, complicated by Hungry Bone Syndrome post operatively.

Clinical Case

A 48 year old gentleman presented with confusion, nausea, vomiting, dehydration, abdominal pain and proximal muscle weakness. His biochemistry revealed a corrected calcium of 5.93 mmol/l (2.2 – 2.6 mmol/l), PTH of 159.4 pmol/l (1.8 – 6.8 pmol/l), Phosphate of 0.69 mmol/l (0.80 – 1.5 mmol/l), ALP of 406 U/l (30 – 130 U/l), and 25-OH Vitamin D of 17 nmol/l (51 – 374 nmol/l); consistent with severe hypercalcaemia in the setting of Primary Hyperparathyroidism with evidence of high bone turnover, and Vitamin D Deficiency. He had an acute kidney injury with Cr of 294 umol/l (59 – 104 umol/l), multiple right renal calculi up to 4 mm and bilateral nephrocalcinosis on CT KUB imaging, suggesting end-organ damage. CT Neck showed a 1.4 cm x 1.2 cm x 2 cm right inferior parathyroid nodule. Despite medical management with intravenous fluids, bisphosphonate therapy, and Cinacalcet, this patient had refractory symptomatic hypercalcaemia, and considering the severity of the presentation, with end-organ disease involvement, the patient was referred for urgent parathyroidectomy as per NICE guidance, and underwent subsequent explorative surgical excision of the right inferior parathyroid nodule, with histology confirming a parathyroid adenoma. Post operatively, he had prompt PTH normalization to 2.1 pmol/l, and Calcium stabilised to 2.46 mmol/l, confirming removal of the culprit lesion was successful. He soon developed persistent hypocalcaemia, along with persistently elevated ALP, and low phosphate levels, in keeping with Hungry Bone Syndrome. He required close monitoring and management with calcium and Vitamin D supplementation, highlighting the predictive value of raised ALP and high bone turnover pre-operatively.

Conclusion

This case highlights the skeletal and renal manifestations of a hypercalcaemic crisis in Primary Hyperparathyroidism. Elevated ALP is a marker of high bone turnover, and a predictor of the risk of developing Hungry Bone Syndrome following parathyroidectomy. Early surgical intervention, where indicated, can be life saving. Careful anticipatory planning, vigilant post operative monitoring and early recognition and management of post operative hypocalcaemia are crucial to optimize patient outcomes.

References

1. National Institute for Health and Care Excellence. Hyperparathyroidism (primary): diagnosis, assessment and initial management. NICE guideline NG132. London: NICE; 2019. Available from: https://www.nice.org.uk/guidance/ng132

DOI: 10.1530/endoabs.113.WF5.1

## WF5.2

### Chronic aches and pains with low ALK phosphatase

Shanza Akram[1] & Paul Cook[2]
[1]University Hospital Southampton, Southampton, United Kingdom; [2]UHS, Southampton, United Kingdom

Introduction

Hypophosphatasia (HPP) is a rare metabolic bone disorder characterized by deficient activity of alkaline phosphatase, resulting from pathogenic variants in the *ALPL* gene. The clinical spectrum can range from perinatal lethal forms to mild adult-onset presentations. Adult HPP is often underdiagnosed, as symptoms overlap with common musculoskeletal and rheumatological conditions. Early recognition is critical, as inappropriate use of anti-resorptive therapies can exacerbate disease and enzyme replacement therapy (asfotase alfa) may offer benefit in selected cases.

