



**DIABETES CANADA/CSEM**  
PROFESSIONAL CONFERENCE  
AT VASCULAR 2023

OCTOBER 25-29, 2023

## CSEM RESIDENT CLINICAL VIGNETTES AND RESEARCH PROJECTS

## CSEM Poster Presentations

## Research Hour in Exhibition Hall

Thursday–Saturday, October 26–28, 2023 | 15:15–16:15

## Clinical Vignettes Oral Presentation

Saturday, October 28, 2023 | 14:00–15:00

## Research Projects Oral Presentation

Saturday, October 28, 2023 | 16:30–17:00



SATURDAY, OCTOBER 28, 2023, 1400–1500 ET

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Tayyab Khan, MD, FRCPC

### 1402 • PRESENTATIONS

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NIVOLUMAB: A CASE REPORT

JANE WANG, MD\*

ENDOCRINE MANIFESTATIONS OF  
ERDHEIM-CHESTER DISEASE: A CASE SERIES

DANIEL (YIQIAO) WANG, MD\*

PREGNANCY INDUCED CUSHING'S SYNDROME

CHAITANYA GANDHI, MD\*

A RARE CASE OF NON-ISLET CELL TUMOUR HYPOGLYCEMIA  
FROM A SOLITARY FIBROUS LUNG TUMOUR

ANNA LIU, MD\*

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ERDHEIM-CHESTER DISEASE?

XING SUN, MD\*

VERY HIGH DHEAS: A CASE OF STEROID SULFATASE DEFICIENCY  
IN A FEMALE PATIENT

SARAH ZANKAR, MD\*

HYPERINSULINISM/HYPERAMMONEMIA (HI/HA) SYNDROME IN  
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IHAB KANDIL, MD\*

FROM OVERDRIVE TO BURNOUT: DEVELOPMENT OF DIABETES  
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AHSEN CHAUDHRY, MD\*

\*AWARD ELIGIBILITY

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\*AWARD ELIGIBILITY



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**JANE WANG\*, JESSICA HADDAD,  
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Université de Montréal

## ISOLATED VASOPRESSIN DEFICIT ASSOCIATED WITH NIVOLUMAB: A CASE REPORT

**Introduction:** While immunotherapy is well known for causing various endocrine complications, isolated posterior pituitary dysfunction has rarely been reported.

**Case description:** We present the case of a 39-year-old female with metastatic gastric adenocarcinoma (lymph node, hepatic and ovarian metastases) admitted for malignant pericardial effusion. She was recently started on the Folfox protocol (folinic acid, fluoracil, oxaliplatin) and nivolumab every 2 weeks starting 7 weeks prior to this admission. Endocrinology was consulted for suspected vasopressin (AVP) deficiency. Following the first dose of immunotherapy, the patient noted a new onset of polydipsia and polyuria. In addition, she complained of nausea and vomiting a few days prior to admission. Calcium, glucose, and potassium levels were within normal ranges. HbA1c was 5.8%. Serum sodium level was 150 mmol/L and urine osmolality was 69 mmol/kg H<sub>2</sub>O. The urinary osmolality increased to a maximum value of 648 mmol/kg H<sub>2</sub>O six hours after administering 2 mcg of subcutaneous DDAVP, confirming the clinical diagnosis of AVP deficiency. Adrenal, thyroid

and lactotroph axes were normal. The gonadotroph axis was considered indeterminate: the patient had a history of amenorrhea for several months prior to chemotherapy and immunotherapy, with undetectable estradiol levels and non-elevated nor suppressed FSH (7.1 UI/L) and LH (9.0 UI/L) levels. While somatotroph axis was not specifically evaluated, IGF-1 was normal. Magnetic resonance imaging revealed a slight thickening of the pituitary stalk with pituitary heterogeneity, suggesting hypophysitis. There were no pituitary lesions suspicious for metastasis. The posterior pituitary bright spot was absent. She was discharged with morning and bedtime oral DDAVP.

**Discussion:** Isolated posterior pituitary dysfunction associated with immunotherapy is a rare condition which needs to be differentiated from pituitary metastasis. Only five similar cases have been reported until now. This case highlights the importance of recognizing this rare condition despite the absence of anterior pituitary deficits. It also illustrates the variety of potential effects of immunotherapy on the endocrine system.



**CHAITANYA GANDHI\*, TAMMY MCNAB, RSHMI KHURANA, TORU TATENO, TODD MCMULLEN, ARIANE DROUIN, CONSTANCE CHIK**  
University of Alberta

## PREGNANCY INDUCED CUSHING'S SYNDROME

**Background:** Pregnancy-induced Cushing's syndrome (CS) represents a rare but emerging entity. The onset of cortisol excess occurs during pregnancy often followed by spontaneous remission postpartum. We describe a patient with pregnancy-induced CS.

**Clinical Case:** A 31-year-old nulliparous woman required admission at 24 weeks gestational age for early-onset pre-eclampsia. She displayed clinical features of CS (acne, hirsutism, dorsocervical adiposity, large striae, face roundness, hypertension, and bruising). Investigations showed elevated 24-hour urine free cortisol (UFC) and serum cortisol, with low adrenocorticotropic hormone (ACTH). Additionally, serum testosterone was increased (Table 1). Pelvic ultrasound revealed bilateral ovarian enlargement with prominent follicles consistent with ovarian hyperstimulation. Unfortunately, she required emergency C-section for intrauterine fetal demise, attributed to placental abruption. Postpartum, she had rapid improvement in biochemistry: serum cortisol, 24-hour UFC, late night salivary cortisol (LNSC), and testosterone normalized within 1 month (Table 1); however 1 mg and 8 mg dexamethasone suppression tests were abnormal with absent diurnal variation in cortisol. Pelvic imaging showed resolution in ovarian enlargement after 3.5 months. Although initial postpartum CT abdomen reported normal adrenals, re-interpretation suggested bilateral adrenal micronodules. Over the next 15 months, she had cyclic symptoms of feeling hot, worsening acne-like lesions, striae, and edema associated with intermittent elevation of

LNSC. During these episodes, ACTH and DHEAS were low. Moreover, there was incomplete cortisol suppression after 2 days of low-dose and high-dose dexamethasone. Adjunctive clues for possible cortisol excess demonstrated normal 24-hour UFC with absence of hypertension, hyperglycemia, and hypokalemia. Dynamic testing did not reveal paradoxical increase in 24-hour UFC with prolonged dexamethasone (Liddle's test) on two occasions and genetic testing for endocrine neoplasia was negative. ACTH 250 mcg stimulation completed one year postpartum revealed 160% and 64% maximal increase in serum cortisol and testosterone, respectively. Stimulation with human chorionic gonadotropin (hCG) 6,500 units showed cortisol and testosterone elevations of 129% (24 hours) and 155% (96 hours), respectively, post administration (Table 2). Interestingly, response to GnRH 100 mcg stimulation was negative. Currently, the patient plans to pursue pregnancy. She is scheduled for a unilateral adrenalectomy for diagnostic purposes and will receive metyrapone intrapartum.

**Discussion:** Hypotheses of pregnancy-induced CS implicate aberrant receptor expression on the adrenal cortex. Such receptors include luteinizing hormone (LH)/hCG, melanocortin-2, or estradiol. In our case, dynamic testing suggests  $\beta$ -hCG mediated stimulation of LH/hCG-receptors. Although rare, pregnancy-induced CS requires awareness given adverse fetal outcomes. Targeted dynamic testing postpartum may help elucidate further mechanisms and identify therapeutic targets.



**ANNA LIU\*, TONY LIU, HERNAN FRANCO LOPEZ**  
Western university

## A RARE CASE OF NON-ISLET CELL TUMOUR HYPOGLYCEMIA FROM A SOLITARY FIBROUS LUNG TUMOUR

**Background:** Non-islet-cell tumour hypoglycemia (NICTH) is a paraneoplastic syndrome caused by high molecular weight ("big") IGF-II production from both benign and malignant tumours. Although rare, NICTH is important to identify because treatment differs from other causes of hypoglycemia. In this case report, we highlight the clinical presentation, pathophysiology, and treatment of NICTH caused by a solitary fibrous tumour, also known as Doege-Potter syndrome.

**Case:** An 89-year-old woman, with a history of CHF and diet-controlled T2DM, presents to hospital with increased shortness of breath, weight loss and fatigue. She was recently diagnosed with a 13 cm biopsy-proven fibrous tumour in the right hemithorax, which is now causing hypoxia. Point-of-care glucose checks in hospital reveal daytime and overnight hypoglycemia (2.3–3.3 mmol/L) associated with fatigue, nausea and diaphoresis. Her symptoms improve with correction of hypoglycemia. Further workup yields a serum glucose level of 2.1 (4–10 mmol/L), C-peptide 67 (370–1470 pmol/L), insulin < 7 (18–173 pmol/L), beta-hydroxybutyrate < 0.1 mmol/L, and IGF-I of 35 (17–167 mcg/L). Glucagon administration results in a glucose rise from 2.9 mmol/L to 4.0 mmol/L (> 1.4 mmol/L). The IGF-II assay is unavailable at our center (n.b. a ratio of IGF-II:IGF-I greater than 3:1 is suggestive of NICTH). Given her clinical presentation and biochemical findings, we make a presumptive diagnosis of Doege-Potter syndrome.

**Results:** With dietary changes and initiation of dexamethasone 6mg p.o. daily, both daytime and overnight hypoglycemic episodes resolve and she is successfully discharged from hospital. She is not a candidate for surgical tumour resection, and is awaiting radiation treatment while continuing on high dose steroid therapy and use of intranasal glucagon as needed.

**Discussion:** Recognition of NICTH is important in the treatment and prevention of hypoglycemic episodes. NICTH from Doege-Potter syndrome is associated with the NAB2-STAT6 fusion gene, which drives big IGF-II production. This IGF-II causes hypoglycemia through activating the IGF-I, IGF-II and insulin receptors to reduce growth hormone release, increase peripheral glucose uptake, as well as suppress gluconeogenesis, glycogenolysis and glucagon secretion. Although the definitive treatment of NICTH is tumour resection, medical therapy may be required to bridge to surgery and for non-surgical candidates. Our case aligns with previous reports demonstrating that treatment with high dose steroids equivalent to prednisone > 20 mg is effective at resolving hypoglycemia. Other treatments include recombinant human growth hormone and glucagon infusion. Somatostatin analogues and diazoxide are not effective in the treatment of NICTH.



**YIQIAO WANG\*, LURDES TSE-AGHA, SARA AWAD,  
JOSHUA LAKOFF**  
Queen's University

## ENDOCRINE MANIFESTATIONS OF ERDHEIM-CHESTER DISEASE: A CASE SERIES

**Introduction:** Erdheim-Chester Disease (ECD) is a non-Langerhans Cell Histiocytosis commonly associated with the BRAFV600 mutation. Approximately 800 cases have been reported in literature. Common endocrine manifestations include pituitary involvement in 70% of patients, and central diabetes insipidus (CDI) in up to 50% of patients. We present two patients with ECD and endocrine-related manifestations.

**Case Presentation:** Patient #1 is a 75-year-old male, who initially presented with shortness of breath secondary to bilateral pleural plaques. Subsequent pleural biopsy revealed histiocytes. Initial workup demonstrated primary hypogonadism with a low total testosterone of  $< 0.4$  (8.4–28.8) and a cortisol level of 283. Subsequent pituitary panel was unremarkable other than an elevated FSH (52.1) and LH (24.7). PET scan showed moderate uptake in adrenal glands bilaterally, without symptoms of adrenal insufficiency. PET and CT scans also revealed soft tissue thickening of the abdominal aorta and perirenal spaces bilaterally, classic radiologic features of ECD. In contrast, patient #2 is a 71-year-old female with a longstanding history of polyuria and polydipsia. She was diagnosed with CDI following an overnight 10-hour water deprivation

test that showed a high morning sodium of 149, serum osmolality of 306, and a dilute urine osmolality of 111. She improved clinically and biochemically with desmopressin. MRI sella showed hypophysitis and bilateral masses near the medulla, encasing the right vertebral artery, and CT scan of the abdomen showed circumferential thickening of the abdominal aorta and proximal common iliac arteries. Bone scan revealed infiltration of vertebrae and long bones, with subsequent biopsy of the distal femur demonstrating foamy histiocytes confirming the diagnosis.

**Management and Outcome:** Patient #1 was managed by endocrinology, hematology, and urology. Regarding his primary hypogonadism, testosterone gel was initiated, and total testosterone improved to 9.6 (6.0–34.0). Repeat AM cortisol was 263 and he will be considered for an ACTH stimulation test. He was also started on trametinib with clinical improvement in symptoms. Patient #2 was started on oral desmopressin with clinical improvement. She is awaiting hematology consult for initiation of immunosuppressive agents and genetic testing. In follow-up, serial adrenal and pituitary scans in addition to hormone panels are important to monitor for new endocrine pathology.



**XING SUN\*, HEATHER LOCHNAN**  
University of Ottawa

## ISOLATED DIABETES INSIPIDUS: HAVE YOU CONSIDERED ERDHEIM-CHESTER DISEASE?

**Background:** Isolated Diabetes insipidus can have an elusive diagnosis and histiocytosis is on the differential. Histiocytosis are rare disorders characterized by the accumulation of cells thought to be derived from dendritic cells or macrophages. They can be classified as Langerhans cell histiocytosis (LCH) or non-LCHs like Erdheim-Chester disease (ECD). LCH are common in the pediatric population, while ECD mainly affects adults, more often males. ECD is a neoplastic disease with mutations in MAPK pathway and can involve multiple organ systems including cardiac, pulmonary, endocrine, retroperitoneal, skin and skeletal manifestations. In recent years a somatic mutation in the BRAF V600E gene has been identified in both LCH and ECD tissue infiltrates, suggesting a common origin of both histiocytosis, and shedding light on new treatment options for ECD which was previously considered an aggressive histiocytic disorder with poor response to therapy.

**Case presentation:** A 41-year-old female initially referred to Endocrinology with polyuria and polydipsia found to have central diabetes insipidus, later developed central hypogonadism and hyperprolactinemia. MRI sella shows thickened pituitary stalk consistent with lymphocytic hypophysitis. Patient was started on desmopressin however despite increasing doses (0.6 mg PO QID) and a trial of prednisone had no significant improvement. 3 years

later she developed fevers NYD and was found to have significant periorbital xanthelasma; macular skin lesions on ankles and flanks; and bony pain with imaging showing osteosclerosis. Biopsy of the skin lesions revealed Langerhans cell histiocytosis, positive for BRAF V600E mutation. Given the constellation of symptoms including recurrent fevers, hypophysitis, serositis, osteosclerosis and xanthelasma, together with skin biopsy results, she was diagnosed with LCH with ECD clinical features. For management, she was initially started on first line chemotherapy with Cladribine with no clinical or radiographic improvement noted. Next step would be to start targeted therapy with Dabrafenib, a BRAF inhibitor.

**Discussion:** This case illustrates a rare presentation of concomitant occurrence of both LCH and ECD in the same patient, and posed significant diagnostic challenges to her care team. Central diabetes insipidus is the most common endocrinopathy associated with ECD, and usually appears early in the disease course. Therefore an initial diagnosis of isolated diabetes insipidus, together with other features such as xanthelasma palpebrarum and bony pain with osteosclerosis, may prompt towards further testing for ECD. Given the rare and aggressive nature of ECD, early diagnosis is crucial to begin treatment and slow disease progression.



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University of Ottawa

## VERY HIGH DHEAS: A CASE OF STEROID SULFATASE DEFICIENCY IN A FEMALE PATIENT

**Background:** Steroid sulfatase deficiency (STSD) is an inherited disease which prevents the conversion of sulfated steroids into their unconjugated forms, such as the conversion between dehydroepiandrosterone sulfate (DHEAS) and its biologically active counterpart, dehydroepiandrosterone (DHEA). The responsible gene is on the X-chromosome and males who inherit this disorder develop X-linked ichthyosis. Female carriers are asymptomatic and often remain undiagnosed.

**Case Description:** A previously healthy 27-year-old female was investigated for unilateral galactorrhea and change in menstrual pattern. She was not on any medications. Prolactin was found to be elevated at 165 ug/L (reference range < 24 ug/L). Screening investigations for other etiologies of menstrual dysregulation revealed very high DHEAS at > 27.00 umol/L (reference range 2.68–9.23 umol/L). Patient had mild hirsutism with no other signs or symptoms of virilization. Menses occurred every 28–36 days. Additional investigations revealed: LH at 2.6 IU/L, FSH at 2 IU/L, 24h urine cortisol at 87 nmol/d, sex hormone binding globulin at 24 nmol/L, 17-Hydroxyprogesterone (17OHPreg) at 1.9 nmol/L and androstenedione (AnS) at 8.5 nmol/L, all within normal ranges. Total testosterone was elevated at 3.2 nmol/L (reference range < 2.0 nmol/L). Magnetic resonance imaging (MRI) of the abdomen noted

unremarkable adrenals and ultrasound of ovaries was normal. MRI sella revealed a microadenoma consistent with prolactinoma and patient was started on cabergoline. Genetics assessment for STSD is pending.

**Discussion:** This patient's significantly elevated DHEAS raised suspicion of possible ominous etiology such as adrenocortical carcinoma, which was fortunately excluded with normal imaging studies and benign clinical presentation. Other possible etiologies, such as congenital adrenal hyperplasia and polycystic ovarian syndrome, were also ruled out. A literature search revealed a similar case of female patient with DHEAS at 20.5 umol/L and otherwise unremarkable work up, and STSD was subsequently confirmed with genetic testing. Female carriers of STSD are rarely identified as they are asymptomatic. Our patient was only discovered incidentally, but a confirmed diagnosis may be useful for family planning. Male offspring can be affected with X-linked ichthyosis, which presents primarily with dark scaly skin, but can also be associated with corneal opacities and rarely cognitive deficits. Furthermore, placental STSD results in very low estradiol production which may hinder progression of labor. Today, this can be addressed with cesarean section but historically resulted in still birth at term. Overall, this condition is relatively benign but should be considered in the differential for elevated DHEAS.





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## HYPERINSULINISM/HYPERAMMONEMIA (HI/HA) SYNDROME IN PREGNANCY: A CLINICAL VIGNETTE

**Introduction:** Hyperinsulinism/hyperammonemia (HI/HA) syndrome is a rare autosomal dominant metabolic disease caused by gain of function mutations in the GLUD1 gene. Over production of mitochondrial enzyme glutamate dehydrogenase (GDH) leads to excess insulin production by pancreatic  $\beta$ -cells and increase in ammonia levels. The most common clinical manifestations are neonatal recurrent severe hypoglycemia and seizures leading to cerebral damage, cognitive impairment and learning disability. In adulthood, management of HI/HA is centered around minimizing hypoglycemia risk through dietary and pharmacologic interventions. Commonly used medications include diazoxide, somatostatin analogues, and calcium channel blockers. Yet, little is known about the management of HI/HA in pregnancy, and the safety of the use of these agents.