Case Presentation

A 31-year-old woman, an intensive care unit (ICU) nurse, was referred for evaluation of chronic musculoskeletal pain. She reported lower back pain with early morning stiffness since adolescence, worsening in 2016. HLA-B27 was positive, though MRI of the lumbar spine and sacroiliac joints (2020) revealed no evidence of inflammation. Non-steroidal anti-inflammatory drugs (ibuprofen, etoricoxib) provided minimal relief. She also described intermittent left shoulder pain since 2012, exacerbated during acute illness, and left knee pain with swelling after prolonged walking. Her past history included a finger fracture, loss of three adult teeth, and frequent dental chipping. She denied childhood skeletal deformities or gait abnormalities. Intermittent tinnitus was reported. Family history revealed rheumatoid arthritis in her mother and stomach cancer in her father. No known familial bone disease was reported. She was a non-smoker, non-drinker, and lived with her partner. During a COVID-19 infection in 2022, routine laboratory testing identified low alkaline phosphatase (ALP) at 6 U/l (reference range: 30–130 U/l). Review of past results confirmed persistently low ALP values (6–17 U/l) over the preceding five years. Serum calcium, magnesium, zinc, copper, liver and renal function, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were consistently normal. Genetic testing confirmed a pathogenic *ALPL* variant, establishing the diagnosis of hypophosphatasia. She was subsequently referred to a rare bone disease clinic. Management included a referral to pain team, physiotherapy and genetic counselling. She reported that a herbal preparation (Devil's Claw) provided superior pain relief compared with pharmacological options.

Discussion

This underscores the importance of considering HPP in patients with chronic pain as treatment modalities could make a considerable difference, Enzyme replacement, alfa asfotase though primarily indicated in pediatric-onset disease, evidence suggests possible symptomatic and radiological improvement in adults. Antiresoptives, especially bisphosphonates, should be avoided due to increased risk of AFF. Genetic counselling is essential given AD inheritance. Options for family members and reproductive planning include non-invasive & invasive prenatal testing and pre-implantation genetic testing.

DOI: 10.1530/endoabs.113.WF5.2

# Workshop G: Disorders of appetite and weight

## WG1.1

### From childhood-onset obesity to adult weight reduction: multi-disciplinary management of a patient with KSR2 mutation

Kiran Rathi, Ehtasham Ahmad & James Greening
University Hospitals of Leicester, Leicester, United Kingdom

Childhood-onset obesity is a complex clinical entity, especially in patients with rare genetic mutations. We present the longitudinal case of a female patient with **KSR2 mutation**, a gene encoding *Kinase Suppressor of Ras-2*, which plays a critical role in cellular energy balance and AMPK signalling. Pathogenic KSR2 variants are associated with early-onset severe obesity, hyperphagia, and insulin resistance, with limited response to conventional therapies. This patient began gaining weight at the age of 3 years and remained >99 th centile for BMI despite structured dietary intervention and active lifestyle. Initial investigations, including thyroid, liver, and lipid profiles, were normal; OGTT revealed normal glucose and insulin dynamics but reduced sex hormone–binding globulin. At age 14, genetic analysis confirmed a **KSR2 mutation**. She was commenced on **metformin (1 g twice a day)**, resulting in ~10 kg weight loss initially, but the effect plateaued within one year despite good adherence. She followed a vegan diet and developed no obesity-related complications such as diabetes, Obstructive sleep apnea, or joint disease. Psychosocial challenges emerged, with low mood, anxiety, and depression, later compounded by a diagnosis of **Autism Spectrum Disorder**; she was treated with sertraline. At age 18, she was assessed for a clinical trial of **setmelanotide (MC4 R agonist)**; however, recruitment ceased due to limited efficacy. Multidisciplinary recommendations included **GLP-1 receptor agonist therapy** and possible bariatric surgery. She was referred to a Tier 3 Specialist Weight Management Service. Investigations showed **ALT 34 U/l, TSH 3.1 mIU/l, normal eGFR**, with an **Edmonton Obesity Staging System score of 2**. She was commenced **semaglutide (Wegovy)**, titrated from 0.25 mg weekly to a dose of 2.4 mg weekly. Her weight trajectory demonstrates significant clinical impact: in **May 2024, she weighed 104.5 kg (BMI 34.2)**, but at her most recent review, she had reduced to **78 kg**. This substantial weight loss, however, has been accompanied by **sagging and loose skin**, leading her to seek **brachioplasty and abdominoplasty**, and she is currently awaiting review by the plastic surgery team. This case illustrates the need for **long-term, multidisciplinary, and precision-based care** in severe genetic obesity. It highlights the evolving role of GLP-1 receptor agonists in monongenic causes of obesity, and the potential place for surgical and reconstructive intervention. The psychosocial burden, especially in the context of neurodevelopmental disorders, underscores the importance of integrated psychological support alongside metabolic management in childhood cases of obesity.