**Methods:** In this report, we present a case of a 26-year-old female with HI/HA and GLUD1 gene mutation. She presented for evaluation with an unplanned pregnancy at 20 weeks gestational age. The patient's clinical history, hospitalization and treatments received during pregnancy are detailed. We review the limited literature on this topic and discuss the risks and benefits of various treatment strategies previously described.

**Results:** The patient was followed closely at our High risk Obstetrics clinic, with weekly monitoring of ammonia and glucose levels. Continuous glucose monitoring device was used to allow the patient to predict and manage low blood sugars. With the assistance of a dietician, the patient implemented a high carbohydrate and leucine restricted diet. She was unable to tolerate cornstarch for hypoglycemia prevention due to symptoms of severe nausea. Prior to pregnancy she was managed with diazoxide 400 mg twice daily and verapamil 80 mg daily. During pregnancy, her verapamil was discontinued and diazoxide dose reduced to 200 mg twice daily due to concern regarding potential teratogenic effects. An attempt to discontinue diazoxide resulted in hospitalization for severe hypoglycemia and seizure. Serial fetal ultrasounds showed normal anatomy with some symmetric growth restriction. She had a successful term delivery at 37 weeks via cesarean section.

**Conclusion:** HI/HA is a rare disorder that is challenging to manage in pregnancy. Optimal management involves a multidisciplinary approach that comprises optimization of dietary and pharmacologic interventions. Diazoxide has limited evidence of safety in human pregnancy but significant risks in animal studies. Octreotide is potentially an alternative option for refractory hypoglycemia, but has limited experience in pregnancy and unclear fetal risks. We recommend preconception counselling to highlight these uncertainties.



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University of British Columbia

## FROM OVERDRIVE TO BURNOUT: DEVELOPMENT OF DIABETES MELLITUS OVER 40 YEARS AFTER DIAGNOSIS OF CONGENITAL HYPERINSULINISM CAUSED BY A HOMOZYGOUS ABCC8 MUTATION

**Background:** Congenital hyperinsulinism (CHI) is a rare disorder characterized by insulin oversecretion and hypoglycemia. Loss-of-function mutations in the ABCC8 gene, which encodes the SUR1 subunit of the ATP-sensitive potassium channel, are the most common genetic cause of CHI. Treatment involves either conservative management, including feeding and diazoxide, or pancreatectomy. Due to its rarity, the long-term metabolic outcomes for patients with CHI, especially those managed conservatively, are not well understood.

**Case Presentation:** A 44-year-old woman presented with a new diagnosis of diabetes mellitus. Her medical history was significant for CHI diagnosed in the neonatal period. Genetic testing later confirmed a homozygous loss-of-function mutation in the ABCC8 gene (c.3992-9G >A). Her CHI was initially managed conservatively and did not require pancreatectomy. She continued to have occasional hypoglycemia into adulthood, including severe hypoglycemic episodes, prompting a dietary pattern of frequent carbohydrate intake to avoid hypoglycemia. She later developed gestational diabetes briefly requiring insulin at the age of 37. At presentation to us, initial investigations revealed an A1C of

8.7%, fasting glucose of 11.6 mmol/L, and 2-hour 75g-OGTT glucose of 19.8 mmol/L. C-peptide was 835 pmol/L with a corresponding plasma glucose of 7.2 mmol/L. Her weight was 100 kg and BMI was 34.6 kg/m<sup>2</sup>. She was started on low-dose metformin and counselled on lifestyle modification. At follow up 6 months later, she had lost 15 kg of weight and had improved glycemic control with a reduction in A1C to 5.9%.

**Discussion:** Although CHI causes recurrent hypoglycemia early in life, there is increasing recognition that it may progress to hyperglycemia and diabetes mellitus over time, as illustrated in our case. Prior studies have suggested that this could be due to prolonged  $\beta$ -cell overactivation and stress leading to perturbations in metabolic pathways and gene expression, as well as cumulative apoptosis and diminished  $\beta$ -cell mass. The impact of genetic predisposition and its complex interplay with acquired factors, such as obesity, in the development of diabetes is also highlighted in this case. Clinicians should be aware of the natural history of genetic CHI and recognize it as a possible risk factor for diabetes in order to effectively screen, monitor, and treat these patients.





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CLAIRE EMILY HIGHAM**  
Université de Montréal

## STROKE RISK IN CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS WHO RECEIVED CRANIAL RADIOTHERAPY

**Background:** Childhood, adolescent, and young adult (CAYA) cancer survivors who received cranial radiotherapy have an increased risk of stroke. Traditional cardiovascular disease (CVD) risk factors likely contribute, but there are no guidelines for the management of stroke risk in this population. It is unclear how general CVD risk calculators (Framingham Risk Score, QRISK3) compare to specific cancer survivors scores such as the Childhood Cancer Survivors Study Stroke Risk Calculator (CCSS).

**Objective:** Our aim is to describe traditional CVD risk factors in an UK CAYA survivor population and to compare the outcomes of 3 risk calculator models (FRS, QRISK3 and CCSS).

**Results:** 99 CAYA patients identified from consecutive late effects clinics at a tertiary oncology center from March–May 2021 were included. The mean age was 35.4 (SD 10.5) years old, with a mean age at the time of cancer diagnosis of 11.8 (SD 5.6) years old. Among the participants, 46% were female and 86%

were of Caucasian ethnicity. Risk factor data were available for 89.9% of the cohort and demonstrate that 7% were active smokers, 12% were diabetic, mean HbA1c was 39.3 (SD 19.8) mmol/mol, mean Chol:HDL was 3.9 (SD 1.1) and mean SBP was 127 (SD 16) mmHg. 90% received cranial radiotherapy with a mean dose of 47.5 (SD 8.9) Gy. The most frequently seen neoplasms included astrocytoma (23.2%), medulloblastoma (22.2%) and germinoma (13.1%). For patients with calculable FRS, QRISK3 and CCSS scores, 94.4% ( $n = 17$ ) and 100% ( $n = 38$ ) who had a CCSS 10-year stroke risk of 5–20% had a lower predicted risk of CVD using FRS and QRISK3, respectively. Patients who had cranial radiotherapy were more likely to have an underestimated common CVD calculator score. Neither FRS nor QRISK3 overestimated the risk calculated by CCSS. 6 patients in our cohort had a stroke, but their CCSS score could not be calculated as their age were  $> 40$  years old.

**Conclusion:** Common CVD risk prediction tools underestimate the risk of stroke compared to the CCSS calculator.



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## TRENDS IN INCIDENCE AND PREVALENCE OF DIABETES IN ADULTS UNDER THE AGE OF 40 IN CANADA: A REVIEW OF NATIONAL SURVEILLANCE DATABASES AND PRE-EXISTING LITERATURE

**Background:** Diabetes represents a key health priority globally and in Canada. Determining population-wide trends is critical in planning public health approaches for prevention and management of diabetes.

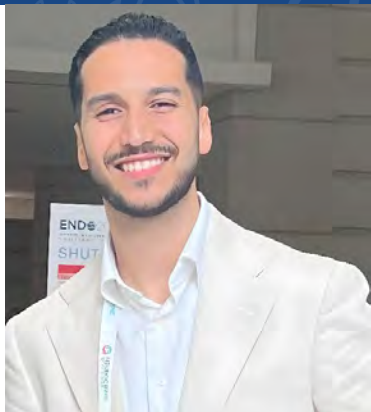
**Objectives:** We aimed to utilize the pre-existing data from the Canadian Chronic Disease Surveillance System (CCDSS) and current literature to determine the annual incidence and prevalence of diabetes in adults under the age of 40 in Canada.

**Methods:** Data from the Canadian Chronic Disease Surveillance System (CCDSS) was utilized, allowing hospital records to be examined according to diabetes diagnosis and age group. We also conducted a systematic review in accordance with the PRISMA guidelines. We searched PubMed, Embase, and CINAHL from January 1970 to December 2022, restricting our articles to those reported in English. Our search identified 8862 studies that upon further screening, identified 73 studies for inclusion.

**Preliminary results:** The latest available data from the CCDSS indicates that currently, 8.2% of Canadians live with diabetes, and approximately 619 new cases are diagnosed each day. Since 2000, the age-standardized prevalence rate has increased by an average of 3.0% per year. The age-standardized

incidence rate has remained relatively stable. Those aged 35–39 saw a 41.9% increase in incidence rates from 2000 to 2020, with a rate increase of 2.2% per year. Those aged 30–34 saw a 27.4% increase in incidence rates, with a rate increase of 1.5% per year. Those aged 25–29 saw a 9.3% increase in incidence rates, with a rate increase of 0.37% per year, and those aged 20–24 saw a 10.0% increase in incidence rates, with a rate increase of 0.4% per year. The highest prevalence and incidence rates were observed in Manitoba (9.54% and 761 per 100 000 respectively), while the lowest rates were observed in Quebec (6.73% and 442 per 100 000 respectively). Our review of the literature indicates that Manitoba has the second largest First Nation population in Canada, and have age-standardized incidence and prevalence rates of diabetes up to 4.5 times higher than those in non-First Nation populations. An increased risk of diabetes was associated with South Asian ethnicity, higher BMI, lower socioeconomic status and lower educational attainment.

**Conclusion:** Our review of national databases indicates that adults under the age of 40 have seen a net increase in both incidence and prevalence rates of diabetes since the year 2000, indicating the need for potential revision of the recommended age for screening, pending further study and analyses of the data.



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## NATURAL HISTORY AND PROGNOSTIC MARKERS OF AGGRESSIVE SUBTYPES AND HIGH-GRADE FOLLICULAR CELL-DERIVED MALIGNANCIES: A RETROSPECTIVE CHART REVIEW STUDY

**Background:** The prevalence of thyroid cancer has increased significantly. Aggressive subtypes of papillary thyroid cancer (AG-PTC) and poorly differentiated thyroid cancer (PDTC) are malignancies that lie between well-differentiated and undifferentiated cancers. The management of well-differentiated cancers has been established in the literature; however, that of AG-PTC and PDTC needs to be clarified because they exhibit characteristics different from those of their less aggressive counterparts.

**Objective:** To describe the clinicopathological characteristics and genomic landscape of AG-PTC and PDTC and to assess their prognostic value.

**Design:** A retrospective chart review of patients with thyroid cancer over the last 10 years.

**Setting:** Single center.

**Participants:** Patients with AG-PTC or PDTC were included in the analysis. Patients with other types of thyroid cancer were excluded. The clinical presentation, pathological characteristics, molecular markers, specific treatments, and clinical outcomes were compared between the groups.

**Results:** Of the 3244 thyroid cancer charts reviewed, 136 met the criteria for AG-PTC and PDTC. The mean age at diagnosis was 49 years, with a

predominance of women. The median follow-up duration was 3 years (0.1–30). Of 75 patients followed up for > 1 year, 42.7% had either a persistent or recurrent disease (52.6% in the AG-PTC group and 32.4% in the high-grade follicular cell-derived malignancy group), 4.5% died of AG-PTC, and 1.8% had PDTC. The presence of vascular or lymphovascular invasion and extrathyroidal extension was associated with a higher incidence of persistent or recurrent disease (Hazard ratio: 2.5, 3.8, and 4.2, respectively;  $p < 0.05$ ). No difference was observed in recurrence based on the presence of BRAF mutations or the percentage of aggressive/poorly differentiated tumor involvement.

**Conclusions and Relevance:** Possible prognostic markers for predicting recurrent and persistent thyroid cancers and guiding therapy for AG-PTC and PTC include vascular/lymphovascular invasion, extrathyroidal extension, response to primary therapy, and the proliferative index Ki-67.

**Keywords:** Thyroid cancer, Ki-67, BRAF, genetic mutation, aggressive variant, poorly differentiated, prognostic marker.



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## A SYSTEMATIC REVIEW ON THE ASSOCIATION BETWEEN DENOSUMAB USE AND THE RISK OF ATYPICAL FRACTURES

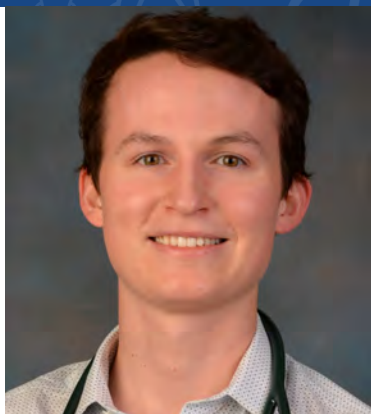
**Background:** Denosumab is a RANK-ligand inhibitor that inhibits osteoclastic activity, reducing bone resorption. It is used in osteoporosis management and has been shown to improve bone mineral density and reduce the risk of fragility fractures. Atypical femoral fractures (AFF) are tensile stress fractures caused by bone remodelling suppression characterized by unique radiographic and clinical features that differ from fragility fractures. Recently, there have been reports of a relationship between denosumab use and AFFs, but the magnitude of this risk remains poorly understood.

**Aim:** To conduct a systematic review to determine the risk of AFF associated with denosumab use.

**Methods:** We systematically searched the Cochrane library, Medline, and Embase for randomized controlled trials (RCTs) and observational studies of denosumab treatment associated with AFF from database inception until October 27, 2022. Two reviewers independently extracted the data and assessed the quality of included studies using the Cochrane Risk-of-Bias (RoB 2) tool to evaluate RCTs and the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS)-I tool to evaluate observational studies.

**Results:** A total of five RCTs, two non-randomized clinical trials, and seven observational studies met our inclusion criteria. A total of 26 811 individuals were included in these studies, of which 9223 had known malignancies. The indications for denosumab use and its dosages varied between studies. Indications included osteoporosis, giant cell tumor of bone and bone metastases. There was a low risk of bias among the RCTs and a moderate risk of bias in the observational studies examined. Overall, the observed incidence of AFFs among individuals receiving denosumab was low, varying between 0 and 4 %. The presence of important clinical heterogeneity prevented the meta-analysis of included studies.

**Conclusion:** The overall risk of AFF in individuals receiving denosumab is low. However, the studies retrieved were few and the populations studied included those with underlying malignancy. Further long-term studies with a focus on assessing denosumab use and AFF risk are needed.



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## IMPACT OF COVID-19 ON POSTPARTUM GESTATIONAL DIABETES FOLLOW-UP AT HÔPITAL MAISONNEUVE-ROSEMONT

**Background:** In order to screen gestational diabetes patients with postpartum glucose abnormalities, it is recommended to perform a 75g oral glucose tolerance test (OGTT) between 6 weeks and 6 months following delivery. The COVID-19 pandemic in March 2020 limited patient access to postpartum tests. In order to continue some form of screening, transiently prescribing glycated hemoglobin (HbA1c) and fasting blood glucose (FBG) tests three months postpartum was suggested. Our center then decided to provide HbA1c and FBG three months postpartum to improve postpartum screening when OGTT was unavailable. The aim of the present study is to evaluate if patients presented to the recommended screening and if postpartum prediabetes and diabetes were diagnosed adequately with the changed screening method.

**Methods:** In this retrospective study, we reviewed the medical records of patients diagnosed with gestational diabetes. We analyzed follow-up tests up to one year postpartum, separated into 2 cohorts of patients who gave birth during the COVID-19 pandemic. The first group, from July 1, 2020, to January 1, 2021, used the OGTT as the main screening modality, compared to the second group, from March 1, 2021, to September 1, 2021, which used HbA1c and FBG as the main screening modality.

**Results:** A total of 592 patient records were analyzed, with 284 in the first group and 308 in the second group. A screening test (either OGTT or HbA1c with FBG) was performed in 39.1% of cohort 1 compared to 46.8% in cohort 2. A positive test occurred in 10.2% of cohort 1 compared to 9.7% in the second group. 7% and 3.5% were diagnosed with prediabetes and diabetes, respectively, in group 1 compared to 7.5% and 3.2% in group 2. In the first cohort, 26.8% underwent a 75g OGTT, and in the second cohort, 38.3% underwent HbA1c and FBG, the favored tests for screening during the respective periods. These tests yielded a positive result in 7.7% of the first group when OGTT was used compared to 3.2% in the second group when HbA1c with FBG was used.

**Conclusion:** The change in screening modality led to an increase in the number of patients undergoing screening tests. However, the lower sensitivity of HbA1c combined with FBG did not provide an advantage to this increase in screened patients.



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## E-CONSULTS AS A TOOL TO IDENTIFY PRIMARY CARE PROVIDER PRACTICE-BASED CONTINUING PROFESSIONAL DEVELOPMENT LEARNING NEEDS IN ENDOCRINOLOGY

**Introduction:** Continuing Professional Development (CPD) activities are designed to address the learning needs of healthcare providers. The use of web-based tools such as electronic consultations (eConsults) provides a unique opportunity to evaluate current practice-based learning needs of primary care providers (PCPs). The purpose of our study was to analyze clinical questions asked by PCPs in Endocrinology eConsult referrals to identify CPD learning needs.

**Methods:** We analyzed the themes of 714 eConsult referrals sent by PCPs across Ontario from March 1, 2017 to July 31, 2023. The data was organized across 18 different clinical topics, and further classified into subcategories based on the clinical question reviewed. The type of question was classified based on previously validated taxonomy.

**Results:** Of a total of 714 questions, 241 (34%) were related to diagnosis and work up of endocrine conditions; 218 (31%) were related to specific

drug treatments and associated side-effects; and 216 (30%) were related to the general management of patients with endocrine disorders. The most common topic was thyroid disease (30%). The majority of questions were related to work up and management of hypothyroidism in different clinical contexts, as well as guidance on work up of thyroid nodules. The second most common topic was type 2 diabetes (17.5%), with questions focusing on selection of antihyperglycemic agents in chronic kidney disease and frail elderly patients. Other questions were related to treatment with GLP 1 receptor agonists and related to side effects. The other most frequently asked questions were related to osteoporosis (8.5%), pituitary gland disorders (6.9%) and women's health (6%).

**Conclusion:** Our study used e-Consults as a valuable tool to identify PCP practice-based learning needs across multiple endocrine conditions. The results will be useful as a needs assessment tool for CPD planning on endocrine-related topics.





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## ELEVATED DKA RISK FOLLOWING ULCER OR AMPUTATION IN T1D: 34 YEAR FOLLOW-UP OF DCCT/EDIC

**Background:** People with type 1 diabetes and advanced neuropathy complications have augmented risk of adverse outcomes including mortality and cardiovascular disease. We aimed to determine if advanced neuropathy independently increases risk of acute complications such as diabetic ketoacidosis (DKA).

**Methods:** We accessed previously-collected data from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study, an interval and open cohort study, through the NIH Public Repository. For advanced neuropathy as the exposure, occurrence of self-reported and verified ulcer or amputation, as well as first DKA from enrolment as the outcome, were evaluated annually throughout follow-up. Multivariable Cox Proportional Hazard models with time-varying exposure and co-variables collected annually were used.

**Results:** 1441 people participated in the DCCT, 1375 of whom joined the EDIC phase, representing 95% of the surviving participants. At baseline of the DCCT, mean age was 26.8 (SD 7.1) years, diabetes duration was 5.6 (SD 4.2) years, HbA1c was 8.9 (SD 1.6) %, 47% were female, and 97% were white. There were 527 foot ulcers noted and 202 amputation events among

226 individuals, and 488 DKA events among 297 individuals. Ulcer/ amputation was associated with increased risk of DKA (Univariable Hazard Ratio 1.8, 95% confidence interval 1.2 to 2.8,  $p = 0.004$ ). In multivariable analysis, ulcer/amputation was independently associated with increased risk of DKA (Hazard Ratio 1.7, 95% confidence interval 1.1 to 2.5,  $p = 0.019$ ). DKA risk was also associated with insulin pump use (HR 3.0, 2.2 to 3.9,  $p < 0.001$ ), higher insulin dose (HR for 1 unit/kg/day 2.4, 1.7 to 3.3,  $p < 0.001$ ), female sex (HR 2.0, 1.5 to 2.6,  $p < 0.001$ ), shorter duration of diabetes (HR for 10 years 1.4, 1.0 to 1.9,  $p = 0.025$ ), and higher time-updated HbA1c (HR for 1 percent 1.4, 1.3 to 1.5,  $p < 0.001$ ). In this model, there was no association with age, baseline HbA1c, weight or time-updated retinopathy or nephropathy.

**Conclusion:** In addition to previously reported augmented mortality and cardiovascular disease risk, this analysis demonstrates a substantially higher risk of DKA independent of possible confounders and other complications in those with a history of foot ulcer or amputation. This implies a need for greater metabolic control, self-management skills and education in those with advanced neuropathy. The mechanism of such acute complications and the other adverse outcomes requires further study.



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## COMPARISON OF CLINICAL CHARACTERISTICS OF PEOPLE LIVING WITH LATENT AUTOIMMUNE DIABETES OF THE ADULT (LADA) AND TYPE 1 DIABETES (T1D) IN THE CANADIAN BETTER REGISTRY

**Introduction:** LADA is known for a slow progression of autoimmune destruction of beta-cells with cases that span a spectrum between classic T1D and T2D phenotypes. To date, lacking a good understanding of LADA has prohibited the release of specific clinical practice guidelines and subsequently an optimal management.

**Methodology:** Cross-sectional analysis of online clinical questionnaires in the Canadian BETTER registry; participants can specify having received a diagnosis of LADA or T1D. Data was analyzed for the first 1464 participants; 131 (9%) reported LADA and 1333 (91%) T1D.

**Results:** At registration; LADA vs T1D were  $49 \pm 13$  y.o. vs  $42 \pm 15$  y.o.; 61% vs. 62% females; diabetes duration  $10 \pm 9$  vs.  $24 \pm 15$  years. LADA vs. T1D were older at diagnosis ( $39 \pm 12$  vs.  $18 \pm 12$  years old;  $p < 0.001$ ), only half started insulin in first year of diagnosis (52 vs. 97%;  $p < 0.001$ ), more often reported a family history of T1D (46 vs. 32%;  $p = 0.001$ ). For comparable glycemic control ( $HbA1c < 8.6$  mmol/L,  $< 7\%$ , 38 vs. 32%), fewer cases with

LADA reported at least an episode in last month of level II hypoglycemia  $< 54$  mg/dL (3.0mmol/L) 63% vs. 77%;  $p = 0.004$ , severe hypoglycemia rates were

8% vs. 12%,  $p = 0.15$ . Diabetes related hospitalizations were 10% in LADA vs. 6%,  $p = 0.11$ , insulin pumps and glucagon were less used in LADA. In a matched analysis for diabetes duration and gender (1:1), glycemic control was still statistically comparable in LADA vs. T1D ( $HbA1c < 7\%$ : 38 vs 35%,  $p = 0.12$ ) as well as rates of nephropathy (6% vs. 11%,  $p = 0.22$ ), neuropathy (12% vs. 7%,  $p = 0.23$ ) and retinopathy (6% vs. 9%,  $p = 0.07$ ) yet with more cardiovascular disease (5% vs. 2%;  $p = 0.02$ ) and less coeliac disease (3 vs. 5%;  $p = 0.001$ ). Data analysis of 3000 participants is ongoing in early 2023.

**Conclusion:** Reported differences may impact LADA management. This study sets the stage for building a prospective Canadian cohort of LADA to undergo deep phenotyping, genotyping and interventional trials.





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McGill University

[VIEW POSTER](#)

## CUSHING'S SYNDROME IN PREGNANCY: NAVIGATING THE DIAGNOSTIC COMPLEXITIES AND MANAGEMENT CHALLENGES

**Background:** Diagnosing Cushing's syndrome (CS) during pregnancy is extremely challenging due to the physiological hypercortisolism present during pregnancy. An accurate diagnosis requires a high index of suspicion, given the overlapping signs and symptoms of pregnancy and CS. It is crucial to approach the interpretation of excess cortisol production tests in pregnant patients with caution, utilizing adjusted upper limits of normal criteria (1). Early identification and management are essential to mitigate maternal and fetal complications.

**Case:** A 33-year-old woman G1 at 29 weeks gestational age (GA) was admitted to our institution for suspected CS based on an elevated 24-hour urinary free cortisol (24-h UFC) level at 2688 nmol/day (reference range: 28–276 nmol/day). Her medical history included type 2 diabetes, adiposity-based chronic disease, heart failure, pulmonary hypertension, and gestational hypertension. Throughout her pregnancy, she had several hospitalizations, including legionella pneumonia, heart failure exacerbation, cellulitis, and pulmonary embolism. The patient did not have the characteristic clinical signs of CS, such as skin fragility, proximal myopathy, or moon facies. Laboratory and imaging investigations confirmed the diagnosis of ACTH-independent CS secondary to a 4 cm right adrenal adenoma, with consistently elevated 24-h UFC and midnight salivary cortisol levels, and a suppressed ACTH. A multidisciplinary team including Endocrinology, Obstetrics and General

Surgery collaborated in managing the patient's diagnosis. After careful consideration, the patient was safely discharged with a plan to induce labour at 34 weeks. Postponing the right adrenalectomy until after delivery was decided due to the high risk of perioperative morbidity associated with the procedure. Endocrinology initiated the process of obtaining metyrapone through Health Canada to medically manage the patient's hypercortisolism. The patient missed her outpatient appointments. During a follow-up fetal ultrasound 3 weeks after her discharge, fetal distress was detected necessitating an emergency cesarean-section. A post-delivery dexamethasone suppression test confirmed persistently elevated cortisol levels and suppressed ACTH, indicating the need for a definitive cure through adrenalectomy. Due to delayed arrival of metyrapone and the patient's refusal of postpartum treatment, medical management was not attempted. Following a stable recovery, the patient was discharged, and a follow-up appointment with general surgery was scheduled to proceed with the pending right adrenalectomy, alongside with repeating the excess cortisol production tests.

**Discussion:** This case highlights the challenges in diagnosing and managing CS during pregnancy. Furthermore, our report highlights the significance of a multidisciplinary approach to optimize patient care and ensure favourable outcomes in both the patient and fetal well-being.



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ROBERT A. HEGELE**  
Western University

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## CASE SERIES OF CANADIAN PATIENTS WITH HOMOZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA TREATED WITH ANGPTL3 INHIBITOR, EVINACUMAB

**Background:** Homozygous familial hypercholesterolemia (HoFH) is an ultrarare, life-threatening condition characterized by markedly elevated levels of low-density lipoprotein cholesterol (LDL-C) due to biallelic LDL receptor variants. Patients have an increased risk of premature atherosclerotic cardiovascular disease (ASCVD). Traditional lipid-lowering agents are minimally effective and the gold standard treatment is serial apheresis. Recently, an angiopoietin-like protein 3 (ANGPTL3) inhibitor, evinacumab, was introduced as a promising new treatment for HoFH. It was FDA-approved in 2021, but is currently available in Canada only through clinical trials or special access programs.

**Case Presentations:** The first five Canadian HoFH patients to receive evinacumab via special access are presented. Their mean age is 25.0 years (SD = 12.3). As of December 2022, they have received evinacumab 15 mg/kg intravenously every four weeks for a mean of 19.2 months (SD = 10.5). Their mean incremental LDL-C reduction is 43.5% (SD = 8.14) on evinacumab along with reduced apheresis frequency for most on serial apheresis. Safety labs for all patients are normal. Brief case summaries are as follows:

**a.** Patient A is a 37-year-old man with severe ASCVD on a statin, ezetimibe, evolocumab and LDL-apheresis. Since starting evinacumab 38 months ago, his time-averaged LDL-C decreased by 42.9%, from 4.76 to 2.72 mmol/L.

- b.** Patient B is a 17-year-old male with elevated LDL-C levels despite being on a statin, ezetimibe and LDL-apheresis. After 21 months on evinacumab, his time-averaged LDL-C reduced by 37.8%, from 8.75 to 5.44 mmol.
- c.** Patient C is a 30-year-old woman with ASCVD on a statin and ezetimibe, but not apheresis. She has been on evinacumab for 18 months with a 54.1% reduction in LDL-C, from 11.43 to 5.25 mmol/L.
- d.** Patient D is a 36-year-old man with ASCVD on a statin, ezetimibe, evolocumab, lomitapide and plasmapheresis. He started evinacumab 9 months ago with a 50.7% decrease in time-averaged LDL-C, from 4.34 to 2.14 mmol/L.
- e.** Patient E is a 5-year-old boy with HoFH and xanthomas on a statin, ezetimibe and plasmapheresis. After 10 months of treatment with evinacumab, his time-averaged LDL-C decreased by 31.9%, from 9.45 to 6.44 mmol/L.

**Discussion:** Five HoFH patients with distinctive histories, baseline treatments and ASCVD have all shown marked improvement in LDL-C levels with a mean reduction of 43.5% on evinacumab on top of existing therapy. Overall, observations from our case series suggest that evinacumab is an effective new treatment for HoFH, a life-threatening condition with few therapeutic options.



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## USE OF PERIOPERATIVE TELOTRISTAT IN A PATIENT WITH CARCINOID HEART DISEASE

Carcinoid heart disease is a rare complication of carcinoid syndrome, resulting in right-sided valvular heart disease and subsequent heart failure due to long-term exposure to vasoactive substances. The management of this condition is complex, often requiring surgical intervention. Intraoperatively, patients are at risk of carcinoid crisis: a life-threatening complication of carcinoid syndrome related to the sudden release of vasoactive substances, resulting in hemodynamic instability, arrhythmias, and subsequent intra- and post-operative complications. Current perioperative regimens entail the use of prophylactic somatostatin analogues to prevent carcinoid crisis, however, regimens vary widely among practitioners and evidence supporting their efficacy in this clinical setting is mixed. This prompts the need for evaluation of novel adjuvant therapies to reduce

the risk of perioperative carcinoid crisis. This clinical case describes the perioperative management of a 65-year-old man with carcinoid heart disease requiring tricuspid and pulmonary valve replacement surgery. As an adjunct to somatostatin analogue therapy, the novel tyrosine hydroxylase inhibitor, telotristat, was initiated preoperatively. This combination resulted in normalization of preoperative urinary 5-HIAA levels, and the patient successfully underwent tricuspid and pulmonic valve replacement without evidence of carcinoid crisis. This clinical case is the first available documenting the use of telotristat in the perioperative period in a patient with carcinoid syndrome and carcinoid heart disease and was associated with a good long-term outcome despite the high-risk nature of the case.



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## A CASE OF HYPERTENSIVE URGENCY DURING BILATERAL ADRENAL ABLATION FOR ECTOPIC CUSHING SYNDROME

**Background:** Ectopic Cushing syndrome is a disorder characterized by cortisol excess due to production of adrenocorticotrophic hormone (ACTH) by a non-pituitary tumour. When resection of the ACTH-producing tumour or adrenalectomy are contraindicated, and medical therapy is unsuccessful, bilateral adrenal ablation may be considered. However, this may result in hypertensive urgency due to systemic catecholamine release. There are no current guidelines to direct whether patients with a negative pheochromocytoma workup undergoing adrenal ablation should be pre-treated with alpha- and beta-blockade with the aim of preventing intraoperative hypertension.

**Case Presentation:** A 61-year-old man admitted to hospital for cellulitis was diagnosed with non-small cell lung cancer (NSCLC). During his admission, he had refractory hypertension (systolic blood pressure [SBP] 150–160s mmHg) and hypokalemia (2.2–3.3 mmol/L) despite aggressive medical management. He was diagnosed with ACTH-dependent Cushing syndrome based on an elevated ACTH (73.7 pmol/L), 24-hour urine cortisol (4514 nmol/day) and non-suppression with a 1 mg dexamethasone suppression test (DST) (serum cortisol 2008 nmol/L). Ectopic ACTH production was likely caused by NSCLC. The patient was not a surgical candidate and ketoconazole was

contraindicated given elevated transaminases (ALT 410 U/L), so bilateral microwave adrenal ablation was performed. Prior to ablation, 24-hour urine fractionated metanephrines were normal. He received pre-treatment with doxazosin (maximum dose 2 mg BID) and bisoprolol (maximum dose 10 mg daily). During ablation of the right adrenal gland, his SBP increased to the high 200s mmHg. During ablation of the left, maximum SBP was 315 mmHg leading to a pause of ablation before completion. He did not require intraoperative anti-hypertensive medications. The adrenal ablation was successful, and his serum cortisol decreased from 2016 nmol/L pre-ablation to 538 nmol/L post-ablation. He was placed on a hydrocortisone taper and off anti-hypertensive agents. Ten days following ablation, he developed hypotension and suffered a cardiac arrest related to massive gastrointestinal bleeding and passed away shortly after.

**Discussion:** This case demonstrates that hypertensive urgency during adrenal ablation for ectopic Cushing syndrome can occur even with pre-treatment with alpha- and beta-blockade. It is important that guidelines are developed for the prevention and management of hypertensive urgency in this population.



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## TSH-SECRETING PITUITARY ADENOMA: 3 CASES WITH CHALLENGING DIAGNOSIS AND MANAGEMENT

**Background:** TSHoma, a rare pituitary tumor with a prevalence of one per million, causes central hyperthyroidism. 30% are co-secreting adenomas (TSH, PRL and GH). Most tumors are macroadenomas ( $\geq 10$  mm) with risk of visual field defects, visual loss, headache, hypopituitarism. Herein we report three cases of TSHoma with challenging diagnosis.

**Clinical Presentation:** A 47-year-old man presented with weight loss, fatigue, muscle weakness and decrease libido. Lab showed increase PRL, and an MRI sella revealed a  $2.2 \times 2.95 \times 1.9$ cm adenoma. No obvious stigmata of acromegaly clinically. Additional Lab showed PRL 45, FT4 23.1, TSH 5.35, GH 2.87, IGF1 0.74ULN, then 2.04 ULN. GH trough during OGTT was 2.74. Alpha SU was 0.5 ng/mL (ref  $< 0.5$ ). A co-secreting pituitary macroadenoma (GH/TSH/PRL) was suspected with improving symptoms on DA and SSA. He showed early normalization of hypersecretion (TSH/GH) post transsphenoidal resection. A 66-year-old man, known for MNG (prominent right benign nodule), HTN, CAD and A. Fib. A CT head done for left hemibody dysesthesias, showed a pituitary mass. MRI confirmed a  $2.4 \times 2.1 \times 1.8$ cm adenoma with left CS and sphenoid sinus extension. Lab showed PRL 29.9, TSH 5.7, FT4 25.8, FT3 6.44, cortisol AM 450, with normal IGF1, LH, FSH, Testosterone. In retrospect, TFT in his file since 2019 were clearly in keeping with central hyperthyroidism. He complained of chronic anxiety, palpitations

and weight loss. Treatment with DA resulted in normalization of TFT. A 17-year-old woman presented with galactorrhea on OCP. PRL was  $> 100$  and an MRI showed a 1.35 cm adenoma. TSH was 5.22, FT4 15.4. She responded well to DA, and 3 years later, after the DA had been tapered off, had severe anxiety, palpitations, weight loss, insomnia. TSH was 2.53, FT4 10.6, FT3 6.29–6.72, PRL 35.6. No adenoma on MRI. Thyroid uptake was increased 48%. Tapazole initiation and DA resumption allowed symptoms resolution.

**Discussion:** The diagnostic hallmark is a persistently high normal or raised free thyroxine and T3 with inappropriately normal or elevated TSH. Exclusion of interfering heterophilic antibodies and increased alpha-SU support the diagnosis. Pituitary surgery for adenoma removal, is the gold standard, but may be incomplete with high volume or local structures invasion. Euthyroidism should be achieved before surgery. SSA are the mainstay therapy for TSH suppression. DA have demonstrated successful results notably in co-secreting adenomas.

**Conclusion:** Clinical hyperthyroidism, monitoring and interpretation of TFTs are essential for early diagnosis of TSHomas and to prevent tumor growth with complications.



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## CHEK2 VARIANT WITH THYROID CANCER AND AUTOIMMUNE ADRENALITIS

**Introduction:** Checkpoint kinase 2 (CHK2; CHEK2 gene) is a protein kinase involved in the DNA-damage-signaling pathway and is an upstream regulator of various DNA-damage-activated protein kinases. Various malignancies have been previously associated with CHEK2 gene mutations including thyroid, breast, colorectal, renal, adrenocortical and prostate cancers. CHK2 has not been previously associated with autoimmune etiologies.

**Case:** A 27-year-old woman presented with a new lump in her neck. Pathology confirmed a 1.5 cm differentiated papillary/follicular thyroid cancer stage T1BN0 after a right thyroidectomy. She underwent completion thyroidectomy and remained stable on TSH suppression with levothyroxine. Six years later, she presented with nausea, vomiting, platypnea and hypotension. Broad work-up was undertaken which included adrenal evaluation. This showed an AM cortisol of  $< 14$  nmol/L and an ACTH 366 pmol/L. CT adrenals showed bilateral small adrenal glands. Her presentation

was consistent with primary adrenal insufficiency and she was treated with IV hydrocortisone until transitioning to PO hydrocortisone and fludrocortisone. Subsequent testing returned positive for anti-adrenal antibodies. Genetic testing was undertaken which revealed a likely pathogenic EX2\_3dup CHEK2 gene variant.

**Discussion:** CHEK2 is classically associated with malignancies, including rare reports of multiple endocrine gland tumours, pancreatic neuroendocrine tumours, and pituitary adenomas (e.g. Cushing's disease and acromegaly). While CHEK2 has not been previously associated with autoimmune adrenalitis, some models have described the potential link between defective DNA repair mechanisms and autoantibody production in other autoimmune diseases. For example, in SLE, lower DNA repair capacity is thought to result in cellular apoptosis and autoantibody production.