DOI: 10.1530/endoabs.113.WG1.1

## WG2.1

### Difficulty identifying clinical signs of cushing's disease with concomitant glucagon-like peptide-1 receptor (GLP-1) agonist use

Demetris Mariannis[1], Carmel Halevy[1], Vassiliki Bravis[1] & Einas Mohamed[2]
[1]Imperial Healthcare College NHS Trust, London, United Kingdom; [2]Imperial College Healthcare NHS Trust, Imperial College Healthcare NHS Trust, United Kingdom

Background
Cushing's disease typically presents with a constellation of symptoms associated with hypercortisolism, including weight gain, hypertension and diabetes. Diagnosis may be challenging with concomitant use of weight loss medications, potentially masking the classical features of Cushing's disease.
Case Presentation
A 53-year-old menopausal woman with a background of asthma presented with weight gain and a large neck lipoma. Her medications included hormone replacement therapy, Symbicort and prednisolone during asthma exacerbations. She was prescribed GLP1- agonist for weight loss by her endocrinologist. Her initial weight was 105 kg, and with semaglutide therapy, she achieved a weight of 85 kg and continuing to lose weight.
Investigations
9 am Cortisol 326 nmol/l, ACTH 53.0 ng/l (RR<30) ONDST: cortisol 304 nmol/l, ACTH not done Midnight Salivary Cortisol: 3.8 nmol/l & 4.0 (RR <2.6) Midnight Salivary Cortisone: 28.8 nmol/l & 30.6 nmol/l (RR <18) LDST: 48-hour cortisol 207 nmol/l. ACTH not done HDDST - ACTH suppressed to 14 ng/l 24-hour urine cortisol - 113 & 206 nmol/day (RR 0-164) HbA1 c 33 mmol/mol (RR <48) MRI pituitary - 5 mm cystic pituitary microadenoma These findings suggest centrally driven hypercortisolemia. However, the patient did not exhibit classic clinical features of Cushing's disease, including hypertension or hyperglycemia (HbA1 c 33 mol/mol), likely secondary to ongoing semaglutide use.
Management and Outcome
The case was discussed at the pituitary multidisciplinary team meeting with the impression of Cushing's disease and given the presence of a target lesion that could be amenable to surgical intervention, the patient will undergo inferior petrosal sinus sampling prior to a neurosurgical consultation.
Conclusion
This case displays the diagnostic challenges in considering potential Cushing's disease when the only presenting feature is obesity, which is being effectively managed with GLP-1 agonist therapy. Given the increasing use of GLP-1 agonist, clinicians should remain vigilant in considering Cushing's disease even when classical features are absent.