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## OPTIMIZING TYPE 2 DIABETES MANAGEMENT IN A MEDICALLY COMPLEX PATIENT: A CASE REPORT OF A PATIENT WITH TYPE 2 DIABETES AND HIV INFECTION

**Background:** The prevalence of diabetes is rapidly escalating, with projections indicating that 783 million individuals aged 20–79 years worldwide will be affected by diabetes. This rise is concurrent with a persistent prevalence of HIV in developing nations. While conventional risk factors such as sedentary lifestyle and unhealthy diet may account for this trend, HIV and its treatment have emerged as potential contributing factors. Achieving optimal diabetes control in patients with HIV necessitates a profound understanding of the intricate interplay between the two diseases and their respective treatments.

**Case Report:** We present a case involving a patient with long standing type 2 diabetes, coexisting HIV infection and hypertension. Despite receiving high doses of insulin, as advised by most diabetes guidelines, the patient's diabetes remained poorly controlled. In lieu of strictly adhering to guidelines, our

primary focus was to conduct a comprehensive reevaluation of the patient's medications, prioritizing the development of streamlined and safe treatment regimens for all three of her medical conditions. Employing this strategy, we observed swift improvement in blood glucose levels, leading to successful diabetes control within one year.

**Conclusion:** This case underscores the importance of individualizing diabetes management in patients with multiple comorbidities. It highlights the significance of reassessing treatment approaches beyond standard guidelines, with a focus on tailoring therapy to suit the unique needs and complexities of each patient's medical profile. Such personalized interventions hold promise for achieving optimal diabetes control in individuals with diverse comorbidities.





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## A CASE OF A SILENT THYROTROPH ADENOMA

**Background:** Silent pituitary adenomas refer to adenomas that express one or more pituitary hormones or transcription factors on immunochemistry, but present as clinically non-functioning adenomas. The subset of silent thyrotroph adenomas remain rare, accounting for less than 2.4% of pituitary adenomas documented in various surgical case series, and often are clinically silent. Over 50% present with extrasellar extension and common clinical symptoms include headaches and visual disturbances.

**Case:** A 52-year-old female who was referred to the Pituitary Clinic in July 2021 for a new pituitary macroadenoma with a maximum dimension of 2.4 cm in craniocaudal direction. There was abutment and uplifting of the optic chiasm and pre-chiasmatic optic nerve. The patient had a chronic history of non-specific neurological symptoms, including weakness, severe dizzy spells, pre-syncope, night tremors and paresthesias over the past six years. At the clinic, she had endorsed that her face had become more swollen and "moon-like" in nature, as well as water retention in her extremities. Additionally, she noted an increase in shoe size, as well as some skin, hair, and

nail changes. Her hormonal panel did not show any objective evidence of overproduction or insufficiency. Given the presence of an early bitemporal visual field defect, she underwent endoscopic transsphenoidal resection in April 2023 during which the entirety of the tumour was removed. On pathology, the tumour was found to be diffusely positive for alpha subunit, Pit-1, TSH and diffuse staining with mixed perinuclear and cytoplasmic pattern for CK8/18. The Ki-67-index was < 1%. Post-operatively she had no pituitary hormone deficiency. Her vision is subjectively unchanged following surgery. She is planned for MRI in October 2023.

**Discussion/Conclusion:** In our case, the silent thyrotroph pituitary adenoma was deemed to be completely resected. Other silent pituitary tumours, including silent corticotroph and silent somatotroph tumors, have a tendency for more aggressive behaviour. In the absence of good information on silent thyrotroph adenomas, we suggest it is prudent to monitor closely for early recurrence.



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## GENETIC CHARACTERIZATION OF A CASE OF PHEOCHROMOCYTOMA IN A PULMONARY TRANSPLANT PATIENT

**Background:** Approximately 40% of PPGL patients carry germline mutations in susceptibility genes. An association was described between hypoxemia and PPGLs, notably in higher altitude exposition and cyanotic congenital heart disease. In the latter, a chronic hypoxemic state can lead to gain of function somatic mutations in the EPAS1 gene that encodes for hypoxia-inducible factor 2-alpha (HIF-2 $\alpha$ ) (1).

**Objective:** To describe and characterize the genetic background of a rare case of PHEO in a pulmonary transplant patient.

**Clinical Case:** A 66 year-old man underwent lung transplant at 47 yo for chronic obstructive pulmonary disease. He required home oxygen therapy for 3 years prior to transplant and was known for new onset diabetes after transplant and hypertension. Nineteen years after transplant, a thoracic CT-scan showed a 6.1  $\times$  3.9 cm right adrenal mass (HU of 7). Diagnosis of PHEO was confirmed biochemically (noradrenaline 713 nmol/d (N < ; 650), adrenaline 588 nmol/d (N < 145), normetanephrines 900 nmol/d (N < ; 600) and metanephrines 1191 nmol/d (N < 370)). Chromogranin A was elevated (3297 ng/mL (N < 104)). The adrenal mass showed no uptake at 18F-FDG PET/CT imaging but fixation at MIBG scintigraphy. The patient received alpha blockers and underwent a laparoscopic right adrenalectomy. The pathology confirmed a PHEO with a PASS score of 8 to 10. Eighteen months following the surgery, the patient showed no signs of recurrence.

### Genetic studies:

- 1) Germline PPGL multigene panel: After consent, the patient underwent a panel of 14 susceptibility genes for PPGLs (INVITAE, CA, USA) that revealed no pathogenic variants.
- 2) Somatic genetic analysis for EPAS1 gene: PHEO DNA was extracted and exons 9, 12 and 16 of the EPAS1 gene were studied by Sanger Sequencing. No pathogenic variants were identified.
- 3) RNA-sequencing: RNA-sequencing of patient tumoral DNA was performed and showed an overexpression of HIF-2 $\alpha$  compared to reference samples.

**Conclusion:** We report a rare case of PHEO in a pulmonary transplant patient. Our genetic analyses demonstrated the absence of a pathogenic germline variant in known susceptibility PPGL genes and no somatic mutations in the EPAS1 gene, but revealed overexpression of HIF-2 $\alpha$ . The mechanism underlying this phenomenon is still unclear. Further work is needed to better understand the genetic and molecular events leading to PHEO in this specific case and determine its possible relationship with hypoxemia.

### References:

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## IGF-2 MEDIATED HYPOGLYCEMIA IN A PATIENT WITH SUSPECTED ADRENOCORTICAL CARCINOMA

**Background:** Insulin growth factor-2 (IGF-2) mediated hypoglycemia is a rare paraneoplastic syndrome caused by tumoral overproduction of IGF-2 or abnormally processed IGF-2 ("big IGF-2"), which binds to the insulin receptor (IR). IGF-2 mediated hypoglycemia secondary to adrenal cortical carcinoma (ACC) is exceedingly rare, with less than 10 reported cases.

**Case:** An 83-year-old man presented to the emergency department for confusion and a blood glucose level of 1.3 mmol/L (3.3–11.0 mmol/L). History was significant for weight loss, early satiety, and abdominal distension over the past 3 months. No Cushingoid features were observed. Serum potassium was 2.7 mmol/L (3.5–5.0 mmol/L) and critical sample (drawn with serum glucose of 3.5 mmol/L) showed insulin < 6 pmol/L (< 120 pmol/L), C-peptide 0.04 nmol/L (0.4–1.40 nmol/L), and beta hydroxybutyrate (BOH) 0 mmol/L. Serum cortisol was 188 nmol/L (170–500 nmol/L) following a 1 mg dexamethasone suppression test, with an adrenocorticotrophic hormone (ACTH) of 2.5 pmol/L (2.0–11.5 pmol/L). Dehydroepiandrosterone sulfate (DHEAS) was 75.5 umol/L (0.4–3.3 umol/L) and estradiol was 241 pmol/L (< 160 pmol/L). Aldosterone-to-renin ratio and 24-hour urine metanephrines and normetanephrines were normal. Insulin growth factor-1 (IGF-1) was 57 ug/L (15–245 ug/L), and IGF-2 was 615 ug/L (333–967ug/L). IGF-2: IGF-1 ratio of 10.8 (< 3). CT scan of the abdomen demonstrated a 14.4 × 12.1 × 17.7 cm mass in the left suprarenal fossa. FDG PET was intensely

hypermetabolic, suggestive of ACC without evidence of other primary malignancy or metastatic disease. The patient was not a candidate for surgery due to tumor invasiveness. Hypoglycemia was refractory to diazoxide and prednisone 60mg daily. Uncooked cornstarch and dexamethasone 4mg twice daily were implemented and successful at preventing severe hypoglycemia. He was referred to radiation oncology and medical oncology for consideration of palliative therapies.

**Conclusion:** We present a very rare case of IGF-2 induced hypoglycemia secondary to ACC. Hypokalemia, suppressed insulin, and undetectable BOH are in keeping with activation of insulin receptors by IGF-2. Interestingly, IGF-2 levels are typically normal, as the structure of big IGF-2 leads to increased bioavailability and binding to IR. IGF-1 is low or low-normal due to negative feedback of IGF-2. Management in this case was focused on preventing hypoglycemia. Glucocorticoids are usually first line of treatment as they stimulate gluconeogenesis and decrease production of big IGF-2 (1). We postulate that dexamethasone was more effective than prednisone due to its longer half-life. Cornstarch is a complex carbohydrate that is digested slowly which helps prevent fasting hypoglycemia. Diazoxide was ineffective because it works by inhibiting pancreatic insulin release and has no effect on IGF-2.



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## A CASE OF 17 ALPHA HYDROXYLASE DEFICIENCY PRESENTING WITH HYPERTENSION AND HYPOKALEMIA

**Background:** We present an interesting case of a 22-year-old female with congenital adrenal hyperplasia (CAH) from a 17 alpha hydroxylase deficiency. 17 alpha hydroxylase deficiency is a rare form of CAH which accounts for about 1% of all cases (1). This case highlights the presentation of this rare deficiency and describes management strategies.

**Case:** A 22 year old female presented with hypertension, hypokalemia, and palpitations. Her past medical history was significant for a prior tumor of the right ovary requiring surgical removal. Her only medication was an oral contraceptive pill which was started after her surgery around age 11–12 prior to any previous spontaneous menses. Her family history was significant for her parents being first cousins. She has 3 siblings; her brother has no medical problems. Neither sister has had any pubertal development and are 12 and 19 years old. Her labs investigations showed hypokalemia (2.4), aldosterone 73 and renin was undetectable. Her LH and FSH were both elevated, estradiol 32, progesterone 34.6, total testosterone less than 0.2, deoxycorticosterone was 53 ng/dL (reference range < 18 ng/dL). A 250 mcg ACTH stimulation test was performed and peak cortisol was 52. A pelvic ultrasound demonstrated uterine hypoplasia and an absent right ovary with a normal left ovary. Given the clinical presentation with hypertension, hypokalemia, absent adrenarche with low cortisol, testosterone, aldosterone and elevated

DOC and progesterone she was diagnosed clinically with CAH from 17 alpha hydroxylase deficiency. Genetic testing showed a homozygous variant of uncertain significance in the CYP17A1 gene confirming the clinical diagnosis. She was initiated on hydrocortisone 10 mg in the morning and 5 mg in the afternoon. On follow up her blood pressure and potassium normalized. There were no further requirements for potassium supplementation. She continued an OCP containing 35 mcg of estradiol.

**Discussion:** This was an interesting presentation of 17 alpha CAH as she never had a period prior to starting an OCP, which when combined with her history of spontaneous hypokalemia and hypertension prompted consideration of 17 alpha CAH. Treatment for hypertension and hypokalemia typically uses corticosteroids or mineralocorticoid antagonists, as evidenced in our case physiologic dosing of hydrocortisone was enough to normalize her blood pressure and potassium. Patients are also treated with hormone replacement therapy.

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## A CHALLENGING CASE OF CUSHING'S SYNDROME

**Background:** Determining the etiology of Cushing's Syndrome can be challenging.

**Case:** A 35-year-old female was referred to Endocrinology Clinic for suspected Cushing's Syndrome. She presented with weight gain and difficult-to-control type 2 diabetes. Past medical history included Celiac disease, hypertension, non-alcoholic fatty liver disease, and a pregnancy 7 months earlier. At her consultation visit, she described unexplained weight gain of 15 pounds, persistent hyperglycemia despite increasing insulin doses, and intermittent episodes of diaphoresis and heat intolerance a few times per week. Her physical exam was remarkable for a dorsocervical fat pad, central obesity and violaceous striae. Investigations prior to endocrinology assessment: HbA1c 12.8%, TSH 1.03, non-HDL cholesterol 7.02 mmol/L, and triglycerides of 5.36 mmol/L. Free androgen index was slightly elevated at 5.4. AM cortisol was 635, ACTH 8.3, and normal metanephrines. Abdominal ultrasound revealed mild diffuse fatty infiltration of the liver. CT scan of the head showed no acute intracranial abnormality.

**Subsequent Investigations:** 24-hour urine free cortisol elevated at 287.4 nmol/d, 1 mg overnight dexamethasone suppression test: showed non-suppressed cortisol of 302 nmol/L. MR Sella showed mildly heterogeneous enhancement of the pituitary gland with a 6 mm relatively hypoenhancing focus suspicious for a microadenoma. Subsequently, inferior petrosal sinus sampling (IPSS) revealed that ACTH levels, both before and after stimulation, were similar in peripheral blood and in the inferior petrosal sinuses and in the left and right petrosal sinuses. This raised suspicion for a non-pituitary source of ACTH, so an enhanced CT chest/abdomen was completed. It revealed no carcinoid or other abnormalities within the chest or abdomen. To look for other possible sources of ACTH, a Gallium-68 DOTATATE PET was ordered; it showed no somatostatin receptor avid disease.

**Comment:** Despite these extensive investigations, no clear source of abnormal ACTH secretion has been identified yet. The current presumed diagnosis is cyclical Cushing's disease of pituitary origin. The patient is now awaiting IPSS to be performed the day after confirmation of an elevated 24-hour urine free cortisol test.



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## AN INTERESTING CASE OF INSULIN RESISTANCE

A 5 month old was evaluated for small head circumference in the context of being below the 3rd percentile for weight and having triangular facies. At 5 years, he was evaluated for short stature. At his initial visit, he had a growth velocity of 5.8 cm/year, which dropped to 4.1 cm/year 6 months later. He was otherwise well, with no concerns for glucose regulation. On exam, he was 98 cm (0.15th percentile) with deep set eyes, and hyperextensible joints. Investigations demonstrated a normal thyroid screen, normal IGF-1 level, an A1c of 5.3% with an appropriate bone age. He had a mid-parental height of 177.3 cm, but a predicted adult height of 150 cm. Whole exome sequencing demonstrated that he has SHORT syndrome (short stature, hyperextensibility, ocular depression, Rieger anomaly, and teething delay). It is an autosomal dominant disorder caused by mutations in the PI3KR1 gene. This gene encodes the regulation of the p85 $\alpha$  subunit. It binds to p110 $\alpha$  activating PI3K which converts PIP-2 to PIP-3, thus activating the membrane bound PDK1. The PDK1 molecule acts on AKT activating it by phosphorylation which inhibits the AS160 protein, allowing GLUT4 transporters to come up to the cell membrane. AKT inhibits GSK-3 $\beta$  allowing for increased glycogen synthesis. AKT activates the mTOR pathway involved in beta cell insulin

production. Downregulation of both mechanisms is why we see both insulin resistance as well as decreased insulin secretion in SHORT syndrome. IGF-1 acts similarly to insulin and requires AKT action, in this case to inhibit TSC2, and thus activate mTOR, allowing for increased protein synthesis and growth. The defects in PI3K are thought to induce lipodystrophy as well because the insulin signaling through AKT to inhibit lipolysis is not functional causing both an inability to maintain adipocytes as well as an increased release of free fatty acids into the serum, worsening insulin resistance. Insulin resistance develops in adolescence, with risk for diabetes in early adulthood. There have been cases of diabetic ketoacidosis reported. Management remains largely empirical including diet, exercise, and insulin. Metformin has sometimes been effective but occasionally paradoxically worsens the insulin resistance. For short stature management, growth hormone is avoided due to adverse impacts on glucose homeostasis. IGF-1 therapy is not well studied but there is known IGF-1 resistance in this population. Metreleptin use has been evaluated in other lipodystrophies, but not in SHORT syndrome. Further research for optimal patient management is needed..





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## SUPRASELLAR MASS: A RARE CASE OF PRIMARY CENTRAL NERVOUS SYSTEM MARGINAL ZONE LYMPHOMA

**Introduction:** Sellar and suprasellar masses are found incidentally on 4–20% of Cranial CTs. Pituitary adenomas, craniopharyngiomas, aneurysms, astrocytomas and meningiomas are the most common lesions in the sellar area, accounting for approximately 80% of cases. Primary central nervous system lymphomas constitute fewer than 5% of suprasellar masses, with only 2 prior cases of CNS Marginal Zone Lymphoma being described in the literature.

**Case:** 39-year-old male with no significant medical, surgical or family history except for corrective eye surgery presented with acute bilateral proptosis, headache and bilateral temporal hemianopsia. Slit lamp exam was unremarkable. CT orbit showed an enhancing suprasellar mass that was iso-intense to the brain parenchyma. MRI Sella Turcica reported a large mass ( $2.2 \times 2.5 \times 3.0$  cm) in the tuberculum sellae with extension into the right cavernous sinus, encasement of the right internal carotid artery, and mass effect on the optic chiasm and the right optic nerve. Pituitary panel showed no hormone excess or deficiency. Serum protein electrophoresis detected a small monoclonal peak [2 g/dl] in the gamma region, confirmed to be IgG lambda light chain by serum immunofixation. Patient underwent transcranial resection of the suprasellar mass, followed by radiation therapy. Pathology revealed B-cell lymphoma with marked plasma cells, suggestive

of lymphoplasmacytic lymphoma (LPL) or marginal zone lymphoma (MZL) with marked plasmacytic differentiation. Immunohistochemistry underscored the large plasmacytic component, positive for CD138 and MUM1, showing lambda light chain restriction (by ISH). At three-year follow-up, patient has not had any recurrence, with marked improvement in his vision and unchanged pituitary hormone function.

**Discussion:** Pituitary adenoma is by far the most common sellar/suprasellar tumor type. Typical MRI findings in primary CNS MZL are mass lesions that are iso- to hypointense on T1- and T2-weighted images. Pituitary adenomas, especially when larger than 1 cm, can have a heterogeneous appearance on MRI depending on hemorrhagic, cystic, and necrotic components. CNS MZL, similar to other primary CNS lymphomas appear homogeneous. Hematological studies intended to uncover monoclonal gammopathy are not in the practice guidelines for the evaluation of pituitary incidentalomas. However, if positive, they lend strong support for primary CNS lymphoma as the underlying etiology. Thus, although primary CNS lymphoma may be indistinguishable from pituitary adenoma on imaging, it should be considered in the differential in the evaluation of an invasive sellar mass that is iso- to hypointense on T2-weighted MRI image.





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## A CASE OF SERTOLI CELL ONLY SYNDROME AND MALE INFERTILITY CONFOUNDED BY HYPERPROLACTINEMIA

The hormonal evaluation of male infertility begins with assessment of hypogonadism. When low testosterone and elevated gonadotropins are present primary testicular failure is suspected. When only one gonadotropin, follicle stimulating hormone (FSH) is elevated, specific testicular anatomic pathology should be considered. Here we highlight a case of an otherwise healthy man in his thirties presenting with infertility. His serum testosterone was noted to be low, with an elevated prolactin. Subsequent imaging confirmed presence of a pituitary macroadenoma. This led to a trial of dopamine agonist therapy (cabergoline) which normalized prolactin and testosterone levels. After 6-months of therapy with cabergoline and a selective estrogen receptor modulator (clomiphene) testosterone levels and sexual function improved, however azoospermia persisted on semen analysis. A normal male karyotype was found, with no Y chromosome microdeletion detected. Decreased testicular volume was noted and a testicular biopsy

was performed. Bilateral testicular biopsy samples showed Sertoli cells within the seminiferous tubules with no spermatogonia, confirming the diagnosis of Sertoli Cell Only Syndrome, also known as Del Castillo syndrome. On retrospective review of the patient's initial hormonal profile, the isolated FSH elevation in context of azoospermia was consistent with primary spermatogenic failure. Interestingly, the patient has an identical twin brother who has fathered two children without fertility concerns. Additional genetic testing for our patient revealed carrier status for a heterozygous CFTR dF508 mutation. Although obstructive reproductive anomalies or congenital absence of the vas deferens are more commonly associated with CFTR mutations, azoospermia has also been described in individuals with heterozygous mutations. This case describes co-occurrence of Sertoli Cell Only Syndrome and heterozygous CFTR dF508 mutation.



**LURDES TSE-AGHA\*, SARA FAROUQ AWAD**  
Queen's University

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## CLINICAL HYPERCORTISOLISM AND PITUITARY ATROPHY FROM ORAL CLOBETASOL RINSE

**Background:** Exogenous glucocorticoids are available in many formulations for numerous indications, and is an important consideration when patients present with Cushing syndrome and central adrenal insufficiency. We describe a case of clobetasol mouthwash-induced hypercortisolism presenting as central adrenal insufficiency.

**Case:** A 49-year-old man presented to the Emergency department with hypotension, generalized weakness, 30-lb weight loss and was found to have low morning cortisol at 53 with a low ACTH  $< 0.3$ . His examination, however, revealed classic Cushing syndrome, including wide violaceous striae, round facies, facial plethora, abdominal and dorsocervical adiposity, and proximal myopathy. He was recently diagnosed with hypertensive heart disease, type 2 diabetes, osteoporosis with vertebral fragility fractures and cataracts. A 250 mcg ACTH stimulation test revealed suboptimal cortisol response with peak cortisol level at 342 nmol/L at 60-minutes. He was started on hydrocortisone replacement. The rest of the pituitary panel revealed central hypogonadism with preservation of his thyroid and growth hormone axes. An MRI sella was initially reported as no pituitary abnormalities. When the patient was eventually seen by Endocrinology as an outpatient, a second opinion was sought — there was evidence of severe

pituitary atrophy, along with other signs of longstanding hypercortisolism including cerebral and cerebellar atrophy, retro-orbital adiposity and fatty bone-marrow infiltration. Abdominal CT-scan showed atrophic adrenal glands and fatty liver infiltration. The patient had initially denied exogenous steroids, including inhalers and creams. On more careful history taking, he stated he had been using a clobetasol 0.15% oral rinse for recurrent aphthous ulcers four-times a day for 8 years. We counseled him to stop this rinse. He lost 12 kg in 6 months, his diabetes improved on metformin alone and his facial plethora, abdominal obesity and proximal myopathy were significantly improved. Hypogonadism reverted to normal range.

**Discussion:** Clobetasol is the most potent exogenous steroid and is significantly systematically absorbed even if used locally such as oral mouthwash rinse. This patient was using a concentration that was 3-times greater than in similar cases that have previously been reported and was using it daily for 8 years. This resulted in clinical hypercortisolism and subsequent central adrenal insufficiency from hypothalamic-pituitary-adrenal axis suppression. Careful history taking and the seeking a second opinion were crucial to obtaining the final diagnosis in this case.



**JESSICA MAK\*, JEANNETTE GOGUEN**  
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## IT'S NOT MY THYROID! A CASE OF TSH-PRODUCING MICROADENOMA (TSH-OMA)

**Background:** Rare TSH-secreting pituitary adenomas (TSH-oma) are predominantly macroadenomas that inappropriately secrete TSH, independent of feedback regulation by thyroid hormone or thyrotropin releasing hormone (TRH) [1,2]. 70% of TSH-omas have an elevated serum glycoprotein alpha-subunit (A-GSU)[3]. Often other pituitary hormones are co-secreted [4].

**Case:** A 33-year-old woman presented with a 3-year history of progressive thyrotoxic symptoms including anxiety, heat intolerance, palpitations, fine tremors and excessive perspiration. Clinical assessment revealed regular tachycardia (112 bpm), fine bilateral hand tremors, brisk upper reflexes, and diffusely enlarged thyroid gland. She had an elevated fT3 8.1 pmol/L (3.1–6.2 pmol/L) and fT4 of 25 pmol/L (9–19 pmol/L) and an inappropriately normal TSH 1.39 mIU/L (0.32–4 mIU/L). Interestingly, her sella MRI demonstrated only a 2–3 mm hypoenhancing nodule in the right pituitary. The rest of her pituitary function was normal, including A-GSU 0.3 ng/mL (normal < = 1.2 ng/mL). Because several features were atypical for a TSHoma, other causes were sought. Laboratory interference was ruled out. In consideration of potential central thyroid hormone resistance (CTHR), the thyroid function of first-degree relatives was screened and was normal. Subsequent investigations were also more suggestive of TSH-oma than CTHR: stimulation with TRH failed to evoke the expected

TSH surge, with levels only rising from 1.81 mIU/L (baseline) to 2 mIU/L (peak) and 1.6 mIU/L (60 minutes post-TRH). Furthermore, on cytomel challenge, her TSH remained unsuppressed at 0.98 mIU/L on day 5, 1.18 mIU/L on day 8 and 1.09 mIU/L on day 11, aligning with a TSH-oma pattern. Upon neurosurgical resection, the pathology demonstrated a thyrotroph Pit-NET dominated by TSH-expressing cells. Post-operatively, she developed central hypothyroidism: TSH levels plummeted to < 0.01 mIU/L, coupled with low fT3 (2.5 pmol/L) and borderline-low fT4 (10 pmol/L), requiring levothyroxine therapy. Her pituitary recovered TSH production 1 year later.

**Discussion:** After ruling out lab interference (supplements, heterophile antibodies) to establish true inappropriate secretion of TSH [1,5], this case illustrates methods to differentiate between key differentials, the TSH-oma and CTHR [1]. This case was unusual because the TSH-oma was a microadenoma and A-GSU was normal [1,2]. Despite its Pit-1 lineage, this case also did not have co-secretion of growth hormone and prolactin [4]. Extra testing was conducted to support TSH-oma diagnosis before proceeding to surgery. The case also demonstrated anticipated central hypothyroidism post-adenoma resection and subsequent thyroid-hypothalamic-axis recovery.



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## LYTIC BONE LESIONS? CALL ENDOCRINOLOGY!

**Case:** A 58-year-old male patient with a history of nephrolithiasis was admitted to Oncology with a 2-month history of right thigh pain. Imaging showed multiple lytic lesions in the proximal femurs, vertebral bodies, and pelvis concerning for multiple myeloma vs. metastatic disease. Initial ionized calcium was 2.35 mmol/L (normal upper limit: 1.28 mmol/L). PTH was 173 pmol/L (normal upper limit: 6.9 pmol/L). Parathyroid carcinoma was suspected given the degree of hypercalcemia, PTH elevation, and apparent bone metastases. A parathyroid scan indicated a possible left parathyroid mass that was surgically removed and found to be a benign 3.9 cm left superior parathyroid adenoma. He underwent right femur intramedullary nail fixation for impending fracture. Pathology of bone fragments noted benign degenerated bone with focal remodeling and fibrosis. The patient developed hemorrhagic shock with 3 liters of surgical blood loss, and upon transfer to the ICU, required pressor support. Following the left parathyroidectomy, PTH normalized to 2.3 pmol/L. The patient then developed severe hypocalcemia (ionized calcium 0.79 mmol/L, normal lower limit: 1.14 mmol/L) with high PTH (13.9 pmol/L), and was started on calcitriol (highest daily dose 3 mcg) and calcium supplementation (highest elemental calcium daily dose 6000 mg). After a 2-month hospital admission, he was discharged home, and within a few weeks was only on elemental calcium dose of 1000 mg twice daily.

**Discussion:** The bony lytic lesions at presentation raised great concern for multiple myeloma or bone metastases. Endocrinology assessment revealed primary hyperparathyroidism with elevated PTH (almost 25 times the upper limit of normal) alarming for parathyroid carcinoma, which can lead to bone metastases and/or osteitis fibrosa cystica (OFC). Pathological analysis revealed this was a parathyroid adenoma with OFC. The right femur lesion bled extensively intra-operatively, and this is not uncommon with surgical intervention for OFC lesions which tend to be very vascular. Furthermore, OFC is a risk factor for developing hungry bone syndrome characterized by prolonged hypocalcemia post-parathyroidectomy, which was the case in our patient. In conclusion, in the setting of critically severe hypercalcemia and elevated PTH, OFC should not be forgotten as a cause of lytic lesions. Coordinated care with Oncology, ENT, Orthopedic Surgery and Endocrinology was vital to determining the etiology of this patient's presentation.



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## HYPOGLYCEMIA UNAWARENESS AND RECURRENT SEVERE HYPOGLYCEMIA IN A PATIENT WITH TYPE 1 DIABETES MELLITUS ON INSULIN THERAPY: A SPECIALIZED MULTI-DISCIPLINARY APPROACH

**Background:** Hypoglycemia is a common complication of insulin therapy in individuals with type 1 diabetes mellitus (T1DM). The combination of beta-cell loss and impaired glucagon response complicates patients' ability to achieve their target HbA1c while avoiding hypoglycemia. In addition, hypoglycemia attenuate the sympathoadrenal response and hepatic glucose release, termed hypoglycemia-associated autonomic failure, which can persist for more than 24 hours and increases the risk of hypoglycemia recurrence. Achieving tight glycemic control while preventing onset of hypoglycemia thus presents a therapeutic challenge to clinicians.

**Case:** A 55 year old man with T1DM was evaluated in a specialist Endocrinology clinic for hypoglycaemia unawareness and recurrent episodes of severe hypoglycaemia requiring almost daily EMS responses and 56 hospitalizations over 4 years. His presenting HbA1c was 4.6%. A multi-disciplinary team (MDT) was formed, comprising an endocrinologist, diabetes nurse educator, registered dietician, family practitioner, emergency department physician and a community paramedic team, with ultimate successful resolution of hypoglycemic crises. In the 1.5 year period post-MDT implementation, the patient required only 5 EMS responses, 1 hospitalization, and repeat HbA1c was 7.2%.

**Discussion:** This case presents a multidisciplinary approach to reduce the incidence of severe hypoglycemia, reduce hospitalization rate and ameliorate

cost-effectiveness of care for a complex patient with hypoglycemia unawareness and severe hypoglycaemia recurrence. Initial strategies to combat hypoglycemia, including insulin regimen titration with permissive hyperglycemia and provision of a continuous glucose monitor (CGM), alone showed limited effect. We therefore employed a multi-disciplinary, patient-centred approach to care that incorporated the following strategies:

1. identification and targeting of patient-specific needs and therapeutic barriers across multiple dimensions of patient well-being, including social, psychological and financial well-being
2. implementation of a dynamic goal-directed approach characterized by frequent inter-provider communication;
3. regular, frequent patient follow-up with a Diabetes clinic team and a community outreach program;
4. patient empowerment, including promotion of diabetes self-efficacy and reduction in patient stigmatization.

**Conclusion:** Severe recurrent hypoglycemia in individuals with T1DM managed with insulin therapy can present a complex therapeutic challenge to care providers. We describe the implementation of a multi-disciplinary team that employed a goal-directed, collaborative, and patient-centred approach to hypoglycemia prevention. We highlight four key themes that were central to the successful resolution of hypoglycemic events requiring hospitalization.



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University of Alberta

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## GONADOTROPH ADENOMA ASSOCIATED WITH CONCURRENT MENINGIOMA

**Background:** Pituitary tumors and meningiomas are two of the most common benign intracranial tumours, and most often associated with sex, age and previous history of irradiation. Pituitary neuroendocrine tumour (PNET) with meningioma (PNET-M) is a rare condition with the mechanism of tumorigenesis unclear. Previous studies have shown possible mechanisms, such as the upregulated mTOR signaling pathway, genetic mutations in MEN1, growth factors from PNET. However, due to the limited number of cases, the mechanisms and features of PNET-M remain unclear.

**Case:** A 49-year-old woman who initially presented in 2018 with symptoms of fatigue, headaches and visual changes in the left eye. She had no family history of MEN. Visual field testing showed a deficit in her left eye. She subsequently had a MR sella which revealed a sellar mass with compression of the optic chiasm and right tentorial leaflet meningioma which local sinus invasion. Endocrine investigations revealed an elevated PRL of 35.6 mcg/L but were otherwise unremarkable. She underwent transsphenoidal surgery on in 2019. Pathology was consistent with a gonadotroph tumour. Post-operatively, her PRL level was normalized. She subsequently underwent an elective craniotomy for tumour resection in 2022 as although her meningioma had stayed relatively stable in size (2.6 cm × 3.4 cm × 2.7cm), it was causing some compression of the right cerebellar hemisphere and vasogenic

edema. Pathology was consistent with meningioma. She was placed on dexamethasone after the surgery, which was weaned off and she has been doing well since. Her most recent MRI showed no evidence of recurrence.

**Discussion:** This is an emerging area of research with preliminary studies showing there may be a common underlying germline mutation in MEN1 causing lower expression of menin and upregulation of the mTOR signalling pathway, leading to the development of PNET-M. In our patient's case, she did not have any elevations in FSH/LH from her gonadotroph tumour but did have some hyperprolactinemia likely from stalk effect. Ciccarelli et al. (*J Neurosurg Sci.* (2001) 45:70–4.) had reported increased prolactin receptors in meningiomas. Other studies, specifically Muccioli et al. (*J Endocrinol.* (1997) 153:365–71) reported in-vitro growth of meningioma cell in-vitro when exposed to prolactin. Interestingly in our case, once the patient's gonadotroph tumour had been removed, her meningioma stayed relatively stable in size.

**Conclusion:** We report a rare case of PNET-M successfully treated with transsphenoidal surgery and craniotomy. More case will be required to understand the nature of this rare condition.





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Western University

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## NOVEL PATHOGENIC GENE VARIANTS IN PATIENTS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 (MEN-1) SYNDROME

**Introduction:** Multiple endocrine neoplasia type 1 (MEN-1) is a rare autosomal dominant tumour syndrome caused by mutations in the MEN-1 gene.

(1) MEN-1 syndrome is characterized by a predisposition to developing tumours, primarily parathyroid adenomas, duodenopancreatic neuroendocrine tumours, and pituitary adenomas. (2) While more than 1200 germline mutations in the MEN-1 gene have been identified, we report two novel gene mutations in MEN-1 that resulted in MEN-1 syndrome.

**Case 1:** A 61-year-old woman was hospitalized for PTH-dependent hypercalcemia. Workup revealed primary hyperparathyroidism and a parathyroid scan showed a parathyroid adenoma. Hypercalcemia persisted despite a left inferior parathyroidectomy, which necessitated a subsequent subtotal parathyroidectomy which led to normalization of her calcium levels. Shortly thereafter, she had GI symptoms, for which a CT abdomen showed a 1.5 × 2 cm pancreatic mass and endoscopic ultrasound guided aspiration revealed a well differentiated pancreatic neuroendocrine tumour. Biochemical work up was suggestive of a gastrinoma. She had a total pancreatectomy with biopsy suggestive of a gastrinoma and subsequent insulin-dependent diabetes. Pituitary MRI showed a 4 mm sellar mass without biochemical evidence of over or underproduction. Genetic testing found a novel MEN1:c.1192delC variant predicted to lead to premature termination of the MEN-1 gene as well as associated with nonsense-mediated decay of the MEN-1 mRNA.

**Case 2:** A 38-year-old woman with a family history consistent with a clinical diagnosis of MEN-1 syndrome, presented to an outpatient endocrinology clinic with recurrent episodes of nephrolithiasis and PTH-dependent hypercalcemia. Given her family history, a subtotal parathyroidectomy was carried out, which has kept her hypercalcemia and renal stones in remission. She had a pituitary MRI which revealed a sellar mass (largest diameter 18mm) with elevated prolactin suggestive of a prolactinoma. Cabergoline treatment led to normalization of prolactin and shrinkage of the sellar mass which now measures 8 mm, even off treatment. Genetic testing found a novel MEN1:c.784-9G > A variant that is thought to affect RNA splicing of the MEN-1 gene. Nearly a decade after her subtotal parathyroidectomy, she had recurrent nephrolithiasis and is currently being considered for parathyroidectomy for recurrent primary hyperparathyroidism.

**Discussion/Conclusion:** The cases above present novel gene mutations associated with MEN-1 syndrome. Further research defining new MEN-1 genetic mutations will provide a larger genetic pool for aiding in the diagnosis of MEN-1 syndrome.

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## ADRENAL INSUFFICIENCY FOLLOWING SUCCESSFUL TREATMENT OF ECTOPIC CUSHING'S SYNDROME IN MEDULLARY THYROID CANCER WITH SELPERCATINIB

**Background:** Medullary thyroid cancer (MTC) is a rare neuroendocrine cancer that arises from the parafollicular cells of the thyroid gland and can be either hereditary or sporadic. All hereditary MTC have rearranged during transfection (RET) mutations, as well as nearly half of all sporadic cases. Selpercatinib is a selective RET-inhibitor that has shown promising results in the treatment of MTC. In rare cases, paraneoplastic Cushing's syndrome may develop in patients with MTC secondary to excess ectopic ACTH production. Here, we discuss a patient with paraneoplastic Cushing's syndrome due to MTC that developed adrenal insufficiency following successful treatment with Selpercatinib.