DOI: 10.1530/endoabs.113.WG2.1

## WG3.1

### Beyond weight loss: transforming outcomes through obesity management

Matus Kalavsky
Watford General Hospital, Watford, United Kingdom

Background
Obesity is characterised by excess adiposity, with or without organ or tissue dysfunction. It increases the risk of metabolic, cardiovascular, respiratory, musculoskeletal, and oncological disease. Obesity management is more than weight loss- it can transform functional capacity and eligibility for critical treatments such as surgery or radiotherapy.
Case
A 68-year-old man was referred to the obesity clinic by his oncology team for weight reduction to facilitate radiotherapy planning, which was limited by body habitus and significant risk of lymphoedema. Baseline weight was 153 F;kg, height 1.78 F;m (BMI 48.3 F;kg/$m^2$). Past medical history included hypertension, dyslipidaemia, prediabetes, osteoarthritis of the knees, and prostate adenocarcinoma. He reported a long history of cyclical weight loss and regain since his mid-40 s, with previous trials of commercial diets and orlistat (discontinued due to gastrointestinal intolerance). He declined bariatric surgery due to caregiving responsibilities. Functional limitations included knee pain restricting mobility. Psychological assessment showed minimal depressive and anxiety symptoms (PHQ-9 3/27; GAD-7 2/21). STOP-Bang score indicated intermediate risk of sleep apnoea, prompting a referral for a sleep study.

Baseline investigations:

| | |
|---|---|
| HbA1 c | 44 mmol/mol |
| fasting glucose | 6.1 mmol/l |
| total cholesterol | 4.5 mmol/l |
| LDL | 2.4 mmol/l |
| HDL | 1.2 mmol/l |
| triglycerides | 1.4 mmol/l |
| LFTs | normal |
| eGFR | 92 mL/min/1.73 $m^2$ |
| TSH | 1.5 mIU/l |
| vitamin D | 36 nmol/l |
| folate | 6.1 µg/l |
| B12 | 305 ng/l |
| Iron studies | Normal |

Following multidisciplinary review, he was initiated on semaglutide (Wegovy®), titrated from 0.25 F;mg to 2.4 F;mg weekly, alongside dietetic guidance (protein adequacy, portion control), pragmatic physical activity (seated exercises, daily walking goals) and vitamin D supplementation. He was reviewed every 8 weeks with metabolic monitoring and behavioural support. At 6 F;months, he achieved 16 F;kg weight loss (around 10%), with increased energy, reduced knee pain, and greater independence, but no significant side effects. HbA1 c decreased to 38 F;mmol/mol and LDL to 1.9 F;mmol/l. His oncology team deemed him fit to proceed with radiotherapy planning.
Discussion
Early multidisciplinary approach to obesity, consisting of endocrinology, dietetics, physiotherapy, psychology and others, improves outcomes. Semaglutide should be used in conjunction with lifestyle interventions in adults with an initial BMI of at least 30 kg/$m^2$, or between 27 kg/$m^2$ to 30 kg/$m^2$ in the presence of at least one weight-related comorbidity. Even moderate, sustained weight loss can produce significant benefits: improved glycaemia, lipids, mobility, quality of life, confidence and eligibility for treatments.

DOI: 10.1530/endoabs.113.WG3.1

## WG4.1

**Ethical and clinical challenges in renal transplant eligibility for a patient with prader-willi syndrome**

Dalhatu Yusuf, Hassan Kahal & Fleur Talbot
North Bristol NHS Trust, Bristol, United Kingdom