**Case:** A 72-year-old female, previously healthy, presented with hypokalemia, bilateral leg swelling, and proximal muscle weakness. Elevated 24-hour urine cortisol (1533 nmol/d) and ACTH (21 pmol/L), along with non-suppressed 8 mg dexamethasone suppression test (AM cortisol 968 nmol/L) confirmed Cushing's syndrome. CT chest demonstrated a large solid mass arising from the left lobe of the thyroid gland. Fine needle aspiration of the thyroid mass demonstrated medullary thyroid cancer. Molecular testing revealed somatic

p.Cys620Arg mutation of the RET proto-oncogene. Surgical resection was deemed too risky as the thyroid mass encased the carotid artery. The patient began treatment with Selpercatinib and had rapid clinical improvements in fatigue and muscle weakness. Morning cortisol levels fell as low as 20 nmol/L, necessitating initiation of hydrocortisone replacement. Levels of the tumour markers carcinoembryonic antigen and calcitonin decreased from baseline. After 5 months of treatment, Selpercatinib elicited sustained clinical and radiographic changes. The patient remains adrenally insufficient at this time.

**Discussion:** Selpercatinib is an emerging treatment option for patients with ectopic Cushing's syndrome due to medullary thyroid cancer, especially when other treatment modalities are contraindicated. This case illustrates the possibility of prolonged hypocortisolism following treatment with Selpercatinib. Further understanding of the time to recovery of adrenal function following treatment with Selpercatinib will help guide appropriate monitoring for patients with paraneoplastic Cushing's undergoing RET-inhibitor treatment.



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## A CASE OF INSULINOMA PRESENTING AS POSTPRANDIAL BIZARRE BEHAVIOUR

Insulinomas are rare neuroendocrine tumours that present with sporadic hypoglycemia events. The diagnosis is often delayed 1–3 years after presentation. Loss of the adrenergic counter-regulatory response to hypoglycemia is known as hypoglycemia-associated autonomic failure (HAAF). HAAF can occur with insulinoma, and hypoglycemic events may lack cardinal signs and symptoms. As a result, patients may be misdiagnosed with primary neurologic or psychiatric disease. A previously healthy 42-year-old woman with a remote history of syncope as a teen presented with an abrupt onset of 6 episodes of exclusively post-prandial bizarre behaviour over a 6-month period. No obvious triggers were identified, but she reported the onset occurring with the diagnosis of terminal cancer in her mother. Episodes occurred 90–120 minutes after eating and resolved spontaneously within 20–30 minutes. The episodes consisted of vocalizations, random limb movements, and unresponsiveness to verbal and tactile cues. The patient could not recall the events but reported feeling irritable prior. She was under investigation for a neurological cause of her paroxysms. Two of the episodes were documented by EMS. The first episode of bizarre behaviour resolved prior to EMS arrival. Her documented blood

glucose (BG) was 3.4 mM, and GCS was 15. With the second event, EMS documented a BG of 1.7 mM and GCS of 6 with normal vitals (pulse 60 bpm). She recovered after IV dextrose. The patient started home BG testing and a low glycemic index diet. Investigations excluded adrenal, thyroid, renal, hepatic, and infectious diseases. Fasting glucose and HbA1c were normal. Home BG testing was normal, and no further spells occurred. She was not taking medications that could cause hypoglycemia. A mixed-meal test was conducted during which serum glucose levels were 2.6–3.7 mM, without any signs or symptoms. She continued her diet and monitoring and was followed closely with no further episodes until 8 months later, the patient was found unresponsive at home with a BG glucose of 1.7 mM. A 72 hr fast documented endogenous insulin hypersecretion with symptomatic hypoglycemia at 12 hrs. Investigations identified a pancreatic lesion. Surgical pathology confirmed a diagnosis of insulinoma. This case illustrates that insulinoma can present with sporadic post-prandial hypoglycemia and HAAF. We propose that clinicians consider insulinoma as a cause of unexplained behavioural postprandial paroxysms and perform a 72 h fast even when symptoms are well-controlled with dietary modification.



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## LEVERAGING CONTINUOUS GLUCOSE MONITORS TO EXPEDITE THE MANAGEMENT OF HYPOGLYCEMIA DUE TO INSULINOMA

**Background:** Neuroendocrine tumors (NETs) are rare neoplasms with an estimated yearly incidence of 6 per 100 000 (Hallet et al., 2015), originating from various sites. Among pancreatic NETs, insulinomas represent the most common functioning subtype and are characterized by neoplastic endogenous hyperinsulinism. Patients with insulinoma often experience significant diagnostic delays (Basuroy et al., 2018) leading to prolonged exposure to hypoglycemia. Despite known diagnostic inaccuracies associated with continuous glucose monitors (CGMs) (Lindner et al., 2021), they are increasingly utilized to investigate nondiabetic hypoglycemia.

**Case:** A 62-year-old man was referred to our institution due to suspected insulinoma, based on recurrent symptomatic hypoglycemic episodes with a positive Whipple's triad. His general practitioner provided him with a Freestyle Libre CGM, which revealed hypoglycemia 82% of the time (including 66% of severe hypoglycemic episodes  $< 3\text{mmol/L}$ ) and normal glucose level 18% of the time over the span of a 4-day period (c.f. attached figures below). The patient had a past medical history significant only for benign prostatic hyperplasia (BPH) and hypertension. He had no history of diabetes, excessive alcohol use and was not on sulfonylureas or insulin therapy. He underwent

a complete fasting challenge, which indicated hypoglycemia ( $2.4\text{ mmol/L}$ ) at 3h, along with inappropriately normal insulin secretion ( $35.5\text{ pmol/L}$  – reference range  $[13 ; 161]\text{ pmol/L}$ ), abnormally elevated C-peptide level ( $0.484\text{ nmol/L}$  – reference range  $[0.400 ; 1.470]\text{ nmol/L}$ ) and suppressed  $\beta$ -hydroxybutyrate levels ( $< 0.1\text{ mmol/L}$ ). Morning cortisol level was within normal limits ( $446\text{ nmol/L}$ ). A CT scan of the abdomen and pelvis revealed a  $1.8\text{ cm}$  hypervascular lesion at the tail of the pancreas, consistent with a NET without evidence of distant metastases. Subsequently, the patient was admitted for treatment with intravenous dextrose and gradual up-titration of diazoxide to manage recurrent hypoglycemic episodes. He is presently awaiting surgical resection of the pancreatic mass.

**Discussion:** Hypoglycemia in non-diabetic patients is a rare condition that can manifest with discrete spells, often challenging to identify in an outpatient setting. Despite the inherent accuracy limitations, this case underscores the pivotal role of CGMs in diagnosing insulinoma and expediting referrals to specialized centers. Furthermore, CGMs may also facilitate identification of unrecognized hypoglycemic events in patients with prolonged hypoglycemia exposure (Unger & Parkin, 2011).



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## MONITORING FOR GONADAL CELL TUMOR RISK IN A MALE PATIENT WITH MIXED GONADAL DYSGENESIS WITH A RING Y CHROMOSOME

**Background:** Mixed gonadal dysgenesis can present with abnormalities in the Y chromosome such as a ring Y chromosome. These children can present with ambiguous genitalia or appear phenotypically male or female. They are at an increased risk of developing gonadal germ cell tumors (GGCTs) that arise from persistent, immature stem cells. The presence of the gonadoblastoma locus (GBY) on the Y chromosome increases this risk, as genes in this locus are involved in cell proliferation. 45X/46XY phenotypic males can present with short stature, cardiorenal malformations and infertility.

**Case:** A 12-year-old boy was referred for assessment of short stature. He had an antenatal diagnosis of IUGR and linear growth was along the 10th percentile until age 1, after which he has been tracking less than the 1st percentile. On examination, he was non-dysmorphic and proportionate with a height of 132.5 cm (- 3.6 SD) and weight of 31.3 kg (- 2.11 SD). His mid-parental height was 170.6 cm (- 0.81 SD) and a bone age scan obtained was within 1SD. He was phenotypically male with a stretched penile length of 5 cm and bilateral descended testes with testicular

volume of 5 cc. Chromosomal microarray revealed a ring Y chromosome with SHOX haploinsufficiency and deletion in the AZF region, which is involved in spermatogenesis. A karyotype revealed 45X/46X(r)Y. The ring Y chromosome includes most of the short arm along with the SRY gene, but there is a loss of the terminal end of the short arm containing the SHOX gene and deletion of the entire long arm. Due to the risk of GGCT associated with mixed gonadal dysgenesis, a baseline testicular ultrasound is being obtained prior to discussing the use of growth hormone therapy for SHOX deficiency.

**Discussion:** The risk of GGCT is lower in phenotypic males with mixed gonadal dysgenesis compared to those with ambiguous genitalia. However, there is an increased risk of GGCT with growth hormone therapy. Whether we use growth hormone therapy or not, this patient will be monitored periodically with physical exams, gonadotropins, serum testosterone, testicular ultrasounds and serum tumor markers. This case highlights the importance of genetic testing for short stature and monitoring closely for tumor risk in male patients with mixed gonadal dysgenesis.



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## GROUP VERSUS INDIVIDUAL DIABETES EDUCATION FOR PERSONS WITH LIVED EXPERIENCE OF HOMELESSNESS IN CANADA

**Purpose:** The purpose of this study was to explore various forms of diabetes self-management education (DSME), including group and individual sessions, for persons with lived experiences of homelessness (PWLEH) in Canada. DSME is essential for improved outcomes for those living with diabetes. PWLEH and diabetes have many barriers to diabetes management including access to appropriate DSME.

**Methods:** We conducted a qualitative descriptive study using open-ended interviews with healthcare and homeless sector service providers with experience in diabetes and/or serving those experiencing homelessness in five cities across Canada. We used NVivo qualitative data analysis software to facilitate thematic analysis, focusing on variations in DSME for persons with lived experience of homelessness.

**Results:** DSME was provided through mainstream diabetes groups, groups focused on PWLEH, and individual sessions. We found four themes, the

first being a harm reduction approach during education tailored to PWLEH. Whether this was in a group or individual session, the harm reduction approach took into account patients' access to food, medications and supplies, as well as other comorbidities including mental health and substance use disorders. The second theme was assumptions in diabetes education, where the curriculum in group education may not meet the needs of an individual patient, especially in mainstream group education. The third theme was community building, where group education created supportive relationships among its members and benefited from peer-to-peer education. The final theme was the importance of trust and confidentiality in DSME, which was most easily met during individual education.

**Conclusion:** PWLEH experience unique challenges in managing diabetes. Diabetes education which is adapted to these individuals' unique needs may be more successful and could be delivered both in individual and group settings.



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## REAL-WORLD APPLICATION OF AMERICAN THYROID ASSOCIATION RISK-ADAPTED DOSING FOR POSTOPERATIVE RADIOACTIVE IODINE IN DIFFERENTIATED THYROID CANCER PATIENTS

**Background:** The 2015 American Thyroid Association (ATA) guidelines recommend a risk-adapted approach to postoperative radioactive iodine (RAI) dosing for differentiated thyroid cancer (DTC). This requires integration of pre-, intra-, and postoperative clinicopathological factors and determination of intent of RAI therapy as either remnant ablation, adjuvant treatment, or treatment of known disease. This study seeks to evaluate the performance of the thyroid cancer triage group at one tertiary care referral centre, in terms of adherence to a guideline-based and risk-adapted approach to RAI dosing recommendations.

**Methods:** We retrospectively analyzed the demographic and clinicopathological data of 1420 adult ( $\geq 18$  years) patients diagnosed with DTC between 2016–2022 after thyroid surgery who were reviewed at an institutional thyroid cancer triage rounds and issued a recommendation for postoperative RAI dosing.

**Results:** Among 1420 patients, the median age at diagnosis was 47 years (range = 18–93 years) and median tumor size was 1.7 cm (range 0.05–16.5cm). ATA risk of recurrence (ROR) was as follows: low 725 (51.1%), intermediate 470 (33.1%), and high 225 (15.8%). The recommended RAI dose in the low risk group was: 0 mCi in 682 (94.1%) patients, 0–30 mCi in 15 (2.1%) patients, 30 mCi in 24 (3.3%) patients, and 30–100 mCi in 4 (0.6%)

patients. The recommended RAI dose in the intermediate risk group was: 0 mCi in 53 (11.3%) patients, 0–30 mCi in 22 (4.7%) patients, 30 mCi in 329 (70.0%) patients, 30–100 mCi in 29 (6.2%) patients, 100 mCi in 36 (7.7%) patients, and 100–150 mCi in 1 (0.2%) patient. The recommended RAI dose in the high risk group was: 30 mCi in 11 (4.9%) patients, 30–100 mCi in 17 (7.6%) patients, 100 mCi in 156 (69.3%) patients, 100–150 mCi in 4 (1.8%) patients, 150 mCi in 34 (15.1%) patients, 150–200 mCi in 2 (0.9%) patients, and 200 mCi in 1 (0.4%) patient.

**Discussion:** In general, our centre followed the ATA risk-adapted approach to RAI dosing. As expected, the vast majority of low risk patients were not recommended postoperative RAI, and all high risk patients were recommended postoperative RAI (median dose = 100 mCi). There was significant variability in the recommended RAI dose among ATA intermediate risk patients (median dose = 30 mCi, range = 0–150 mCi), reflecting the heterogeneity in ROR among this cohort. At times, the triage group recommended an RAI dose range in order to incorporate postoperative thyroglobulin values, postoperative staging imaging, or patient values/preferences.





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[VIEW POSTER](#)

## BITES FOR BONES

**Background:** An estimated 1 in 2 women and 1 in 5 men experience a fragility fracture after age 50 due to osteoporosis. Diet is an important mediator of bone health but individuals with or at risk of osteoporosis do not always meet recommendations regarding intake of specific nutrients (protein, calcium, vitamin D) and whole foods. Culinary Medicine aims to improve dietary quality through the delivery of practical, evidence-based information and skill development and may improve nutritional knowledge acquisition and application for individuals with or at risk of osteoporosis.

**Objective:** We aimed to identify barriers and facilitating factors to adopting a bone-healthy diet among adults with or at risk of osteoporosis, and to assess interest in attending a bone-focused Culinary Medicine program.

**Methods:** From Oct 2021–Feb 2022, we recruited adults aged  $\geq 45$  years referred to our specialty osteoporosis clinic to complete an electronic survey and participate in virtual focus groups exploring barriers and facilitators to following dietary recommendations for bone health. Interest in a practical, bone-health focused Culinary Medicine program was also assessed. Survey data was summarized using descriptive statistics and participant responses from the focus groups were grouped thematically and coded for frequency.

**Results:** Among survey respondents ( $n = 26$ , 22 female, age range 56–85 years), the most frequently reported barrier to adopting a bone-healthy diet was lack of time and convenience (reported by 11 [42%]). Principal barriers highlighted by focus group participants ( $n = 24$ ) were:

1. living alone and cooking for one
- b. low motivation to prepare meals, and
- c. dietary restrictions due to comorbidities.

Principal facilitators identified in the focus groups were:

- d. preparing meals in advance
- e. online grocery shopping, and
- f. exercise.

Focus group participants expressed enthusiasm about a Culinary Medicine program for bone health.

**Conclusion and Implications:** Adults with or at risk of osteoporosis and fragility fracture face multiple barriers to adhering to dietary recommendations. Bone-focused Culinary Medicine programming may help to address these barriers and is likely to be well-accepted.





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[VIEW POSTER](#)

## VITAMIN D LEVELS IN TRANSGENDER PATIENTS: A CANADIAN PERSPECTIVE

**Objectives:** In Canada, reported rates of vitamin D deficiency are as high as 70–97% (1). Current data on prevalence of vitamin D deficiency in transgender populations noted lower levels of 25 (OH) vitamin D levels in transgender women compared to age-matched cisgender men prior to initiation of gender affirming hormone therapy (GAHT) and low BMD Z-scores associated with vitamin D deficiency in transgender adolescents (2,3). Furthermore, transgender individuals are burdened by a higher rate of mood disorders compared to the general population (4) and vitamin D deficiency may be associated with depression (5). Thus, it is important to ensure that transgender patients receive adequate vitamin D supplementation. Current guidelines stipulate that transgender patients should be reminded of the importance of vitamin D repletion and ensure daily intake of 1000 IU (6), but this may be insufficient if severe deficiency is more common in these patients.

**Methods:** A retrospective chart review of patients referred for GAHT at one endocrinology private practice office was conducted. Patients referred for initiation of GAHT, and those already established and needing transfer of care, were included. Data collected included vitamin D level, patient's assigned sex at birth, and age. Vitamin D was classified as replete at  $> 75$  nmol/L,

insufficient at 50–75 nmol/L, deficient at 22–49 nmol/L and severely deficient if  $< 25$  nmol/L. Results A total of 438 patients were assessed, 394 of which had vitamin D data. Only 17.8% of patients were found to be vitamin D replete, compared to 34.3% insufficient, 33.5% deficient, and 14.5% severely deficient. There was a strong correlation between increasing age and vitamin D levels in transgender patients ( $R = 0.22$ ,  $p < 0.0001$ ). Patients who were transferred for ongoing on GAHT were more likely to have higher vitamin D levels than those who had yet to start (23.5% vs. 14.7%,  $p = 0.0372$ ). There was no correlation between vitamin D levels and sex assigned at birth.

**Conclusion:** The current study demonstrates high rates of vitamin D deficiency in transgender Canadians, especially those who are younger. Current recommendations regarding vitamin D supplementation may be insufficient to adequately replenish levels in this population. This data may not be relevant to transgender patients in other regions, especially in countries at lower latitudes. To Canadian practitioners and patients, it is important as the impacts of GAHT on bone health and the effects of vitamin D on general health are still being studied. Please note references are not included but available upon request.



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## VALIDITY OF ADMINISTRATIVE HEALTH DATA CASE DEFINITIONS FOR IDENTIFYING POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW

**Background:** Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in females of reproductive age. Administrative health data offer the opportunity to evaluate health outcomes and disease epidemiology at a population-level, but variable administrative health data case definitions for PCOS have been used to date.

**Objective:** To estimate the validity of published administrative health data case definitions of PCOS compared with reference standards.

**Methods:** Studies published up until July 4, 2023 were searched from Medline and Embase. Abstracts and full texts were reviewed in duplicate using Covidence. Studies were included if they compared the accuracy of codes for PCOS in an administrative database with a reference standard and had validity indices (sensitivity, specificity, positive predictive value (PPV), negative predictive value or measure of agreement). Original studies in English with human subjects and at least five PCOS patients (and  $\geq 30$  patients overall) were included. Quality was determined using the Quality Assessment for Diagnostic Accuracy Studies 2 tool. A meta-analysis was planned if there were sufficient data available.

**Results:** Of 6266 screened abstracts and 70 screened full texts, four studies met inclusion criteria. All four studies compared administrative health data definitions of PCOS to chart review as a reference standard. Two studies defined PCOS using Rotterdam Criteria, one study used self-report, and one used a clinical gold standard. All case definitions included the ICD-9 code 256.4 in the PCOS case definitions presented and three case definitions also included ICD-10 code E28.2. Two case definitions included ICD codes for related disorders, such as hirsutism, female infertility, or irregular menses. The range of ICD codes used in the case definitions was 2-17. Of the three studies that reported PPV for case definitions, PPV ranged from 68% to 96%. One study did not report PPV but found high agreement (Percent agreement = 90.3,  $\kappa = 0.21$  and percent agreement bias adjusted  $\kappa = 0.81$ ). Overall, the risk of bias of included studies was low. There were insufficient data for meta-analysis.

**Conclusions:** We identified four studies that reported the validity of one or more administrative health data case definitions for PCOS in administrative databases compared with reference standards. The majority of case definitions for PCOS had a high PPV ( $> 70\%$ ), suggesting that these case definitions are valid. Further validation of these case definitions is required in other administrative health databases to assess and compare their external validity for use in population health studies.



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[VIEW POSTER](#)

## CUSHING'S DISEASE MANAGEMENT AT THE CHU DE QUÉBEC UNIVERSITÉ LAVAL: A RETROSPECTIVE COHORT STUDY

**Background:** Cushing's syndrome is a rare clinical entity characterized by a high secretion of endogenous cortisol. It is classified as Cushing's Disease when it is caused by a pituitary adenoma. When untreated, the mortality rate is increased by 1,4–3,8 times. The first line of treatment is transsphenoidal surgery. Reported postoperative remission is between 65 to 98%. It varies according to neurosurgeon expertise, adenoma size and location, and remission criteria. Long term recurrence is also possible. When surgery is not curative, medical treatment is indicated. The objective of this study was to determine remission and control rates of Cushing's Disease one year after initial treatment and at the last follow-up in a perspective of quality of care assessment.

**Methods:** This is a unicentric retrospective descriptive cohort study. Adults with Cushing's Disease treated at the CHU de Québec – Université Laval between January 2000 and June 2022 and followed by the endocrinology service were included. Silent corticotropic adenomas were excluded. The remission status was defined by the endocrinologist after surgery or other permanent treatment. Patients on active corticosteroid replacement were considered in remission. When on medical treatment, disease's control

(either persistent endogenous hypercorticism or not) was assessed at each follow-up visit. The control status of medical comorbidities was also assessed.

**Results:** 75 records were screened and 40 patients were included. 57.5 % had a microadenoma, 40% had a macroadenoma and 2.5% had no visible tumor on MRI. 95% of patients underwent transsphenoidal surgery, 25% had radiation therapy, 55% received pharmacological therapy and 15% underwent bilateral adrenalectomy. The median follow-up length was 79.5 months. The combined remission and disease control rate at one year of treatment was 87.5% and it was 92.5% at the last follow-up visit. Six patients (15%) died during the follow-up but only one of them was not in remission.

**Conclusion:** In our study, the combined remission and disease control rate after several years of follow-up at CHU de Québec-Université Laval was 92.5% using multiple treatment modalities for patients with Cushing's Disease.



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## THE ROLE OF ANTI-GLUTAMIC ACID DECARBOXYLASE ANTIBODIES IN PATIENT CARE: IDENTIFYING CURRENT PRACTICE AND FUTURE POTENTIAL FOR PATIENTS WITH DIABETES

**Background:** Diabetes mellitus (DM) encompasses Type 2 DM (T2DM), characterized by insulin resistance, Type 1 DM (T1DM) and Latent Autoimmune Diabetes in Adults (LADA) — both of which are characterized by autoimmunity. Anti-glutamic acid decarboxylase (anti-GAD) antibodies are positive in up to ~ 80% of newly diagnosed T1DM patients and may also be positive in patients with LADA. To improve clarity on the indications to test for anti-GAD antibodies in DM patients, we are studying the current clinical utility of these antibodies and how their results impact patient care.

**Methods:** We are performing a retrospective chart review for patients who had anti-GAD antibodies ordered between 1 January 2020 and 31 December 2021. Data collected include the titre of anti-GAD antibodies, patients' age, sex, type of DM, and the specialty of the ordering physician. We categorized patients based on the clinical context in which the anti-GAD antibodies were ordered. Furthermore, we documented patient cases where the anti-GAD antibodies were instrumental in changing the patient's diagnosis for type of DM from T2DM to T1DM or LADA.

**Results:** Interim results (January 2020 – June 2021) show that the top reason (39% of cases) for ordering anti-GAD antibodies is to detect possible autoimmunity in T2DM patients who develop diabetic ketoacidosis (DKA) or other signs of insulin insufficiency, or who have inadequate glycemic control on non-insulin forms of anti-hyperglycemic medications. Anti-GAD antibodies are also ordered in patients with a first presentation of DKA / signs or symptoms of insulin insufficiency, and for confirmation in T1DM patients. In 22 out of 243 patients with diabetes (9.1%), a positive anti-GAD antibody result led to a change in diagnosis from T2DM to LADA.

**Conclusion:** Anti-GAD antibodies' positivity can support a change in diagnosis from T2DM to LADA, which has substantial impact on patient care. More in-depth understanding of anti-GAD antibodies will clarify their role in future guidelines for DM diagnosis.



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## SUPPORTED OPEN-SOURCE AUTOMATED INSULIN DELIVERY: RANDOMIZED MULTI-ARM PLATFORM TRIAL PROTOCOL

**Background:** Commercial automated insulin delivery (C-AID) pump systems have demonstrated improved outcomes in type 1 diabetes (T1D), but have potential drawbacks including cost, delays to innovation related to regulatory processes, and device ecosystem constraints. Given these limitations, unregulated open-source automated insulin delivery (OS-AID) systems are used by some people with diabetes. The benefits of OS-AID have been demonstrated in several observational studies and in randomized trials against non-AID controls. To date there are no randomized trials comparing OS-AID and C-AID, nor comparing different OS-AID systems with one another. When supported in a clinic setting, OS-AID is referred to as supported OS-AID (SOS-AID).

**Methods:** This protocol is in development and has not yet been submitted for Research Ethics Board approval. The SOAR-UP (Supported Open-source Automated insulin delivery Randomized mUlti-arm Platform) trial is a 90-day non-inferiority, open-label, randomized platform trial assessing multiple C-AID and SOS-AID systems. Participants naive to automated insulin delivery will be allocated randomly to either SOS-AID or C-AID. Each participant will retain their existing pre-study hardware (smartphone and insulin pump), and be allocated randomly among the SOS-AID/C-AID systems available for that hardware, see Figure 1. They will use the allocated system for 90 days

with standardised installation procedures and regular clinician support in an experienced centre. Those who do not wish to be randomized may participate in a separate observational arm for C-AID. The primary outcome measure is the sensor glucose percentage time-in-range (3.9–10 mmol/L) at end-of-study (days 76 through 90) in the randomized SOS-AID and C-AID groups. Secondary outcomes include other glycemic measures, quality-of-life measures, adverse events and system performance. Participants with T1D aged 2–80 years using continuous glucose monitoring will be recruited from a single centre in Canada. The C-AID systems planned for inclusion in this study (Omnipod 5 and mylife CamAPS FX) await Health Canada approval. The SOS-AID systems planned for inclusion (Loop, iAPS and AAPS) are currently in clinical use at the study centre in the context of a detailed consent form and waiver. Expected results based on available data (see Table 1) include a mean time-in-range of > 70% for all SOS-AID groups and the C-AID Omnipod 5. Adverse events and system performance are expected to show safety of SOS-AID systems.

**Conclusion:** The SOAR-UP trial will compare the efficacy and safety of SOS-AID with C-AID systems. The results will be of assistance to people with diabetes and clinicians in their assessment of available therapies.



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## PREVALENCE AND CHARACTERISTICS OF ADRENAL INCIDENTALOMAS IN PATIENTS WITH LUNG TRANSPLANTS: A RETROSPECTIVE COHORT STUDY

**Background:** Adrenal incidentalomas are adrenal lesions found on imaging performed for reasons other than suspected adrenal disease. The prevalence of adrenal incidentalomas is about 3% in patients. Hormone assessment is recommended in patients with adrenal incidentalomas by current guidelines. Recently, chronic hypoxemia exposure such as in cyanotic congenital heart disease and high altitude was found to be a risk factor for pheochromocytomas and paragangliomas. However there is no data available on adrenal incidentalomas in lung transplant patients.

**Objectives:** To evaluate the prevalence of adrenal incidentalomas in lung transplant patients, and to assess the proportion evaluated according to guidelines.

**Design:** In this retrospective single-center study, we reviewed the records of adult patients who underwent pulmonary transplant at our hospital center from 2014 to 2020. Data was collected using hospital database and the presence of adrenal incidentalomas was assessed using the most recent thoracic and abdominal CT-scans.

**Results:** Our study included 398 patients who underwent lung transplant. Our cohort consisted of 163 females (41%) and 235 males (59%). Mean

age was of 53 yo (median: 58 yo). Before transplant, 94% of patients were hypoxemic, with a mean of 4.3 years and a median of 2 years of home oxygen-therapy. Thirteen cases of adrenal incidentalomas were identified (prevalence of 3.3%). Among the 13 patients, 9 were female (69%) and the mean age was of 52 yo (median: 58 yo). All of these patients were hypoxemic before transplant, with home oxygen-therapy for a mean time of 5 years and a median time of 2 years. Prior to transplant, 3 patients with incidentalomas were known for hypertension, 1 for diabetes and 3 for coronary artery disease. Two out of 13 patients (15%) had bilateral adrenal incidentalomas. The radiologic mean adrenal mass size was 15.7 mm (range from 11 to 34 mm) and Hounsfield Units (HU) ranged from -7 HU to 26 HU (N:5). No patient had hormonal work-up according to guidelines, and none were referred to an endocrinologist.

**Conclusion:** We found a prevalence of 3.3% of adrenal incidentalomas in our cohort of pulmonary transplant patients, which is similar to the general population. As in the majority of patients with adrenal incidentalomas, adrenal hormonal work-up is lacking in lung transplant patients. Hormonal investigations are currently being conducted to determine hormonal profiling of these adrenal masses and to determine the prevalence of pheochromocytomas in this cohort of hypoxemic lung transplant patients.





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## QUALITY IMPROVEMENT INITIATIVE TO ENHANCE PERIOPERATIVE CARE AND MONITORING AFTER PITUITARY SURGERY

**Background:** The pituitary gland plays a critical role in regulating various hormones. Following pituitary surgery, patients may develop hormone abnormalities, including syndrome of inappropriate antidiuretic hormone and central adrenal insufficiency. These complications could lead to hospital readmissions, morbidity and even mortality without early recognition and prompt treatment. Current endocrine guidelines recommend outpatient sodium and cortisol monitoring on postoperative day 7 (POD7) and comprehensive pituitary function assessment around 6 weeks post-surgery (POW6). However, there is currently no standardized postoperative protocol in place at our local tertiary care hospital, and it is unclear how often the recommended bloodwork is being performed at our hospital.

**Objectives:** To evaluate the frequency of outpatient bloodwork on POD7 and POW6, before and after implementation of a standardized endocrine discharge protocol.

**Methods:** Through collaboration with relevant stakeholders and using quality improvement tools, we created a standardized endocrine discharge protocol that included clear patient instructions and pre-filled laboratory requisitions. For the baseline cohort, we retrospectively reviewed all postoperative outpatient bloodwork from all pituitary surgeries at our hospital from September 1, 2021, to August 31, 2022. We then prospectively collected data for all patients who had surgery after the implementation of our protocol

starting on January 1, 2023 (intervention cohort). Our main outcome measure was completion of POD7 and POW6 bloodwork. We defined POD7 bloodwork as cortisol or sodium level by POD7, excluding patients who were still admitted on or after POD5, and POW6 bloodwork as cortisol by POD90 and free T4 between POD30-90. We compared outcomes between the two cohorts using statistical process control charts. We also contacted a subset of intervention patients for their feedback on the process and their postoperative experience.

**Results:** In the baseline cohort, only 17% of patients (9/52) completed POD7 bloodwork, and 52% (28/54) completed POW6 bloodwork. In the intervention phase thus far, this increased to 77% (17/22) for POD7 bloodwork and 75% (12/16) for POW6 bloodwork. Importantly, we found that 35% of intervention patients (6/17) had hyponatremia on POD7. In addition, all 13 interviewed patients expressed high satisfaction and found the discharge instructions to be clear and comprehensive.

**Conclusion:** The introduction of a standardized endocrine discharge protocol at our tertiary care hospital improved the completion rates of guideline-recommended outpatient bloodwork following pituitary surgery. This improvement is crucial for the early detection and prompt treatment of postoperative endocrine complications.





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[VIEW POSTER](#)

## TREATMENT OF INPATIENT HYPOGLYCEMIA – CURRENT ISSUES AND QUALITY IMPROVEMENT OPPORTUNITIES

**Background:** Inpatient hypoglycemia increases morbidity, mortality, and length of hospital stay (Carvalho, 2020; Lake, 2019). The Ottawa Hospital (TOH) inpatient hypoglycemia treatment protocol (juice if can drink or intravenous dextrose if unable to drink, and re-check in 15 minutes) was designed for diabetes mellitus (DM) inpatients when blood glucose (BG) is  $< 4$  mmol/L, according to consensus guidelines (AMA, 2018; Yale, 2018). For inpatients without DM, hypoglycemia is considered BG less than  $\sim 3$  mmol/L, and this protocol can also be applied. Electronic Medical Record auditing of hypoglycemia is an effective strategy for improving patient safety outcomes (Cruz, 2020).

**Objectives:** To audit for adherence to the hypoglycemia protocol at TOH, and to inform quality improvement initiatives for timely resolution of inpatient hypoglycemia. Methods: Retrospective chart review for inpatients with point-of-care glucose meter reading  $< 4.0$  mmol/L, from January to April 2021 at TOH.

**Characteristics collected for each event:** DM status known or unknown, value of BG before and after treatment, capability to tolerate oral intake, whether hypoglycemia protocol was ordered, treatment given, time to BG re-check. Results: 25% of BG  $< 4$  mmol/L events occurred in patients with known

DM and yet the hypoglycemia protocol was not ordered. In 59% of patients without known DM who had a BG  $< 4$  mmol/L event, the hypoglycemia protocol had been ordered. While patients without DM are only considered hypoglycemic at BG  $< 3$  mmol/L, inpatients without DM were treated with this hypoglycemia protocol for BG 3.1 to 3.9 mmol/L in 66% of cases. The protocol's treatment type was followed 74% of the time. However, 7% of BG  $< 4$  mmol/L events received intravenous dextrose in a patient able to tolerate oral intake. 85% of blood glucose re-checks were delayed (over 15 minutes after initial event). 22% of BG re-checks exceeded 60 minutes after initial event. 20% of treated BG  $< 4$  mmol/L events were unresolved on re-check.

**Conclusions:** TOH hypoglycemia protocol is frequently not followed with regards to the intended population, treatment chosen, and BG re-checks. Future directions for optimizing inpatient hypoglycemia management to improve patient safety include analyses of barriers to appropriately ordering and following the hypoglycemia protocol through stakeholder focus groups. In addition, this study also reflects on the clinical effectiveness of this commonly used hypoglycemia protocol which had been based on small sample sizes, and may benefit from evaluation in the modern inpatient DM population (Brodows, 1984; Slama, 1990).



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[VIEW POSTER](#)

## INCREASED PROLACTIN SECRETION IN INFERIOR PETROSAL SINUS SAMPLING FOLLOWING DESMOPRESSIN ADMINISTRATION IN PATIENTS WITH ACTH-DEPENDENT CUSHING'S SYNDROME

**Background:** Previous studies have described an increase in central prolactin (PRL) secretion in response to corticotropin-releasing hormone (CRH) during inferior petrosal sinus sampling (IPSS) in a proportion of patients with Cushing's disease (CD). Desmopressin is now used instead of CRH because of its wider availability, lower cost, and similar accuracy. It is unknown whether central PRL secretion can also increase after desmopressin as it does after CRH.

**Objectives:** Evaluate the central PRL response to desmopressin administration in patients with ACTH-dependent Cushing's syndrome (CS) undergoing IPSS.

**Method:** We conducted a retrospective study of patients who underwent IPSS in our center between 2015 and 2022. IPSSs using desmopressin were collected, as well as those using either CRH or CRH + desmopressin for comparison. ACTH and PRL were measured in bilateral petrosal sinuses before and 3, 5, and 10 minutes after a 10 mcg IV desmopressin bolus; and simultaneous peripheral ACTH, PRL and cortisol were measured. A > 50% central PRL increase was considered a positive response.

**Results:** 30 IPSSs performed with desmopressin were included: 24 patients with CD and 6 patients with ectopic ACTH secretion (EAS). 73.3% were

women and mean age was 48 yo. 12 patients with CD (50%) had a > 50% PRL increase on at least one side. The peak PRL value and highest central/peripheral (C/P) ACTH ratio after desmopressin were ipsilateral in 10 out of 12 patients (83%). Among the 9 patients whose pathology was available, only one showed co-expression of ACTH and PRL on immunohistochemistry (IHC). No somatic genetic USP8 analyses were performed. Among the 6 patients with EAS, none had a central or peripheral PRL response after desmopressin. 21 IPSSs with CRH or CRH + desmopressin were collected. 14 out of 18 patients (77.8%) with CD had a > 50% PRL increase after stimulation. For 10 out of these 14 patients (71.4%), peak PRL value and C/P ACTH ratio were ipsilateral. 2 out of 3 IPSSs with CRH or CRH + desmopressin in patients with EAS had a > 50% PRL increase after stimulation.

**Conclusion:** In our study, 50% of IPSSs showed a significant central prolactin increase after desmopressin in patients with CD, but none in patients with EAS. In pathology of corticotroph adenomas from patients with prolactin stimulation by desmopressin, there was no expression of prolactin by IHC. Further research is needed to better understand the mechanisms for prolactin secretion following ACTH secretagogue administration and its potential clinical implications.



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[VIEW POSTER](#)

## TREATMENT OF SUBCLINICAL HYPERTHYROIDISM AND INCIDENT ATRIAL FIBRILLATION

**Background:** Treating overt hyperthyroidism can prevent and leads to resolution of atrial fibrillation (AF). While subclinical hyperthyroidism (SH) is also associated with AF, it is unknown if treating SH can prevent AF.

**Objective:** We aimed to assess the association between treatment of SH and incident AF.

**Methodology:** In a single-centre retrospective cohort study, patients  $\geq 18$  years with biochemical SH were identified from the Regional Laboratory database 2000–2021. Those with prior AF, thyroid or pituitary disease, or pregnancy were excluded. Patients treated for SH (medications, radioactive iodine, or surgery) were compared to untreated patients. The primary outcome was incident AF. The secondary outcomes were ECG p wave duration and echocardiographic ventricular and ascending aorta size. More rigorous pharmacoepidemiologic analyses to account for immortal time bias will follow.