Prader-Willi syndrome (PWS) is a rare, complex genetic disorder resulting from the absence of expression of paternally inherited genes in the chromosome 15 q11.2 q13 region. It's characterised by hypothalamic dysfunction, hyperphagia, and severe obesity, alongside endocrine and neurodevelopmental complications. Obesity remains the leading cause of morbidity and mortality in adults with PWS, and its management is complicated by behavioural rigidity, impaired satiety regulation, and metabolic dysregulation. While bariatric surgery is considered for some cases, its effectiveness in PWS is limited. Wolf *et al*'s meta-analysis reports initial excess weight loss of 50-60% at one year, comparable to BMI-matched controls, but with substantial weight regain by year three (down to 20-30%), with outcomes strongly influenced by the type of procedure performed. We present the case of a 30-year-old woman with genetically confirmed PWS and end-stage renal disease (eGFR 9). Her comorbidities include growth hormone deficiency, duplex kidneys, type 2 diabetes, autistic spectrum disorder, hypertension, and obstructive sleep apnoea on CPAP. Her BMI was 52 kg/m$^2$ (weight 139.5 kg, height 1.60 m). Despite meeting eGFR criteria for renal transplant, her BMI exceeded the threshold for referral. A target weight of 90 kg (35% reduction) was required for eligibility. She was therefore referred to weight management services. The BMI threshold was established to reduce surgical risk and outcome, as excess weight can affect graft vasculature and increase the risk of graft loss. As she had no living donor, coordinating transplant timing with nadir weight was unpredictable, which complicated eligibility. Furthermore, achieving 35% weight reduction was deemed unfeasible, especially in PWS, where hyperphagia and behavioural rigidity hinder success. Based on these considerations, the Tier 3 and Tier 4 MDT concluded that she is not a candidate for bariatric surgery. She was therefore commenced on haemodialysis and Semaglutide along with behavioural and nutritional support. Her most recent weight is 121 Kg with a BMI of 48, following 11 months on this regimen. This case highlights the ethical tension between transplant eligibility criteria and equitable access to care. While BMI thresholds aim to optimise surgical outcomes, they may inadvertently exclude patients with syndromic obesity whose physiological and behavioural profiles limit weight loss potential. Conversely, proceeding with surgery in the context of poor expected outcomes and increased risk may not be justified. Future research should focus on refining transplant eligibility frameworks, assessing long-term outcomes of weight loss methods in syndromic populations, and creating equitable care pathways.

DOI: 10.1530/endoabs.113.WG4.1

# Workshop H: Miscellaneous endocrine and metabolic disorders

## WH1.1

### A MEN1 family

Cristina Eliza Grigoras
Kent and Canterbury Hospital, Canterbury, United Kingdom

A 38 year old man was referred by his GP to the endocrinology clinic to investigate mild hypercalcemia and hyperparathyroidism. He had a history of recurrent kidney stones and had 3 1/2 parathyroid glands removed more then 10 years before. He also had a strong family history of hypercalcemia and hyperparathyroidism affecting his mother and 2 siblings (an older brother and a younger sister), none of them under regular specialist follow-up. The patient initially reported no family history of neuroendocrine tumours or pituitary tumours. The family had never been offered a genetic test. Patient's biochemical and hormone investigations showed a high normal albumin adjusted calcium of 2.6 mmol/litre with inappropriately elevated PTH 7.1 pmol/litre. The genetic test confirmed a genetic diagnosis of MEN1 syndrome. Patient's mother aged 60 had a history of hypercalcemia and hyperparathyroidism with 2 parathyroid surgeries more than 20 years before. She had a low, but detectable PTH and was treated with alfacalcidol and Adcal-D3 for hypocalcaemia. She had a recent presentation with acute bowel obstruction and was diagnosed with metastatic bowel NET. During the first consultation in the endocrine clinic she disclosed that her father also had hyperparathyroidism and died of a brain tumour and that her paternal uncle died of pancreatic tumour. The genetic test confirmed a genetic diagnosis of MEN1. The patient was commenced on Somatostatin analogues and later on Lu Dotatate PRRT. Unfortunately she passed away a couple of months later after developing small bowel obstruction. Patient's brother aged 42 had a history of hypercalcemia and hyperparathyroidism and had a right lower parathyroid adenoma removed in 2004. He had a history of kidney stones and fibrous tumours removed from the nose and scalp. He has 2 children aged 8 and 11. The genetic test confirmed a genetic diagnosis of MEN1. This patient was referred to Guy's Genetic department for counselling regarding genetic testing for his children. Patient's sister aged 35 had a history of hypercalcemia and hyperparathyroidism with 3 1/2 parathyroid glands removed 15 years before (parathyroid hyperplasia). Biochemical and hormone investigations showed an albumin adjusted calcium of 2.4 mmol/litre and an elevated PTH 14 pmol/litre. The genetic test confirmed a genetic diagnosis of MEN1. Further hormone investigations showed an elevated glucagon and an unsuppressed cortisol after overnight dexamethasone. The abdominal imaging reported multiple small pancreatic cysts compatible with neuroendocrine tumours. The patient was started on Somatostatin analogues. She was referred to Guy's genetics clinic for counselling regarding genetic testing for her 2 children. All 3 surviving patients continue to have regular hormone and imaging investigations according to MEN1 management guidelines.

DOI: 10.1530/endoabs.113.WH1.1

## WH2.1

### Recurrent primary hyperparathyroidism during pregnancy revealing MEN1 syndrome: diagnostic and surgical challenges

Aisha Hashmi, Soe Nyi Nyi Htet, Ioannis Dimitropoulos & Patrick Chong
Department of Endocrinology & Diabetes, University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom

Background
Primary hyperparathyroidism (PHPT) is a common endocrine disorder characterised by hypercalcemia and elevated parathyroid hormone (PTH) levels. Multiple Endocrine Neoplasia type 1 (MEN1) is a hereditary syndrome associated with multiglandular endocrine tumours, including recurrent or multigland parathyroid disease. Management of PHPT during pregnancy presents significant diagnostic and therapeutic challenges, particularly in the context of MEN1.
Case Presentation
We report a case of a 24-year-old woman initially diagnosed with PHPT, presenting with hypercalcemia (2.76 mmol/l), elevated PTH (13.2 pmol/l), and associated symptoms including palpitations and near-syncope. Imaging identified two parathyroid adenomas, which were surgically removed. Postoperative calcium and PTH levels improved but remained mildly elevated. The patient was lost to follow-up and subsequently had two pregnancies. During her second pregnancy, she re-presented with recurrent hypercalcemia (2.68 mmol/l), elevated PTH (22.6 pmol/l), and a neck mass. Genetic testing confirmed a MEN1 mutation.
Management and Outcome
Following multidisciplinary discussion, parathyroidectomy was performed during the second trimester to reduce maternal and fetal risks. Postoperative calcium and PTH were normalised without complications. The patient remains under endocrine and obstetric care, with ongoing surveillance for MEN1-associated tumours. Genetic counselling has been provided to assess familial risk and guide screening in offspring.
Discussion
Recurrent or multiglandular PHPT in young individuals should prompt evaluation for MEN1. During pregnancy, hypercalcemia increases the risk of miscarriage, preeclampsia, intrauterine growth restriction, and neonatal hypocalcemia. While conservative management may be considered in mild cases, surgery is the definitive treatment for symptomatic or persistent hypercalcemia, ideally performed in the second trimester to minimise obstetric and anaesthetic risks. This case highlights the importance of a coordinated, multidisciplinary approach and early genetic diagnosis in managing complex endocrine conditions during pregnancy.
Conclusion
This case underscores the diagnostic and therapeutic complexities of recurrent PHPT in pregnancy and the critical role of recognising MEN1. Timely surgical intervention during pregnancy, along with multidisciplinary and genetic input, is essential to optimise maternal and fetal outcomes.

DOI: 10.1530/endoabs.113.WH2.1

## WH3.1

### Autosomal dominant hypocalcaemia type 1 in a family with autoimmune endocrinopathies: importance of genetic testing

Zaiem Zarkasi[1], Rajshekhar N. Mudaliar[2,3] & Akheel A. Syed[2,3]
[1]Endocrinology, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, United Kingdom; [2]Endocrinology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, United Kingdom; [3]Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom

Hypocalcaemia is most commonly caused by hypoparathyroidism, vitamin D deficiency, or renal disease. In young patients with a strong family history and co-existing autoimmune endocrinopathies, autoimmune polyglandular syndrome type 1 (APS-1) is often suspected. APS-1, caused by pathogenic variants in the *AIRE* gene, classically presents with autoimmune hypoparathyroidism, chronic mucocutaneous candidiasis, and adrenal insufficiency. Autoimmune hypothyroidism and type 1 diabetes can also be associated with APS-1. However, genetic causes of hypocalcaemia can also be present, and distinguishing them is crucial for diagnosis, prognosis, and management. We describe a 57-year-old woman with chronic hypocalcaemia due to childhood-onset hypoparathyroidism. She was diagnosed with type 1 diabetes at the age of 10 and autoimmune hypothyroidism in her 40 s. The coexistence of multiple autoimmune endocrinopathies, combined with a younger sister who also had chronic hypocalcaemia, initially raised suspicion of APS-1. However, genetic testing was negative for pathogenic variants in the *AIRE* gene. Subsequent genetic testing of the sibling and the index patient revealed a heterozygous activating mutation in the *CASR* gene, establishing a diagnosis of autosomal dominant hypocalcaemia type 1 (ADH1). ADH1 is a rare, inherited form of non-surgical hypoparathyroidism caused by heterozygous gain-of-function mutations in *CASR* (Roszko *et al*., 2022; Roszko *et al*., 2016). These mutations increase CaSR sensitivity to extracellular calcium, resulting in suppression of parathyroid hormone secretion and enhanced renal calcium excretion. The biochemical hallmark is hypocalcaemia with hyperphosphataemia, low or inappropriately normal PTH, and frequent hypercalciuria (Roszko *et al*., 2022; Chang *et al*., 2025; Dershem *et al*., 2020). Clinical expression is variable: some individuals remain asymptomatic, while others develop neuromuscular irritability, muscle cramps, or seizures. Chronic complications include nephrocalcinosis, nephrolithiasis, renal impairment, and occasionally basal ganglia calcifications (Roszko *et al*., 2022; Kinoshita *et al*., 2014). ADH1 is increasingly recognised as a cause of hypoparathyroidism but remains underdiagnosed, as shown by population-based studies (Chang *et al*., 2025; Dershem *et al*., 2020). Management is challenging: conventional treatment with calcium and calcitriol may exacerbate hypercalciuria and renal complications, so therapy aims to maintain calcium at the lowest level that prevents symptoms. Thiazide diuretics can reduce urinary calcium, and calcilytics (CaSR antagonists) are under investigation but are not yet in routine use (Roszko *et al*., 2016; Gafni *et al*., 2019). This case highlights a diagnostic pitfall, where coexisting autoimmune endocrinopathies initially suggested APS-1 but genetic confirmation revealed ADH1. Importantly, ADH1 and APS-1 require different counselling and management strategies. This underscores the importance of

considering genetic causes of hypocalcaemia, even in the presence of autoimmune conditions, and of incorporating *CASR* mutation analysis into the diagnostic pathway for familial hypocalcaemia.

DOI: 10.1530/endoabs.113.WH3.1

## WH4.1

**Advanced adrenocortical carcinoma with severe hypercortisolemia-role of debulking surgery**

Louise Sarr[1], Fiasal Hassan[2] & Salah Alhbuheissi[2]
[1]University Hospital Bristol and Weston, Bristol, United Kingdom; [2]North Bristol Trust, Bristol, United Kingdom

Adrenocortical carcinoma is a rare and aggressive malignancy, with an incidence of 1–2 cases per million annually. Approximately 50% present with advanced disease, and 60% of cases are hormonally active—most commonly with cortisol excess. This case describes a 63-year-old male farmer who initially presented with chest pain and elevated troponin levels, and was treated for NSTEMI. Further investigation revealed bilateral lung nodules and a right adrenal mass with inferior vena cava (IVC) thrombus. Clinical features included significant weight gain, cushingoid appearance, uncontrolled hypertension on four agents, and hyperglycaemia. Biochemical assessment showed severe hypercortisolaemia with suppressed ACTH, negative plasma metanephrines, and a urine steroid profile suggestive of cortisol excess only. Imaging confirmed a large right adrenal mass invading the adrenal vein and IVC, with indeterminate liver lesions and pulmonary metastases. Metyrapone was initiated for cortisol control and anticoagulation commenced for the IVC thrombus. The case was referred to a specialist Neuroendocrine Tumour (NET) multidisciplinary team (MDT), which recommended debulking surgery following adequate cortisol suppression. Peri-operative management was high-risk, given the background of recent NSTEMI and severe hypercortisolaemia. Metyrapone was stopped preoperatively; hydrocortisone was administered peri-operatively alongside steroid-sparing measures and PCP prophylaxis. The patient underwent open right adrenalectomy, with complete resection of the adrenal mass. Liver nodules were left in situ. Post-operatively, the patient showed significant clinical improvement, including weight loss, better glycaemic and blood pressure control, and improved functional status. Histopathology confirmed adrenocortical carcinoma with lymphovascular invasion, a high Ki-67 index (30–40%), and R2 resection margins. Final staging was ENSAT Stage IV (pT4 pNX pMX). This case highlights the complexity of managing advanced ACC, especially in the context of life-threatening hypercortisolaemia. Debulking surgery, although not curative in metastatic ACC, may offer meaningful symptom relief, improved quality of life, and facilitate subsequent oncological treatment. Early identification and control of cortisol excess are crucial to reducing surgical risk

DOI: 10.1530/endoabs.113.WH4.1

## WH5.1

**A hidden syndrome behind hypertension: a case of von hippel-lindau in a young adult**

Matus Kalavsky
Watford General Hospital, Watford, United Kingdom

Background
Von Hippel-Lindau (VHL) is a genetic syndrome caused by mutations in the VHL tumour-suppressor gene, that predisposes individuals to CNS and retinal haemangioblastomas, pheochromocytomas, neuroendocrine tumours of pancreas, renal and pancreatic cysts and other benign tumours. VHL may initially present subtly, but early recognition is essential to prevent serious complications and guide lifelong follow-up.
Case
A 32-year-old man was referred to Ambulatory Care Unit with 6-month history of recurrent headaches, palpitations, and persistent high blood pressure despite ramipril 5 mg once daily. He also reported intermittent episodes of flushing and sweating lasting 10–15 minutes, often triggered by stress or exertion. On examination, the blood pressure was 180/110 mmHg and the resting heart rate was 110 bpm. No other abnormalities were noted on physical examination. There was no evidence of end-organ damage. Serum electrolytes, PTH, renal/liver/thyroid function, cortisol and renin/aldosterone ratio were all within a normal range. However, plasma-free metanephrine was significantly elevated at 2.5 nmol/l (normal $<0.5$), as was normetanephrine at 3.8 nmol/l (normal $<0.9$). MRI of the abdomen revealed a 4 cm right adrenal mass in keeping with a pheochromocytoma, along with incidental pancreatic and renal cysts. MIBG scintigraphy showed a high accumulation of the tracer in the right adrenal lesion. MRI brain and spine showed multiple posterior fossa haemangioblastomas. Fundoscopy showed no abnormality. A detailed family history revealed that patient's father died in his 40 s from a brain tumour. The patient was started on alpha-blockade with phenoxybenzamine for blood pressure control prior to surgery. Once adequate alpha-blockade was achieved, a beta-blocker was added. He subsequently underwent laparoscopic adrenalectomy without complications. Postoperatively, blood pressure normalised and his episodes of flushing and palpitations resolved. Patient was referred to the neurosurgical team for an assessment for the CNS haemangioblastomas. He was started on prednisolone for headaches and was offered a neurosurgical intervention. Genetic testing confirmed a pathogenic VHL mutation. On discharge, he was enrolled in a structured surveillance program including periodic MRI scans of abdomen, brain and spinal cord, regular eye exams by ophthalmologist, regular bloods for plasma metanephrines and urine for catecholamines. First-degree relatives were offered genetic counselling and testing.
Discussion
This case demonstrates that hypertension in young adults can rarely be a clue to an underlying hereditary tumour syndrome. Pheochromocytomas may present subtly- a careful analysis of symptoms, biochemistry and imaging is essential for diagnosis.

DOI: 10.1530/endoabs.113.WH5.1

# Author Index