**Results:** 360 of 5567 patients with SH met inclusion criteria (131 (37%) treated, 229 (64%) untreated). 5 treated and 15 untreated SH patients developed AF (3.8 % and 6.6%, respectively,  $p = 0.26$ ). In the treated group,

we excluded time from SH diagnosis to SH treatment: 224.49 person-years (py) (median 0.56 years; IQR 0.19, 2.01) from analysis. Follow-up time in the treated group from SH treatment start was 496.36 py (median 2.85 years; IQR 1.26, 5.31), and in the untreated group from SH diagnosis was 920.44 py (median 3.12 years; IQR 0.82, 6.18). Incidence rate of AF was 1.0 %/year in the treated and 1.6 %/year for the untreated group (IRR 0.62, 95% CI 0.17–1.79,  $p = 0.62$ ). Mean p-wave duration, ventricular size and ascending aorta size in the treated vs untreated groups were 88.97 vs 84.95 ms ( $p = 0.15$ ), 4.18 vs 4.31 cm ( $p = 0.81$ ), and 3.36 and 3.21 cm ( $p = 0.24$ ), respectively. In a sensitivity analysis, patients diagnosed with AF  $< 30$  days after starting treatment for SH were included in the untreated group. In these treated and untreated groups, 3 versus 17 patients developed AF (2.3% versus 7.4% respectively,  $p = 0.04$ ), and incidence was 0.6%/year in the treated and 1.8%/year in the untreated group (IRR 0.33, 95% CI 0.06–1.14,  $p = 0.06$ ).

**Discussion:** Although there was an overall trend towards less AF in the treated group, there were no significant differences in AF incidence, or ECG or echocardiographic characteristics following SH treatment. Our small retrospective study does not support that treating SH directly prevents AF. Future larger prospective studies are required to further assess this question.



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[VIEW POSTER](#)

## INVESTIGATION AND MANAGEMENT OF PRIMARY ALDOSTERONISM WITH ADRENAL VEIN SAMPLING AT THE CHU DE QUÉBEC-UNIVERSITÉ LAVAL

### Investigation and Management of Primary Aldosteronism with Adrenal Vein Sampling at our centre.

**Background:** Adrenal vein sampling (AVS) is the gold-standard test to assess for lateralization in primary aldosteronism (PA). In case of unsuccessful right adrenal vein (RAV) cannulation, our tertiary care centre uses a multinomial regression model to extrapolate the RAV cannulation results.

#### Objectives:

1. To determine the proportion of successful RAV cannulation during AVS at our hospital
2. To evaluate the management and clinical evolution of patients with PA who underwent AVS, including those who were treated based on the multinomial regression model results.

**Methods:** This retrospective cohort study included patients aged  $\geq 18$  years with a diagnosis of PA who underwent AVS between January 2017 and September 2022 at our centre. Epidemiological data at diagnosis were collected, as well as data on AVS cannulation, AVS complications and PA clinical evolution. Successful RAV cannulation was determined by the interventional radiologist and by cortisol ratios. Results are presented as percentage or mean  $\pm$  SD.

**Results:** 39 patients were included (33.3% women; mean age  $51.1 \pm 11.5$  years; 89.7% with hypertension treated with a mean of  $2.5 \pm 1.1$  antihypertensive drugs; 74.4% with hypokalemia), for a total of 40 AVS procedures. 3 procedures (7.5%) selectively cannulated both adrenal veins. 3 procedures (7.5%) led to complications (subcutaneous hematoma). Of the 33 incomplete AVS procedures, the clinical management after 6 of these procedures was unavailable due to follow-up in other hospital centres. Among the remaining 27 patients, 5 (18.5%) had a second complete AVS in another tertiary care centre, 12 (44.4%) were medically treated, 1 (3.7%) had an adrenalectomy and 11 (40.7%) were treated according to the multinomial regression model results. The model lateralized aldosterone secretion in 5 patients, who then all had adrenalectomy, after which 4 were diagnosed adrenal adenomas and one was diagnosed adrenal hyperplasia on pathology. The 8 complete AVS procedures led to 6 diagnoses of unilateral disease and 2 diagnoses of bilateral disease. Applying the multinomial regression model to the initial AVS procedure of these 8 cases would have correctly predict aldosterone lateralization in 7 cases (87.5%).

**Conclusion:** AVS success rate in our tertiary care centre was low. The multinomial regression model appeared to adequately detect unilateral disease in our small sample. It is necessary to reevaluate our AVS technical protocol to increase our AVS successful cannulation rate.



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## DIAGNOSIS AND MANAGEMENT OF PRIMARY ALDOSTERONISM AT A TERTIARY CARE CENTER: A DESCRIPTIVE AND QUALITY ASSURANCE STUDY

**Background:** Primary aldosteronism (PA) is under-diagnosed despite having a global prevalence as high as 12.7% in primary care<sup>1</sup> and 11.2% in newly diagnosed hypertensive patients<sup>2</sup>. Excess aldosterone can lead to increased morbidity and mortality if left untreated, particularly on cardiovascular, cerebrovascular, and renal outcomes, independent of its effect on blood pressure<sup>1</sup>. Despite international guidelines for the diagnosis and management of PA<sup>3</sup>, there exists individual provider variability. Many patients go on to receive invasive diagnostic and therapeutic procedures such as adrenal vein sampling (AVS) and adrenalectomies in the absence of a standardized workup algorithm. We aimed to assess the diagnostic workup and management of patients undergoing testing for PA at a tertiary care center and identify gaps in the use of diagnostic tests.

**Methods:** A retrospective chart review of patients > 18 years who underwent adrenalectomy and/or AVS from 2012–2023 at a tertiary care center was performed. Laboratory data including aldosterone, renin, aldosterone-renin ratio, electrolytes, renal function tests, medications (number and type of antihypertensives and potassium supplementation), confirmatory tests, imaging results, AVS results, surgery details, postoperative laboratory data and outcomes post-adrenalectomy were reviewed.

**Results:** We identified 104 patients who underwent laparoscopic adrenalectomies. Of these, 18 had a diagnosis of PA. Twelve did not have relevant investigations for PA despite having a history of hypertension and/or hypokalemia. For those with PA, the average pretreatment potassium and creatinine levels were 3.2 (SD = 0.7) and 92 (SD = 35) respectively. The average ARR of these patients was 676.6 (SD = 773.5), with none in the intermediate range (5–15 ng/dL) yet three had confirmatory testing done, nonetheless. The average number of anti-hypertensives before treatment was 2.94 (range 1–5, SD = 1.21) and 14 of them were on potassium supplementation. Three patients did not have AVS prior to their adrenalectomy despite being over 35 years of age. The average post-treatment potassium (off supplementation) and creatinine were 4.4 (SD = 0.4) and 105 (SD = 35) respectively. Seven of the 18 patients were cured (off hypertension or potassium supplements), while 5 improved with reduction in the anti-hypertensive agents and discontinuation of potassium supplements.

**Conclusion:** Most patients diagnosed with PA undergo the appropriate biochemical, imaging and AVS investigations. Some patients undergoing adrenalectomies may not be appropriately screened for PA which may represent an area for improvement given the under recognition of PA. These results will help to improve the consistency of diagnosis and treatment of PA according to evidence-based guidelines at our center.





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## EXPERIENCES OF SPECIALIST PHYSICIANS WITH E-CONSULTATIONS IN A SMALL ACADEMIC CENTRE

**Background:** E-consultation (e-consult) is an electronic service which allows primary care providers to interact with specialist physicians over a secure web-based platform. The purpose is to reduce specialist wait times and enhance access to expert care. Endocrinology is well suited to the use of e-consults, which have been implemented successfully in larger Canadian centres. The experiences of specialist physicians with e-consults are generally positive, although most studies are from large academic centres. The perspectives of specialist physicians regarding e-consults in small academic centres are unknown.

**Objectives:** To explore the experiences of specialists with e-consults in a small academic centre. **Methods:** An electronic questionnaire was emailed to specialists who participated in the local e-consult service between 2018 and 2022. The questionnaire assessed time, technology, consult quality and future improvements. Data was analyzed for descriptive results and themes (Qualtrics XM software).

**Results:** A total of 36 physicians completed the questionnaire (response rate 55%). Respondents were predominantly Internal Medicine specialists (53%), including Endocrinologists (8%). The majority work in departments of 5-10 people (92%) and have no protected time (89%) or dedicated financial compensation (56%) to complete e-consults. Most specialists complete e-consults outside of working hours (92%). Three quarters (75%)

of respondents need to do a chart review at least occasionally, and report this takes on average 5-15 minutes to complete. In addition, 44% reported the current electronic platform is a barrier to participation. Participants reported that financial remuneration (81%) and addition of electronic templates (56%) would improve long-term participation by specialists.

**Discussion:** While e-consults have the potential to increase timely access to care, specialists who complete these e-consults require sufficient time to participate in the service. Specialists in small academic centres have limited resources and e-consults may contribute to increased workload and potential for burnout. Indeed, the majority of participants required time outside of working hours to complete these e-consults, which is not feasible over the long term. Study limitations include a small sample size and the potential selection bias, as participants with negative experiences with e-consults may have been more likely to respond. Furthermore, the responses of participants who had stopped using the system may not reflect the most recent platform upgrades.

**Conclusion:** Specialists in this small academic centre identified a need for protected clinical time, adequate financial remuneration, electronic platform improvements, and use of templates to ensure ongoing provision of e-consults.





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## DIABETIC KETOACIDOSIS SUBCUTANEOUS INSULIN PROTOCOL: A QUALITY IMPROVEMENT PROJECT AT A CANADIAN TERTIARY CARE CENTER

**Background:** Diabetic ketoacidosis (DKA) is a life-threatening hyperglycemic emergency in patients with diabetes mellitus. The current standard of care in Canada is intravenous (IV) insulin infusion, which poses a significant cost to the healthcare system. There is growing interest in using subcutaneous (SC) insulin as an alternative. The objective of Phase 1 of this study was to implement and evaluate a SC insulin protocol for management of DKA.

**Methods:** A DKA SC insulin protocol was developed and piloted in the Emergency Department (ED) and Intensive Care Unit (ICU) at a tertiary care center. Phase 1 of this study involved retrospective chart review of patients with DKA treated with either SC or IV insulin to characterize safety and efficacy of the protocol. Patients admitted between March 2022–May 2023 were considered for inclusion if they were 18 or older, non-pregnant, and diagnosed with DKA. Patients who were clinically unstable, had a reduced level of consciousness, or had a weight greater than 160 kilograms were excluded. Treatment involved simultaneous administration of weight-based long-acting and short-acting subcutaneous insulin. Demographics and clinical parameters including time to anion gap (AG) closure, length of stay (LOS) and complications (hypokalemia, hypoglycemia, AG re-opening) were analysed with independent t test and Chi-squared test. Preliminary analyses were unadjusted.

**Results:** After excluding 27 patients, 41 patients were included for analysis; 10 were treated with SC insulin and 31 were treated with IV insulin. Preliminary analyses showed that the SC insulin group had significantly higher pH ( $7.30 \pm 0.05$  versus  $7.18 \pm 0.14$ ,  $p = 0.008$ ) and bicarbonate ( $20.2 \pm 3.39$  versus  $13.6 \pm 5.99$ ,  $p = 0.002$ ) at presentation compared to the IV insulin group. There was no significant difference in time to AG closure. Notably, patients treated with SC insulin had significantly lower rates of hypoglycemia compared to those treated with IV insulin (0% versus 39%,  $p = 0.019$ ) with no difference in rates of hypokalemia or AG re-opening. There was no significant difference in LOS in ED or hospital admission.

**Conclusion:** To our knowledge, this is the first implementation of a DKA SC insulin protocol at a Canadian tertiary care center. Interim data show that the use of SC insulin results in similar time to AG closure and LOS as compared to IV insulin without increased rates of hypoglycemia, hypokalemia, or AG re-opening. Next steps include formalizing implementation of the protocol and conducting additional analyses to further establish the safety and efficacy of SC insulin for treatment of DKA.



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## USE OF RADIOTHERAPY FOLLOWING SURGICAL RESECTION OF NON-FUNCTIONING PITUITARY ADENOMAS IN ONTARIO

**Background:** Non-functioning pituitary adenomas (NFAs) affect 3 to 10% of the population. Surgery is often first line therapy, with radiotherapy (RT) used to treat incomplete resections, tumor progression, or as first line for inoperable cases.

**Purpose:** We describe a population of patients with NFAs in Ontario, as well as the use and timing of RT in this cohort.

**Method:** Patients with a diagnosis of NFA were identified between January 1999 and December 2018 using administrative health data from the Institute for Clinical Evaluative Sciences. Specifically, radiotherapy data were accrued through Cancer Care Ontario's Activity Level Reporting (ALR), and the National Ambulatory Care Reporting System (NACRS).

**Results:** A total of 5083 patients had surgery for NFA ('index surgery'). Mean follow up was  $10.8 \pm 5.6$  years. Out of these patients, 322 (6.3%) received one or more courses of RT. The most commonly used RT modality was Intensity-Modulated Radiotherapy (IMRT;  $n = 81$ ; 37.5%). One hundred ninety-four out of 322 (60.2%) patients who had RT received it directly after index surgery, within a median of 2.4 years (range 0.6 to 5.1 years), and the rest

received RT after subsequent repeat surgeries. Only 40 out of 322 patients (0.8%) received RT within a year. Ten patients required repeat radiation after their first course; none in this cohort required a third course. Mean duration between repeat RT courses was  $816.3 \pm 1113.6$  days. In addition, 728 patients required repeat surgery after index resection, and 123 patients required two or more repeat surgeries. The need for repeat surgeries was correlated with the use of RT, as 43.2% of patients in the RT group also required repeat surgeries, versus only 12.2% of patients who only had index surgery ( $p$ -value =  $< 0.001$ ).

**Discussion:** Only 6.3% of patients required RT after index surgery in this cohort. Based on these findings, it seems that use of RT in Ontario is mainly reserved for cases of tumor progression, since most patients received RT more than 1 year after index surgery. Regardless of timing, very few patients required any further interventions following RT, suggesting its effectiveness at controlling tumor progression. Whether the timing or technique of RT corresponds to differences in long-term outcomes such as hypopituitarism, stroke risk, cognitive impairment, secondary tumors, or increased mortality requires further exploration.



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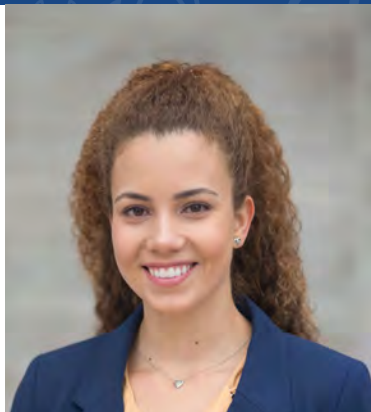
## COMPARISON OF THE EQUIVALENCE OF INTRAVENOUS AND ORAL SODIUM OVERLOADS FOR THE DIAGNOSIS OF PRIMARY ALDOSTERONISM: PRELIMINARY RESULTS

**Introduction:** Primary aldosteronism (PA) is the most common cause of secondary hypertension and is currently underdiagnosed. Consequently, it represents a significant cause of mortality and increased morbidity among hypertensive patients, which could potentially be prevented. Salt Infusion test (SIT) and oral salt loading (OSLT) are two recommended methods to confirm the diagnosis of PA, according to the "Endocrine Society Clinical Practice Guideline." However, several studies have reported divergent results regarding their performance, with insufficient evidence to definitively favor one approach. Also, up to now, no study compares the diagnostic performance of those two.

**Method:** Our retrospective study include hypertensive patients assessed by the Endocrinology Department of CIUSSS-de-l'Estrie-CHUS, who had a positive RRA (renin-to-aldosterone ratio) screening test (N 79) between 2015 and 2023. These patients subsequently underwent both SIT and OSLT, and we directly compared the rates of positivity. The standard positive threshold for the SIT was an aldosterone of 163 pmol/L at the end of the 4h of salt infusion. For the OSLT the standard threshold for a positive test was a 24h urinary aldosterone of 33 pmol with a 24h urinary sodium excretion of 170 mEq or more. An intermediate threshold of 27 pmol was also considered. We compared the rate of positivity for both threshold for the SIT compared to the OSLT.

**Results:** Up to now, among the 79 included patients, 49 had at least one positive diagnostic test using the standard threshold (28 with SIT and 35 with OSLT). When using the intermediate threshold for the OSLT, 45 were positive. Comparing positive cases between SIT and OSLT, we found that the average screening RRA was significantly higher in cases detected by the intravenous method than the oral one, 268.89 vs. 193.50 ( $p = 0.025$ ). Using standard threshold, the SIT and OSLT were concordant in 73.4% (95% CI: 62.8–81.9) of cases. When using intermediate threshold, they were concordant in 68.4% (95% CI: 57.5–77.6). The McNemar test suggests that the OSLT with an intermediate threshold is not equivalent to the SIT ( $p < 0.001$ ), while there is no significant difference with the standard threshold ( $p = 0.189$ ).

**Discussion:** These results suggest that OSLT using an intermediate might be more sensitive to confirm PA than SIT, likely due to an increased detection of milder cases. We also think it is explained by the integration of all the aberrant stimuli that regulate aldosterone in PA over a day instead of 4 hours during SIT.



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## HOW HAS VIRTUAL CARE DELIVERY CHANGED THE PATTERNS OF CARE IN DIABETES MANAGEMENT PRE AND DURING THE COVID-19 PANDEMIC?

**How has virtual care delivery changed the patterns of care in diabetes management pre and during the COVID-19 pandemic?**

**Background:** The COVID-19 pandemic accelerated the use of virtual care for management of many health care conditions including diabetes.

**Objective:** This study aimed to compare how patterns of care for diabetes have changed as a result of virtual care and the COVID-19 pandemic at a large academic ambulatory care facility.

**Methods:** Patients were included who had an initial diabetes visit in the endocrinology practice between September 15, 2019 and September 14, 2020. Chi-square test and Fisher's exact test were used to determine differences in care patterns between visits pre (September 15, 2019 – March 14, 2020) and during COVID-19 (March 15, 2020 – September 14, 2020).

**Results:** This study included 120 patients with an initial visit for diabetes pre COVID-19 (mean age 54.2; mean A1C 8.7%; 56% women) and 155 patients with an initial diabetes visit during COVID-19 (mean age 48.7; mean A1C 9.1%; 60% women). Majority of initial visits during the pandemic were completed by phone (83.2% vs. 7.1% in person vs. 9.7% video). There were more

no-shows pre COVID-19 (17.5% vs. 12.3%;  $p = 0.0351$ ); however there were more patients lost to follow-up (28.4% vs. 23.3%;  $p = 0.0155$ ) during COVID-19. In a 1 year period, patients had more follow-up visits during COVID-19 compared to pre COVID-19 (2.93 vs. 2.14;  $p = 0.00006$ ). During COVID-19, 54.2% of patients had no weight measured or reported at initial visits compared to 4.2% pre COVID-19 ( $p < 0.0001$ ). Similarly, the proportion of patients that had no blood pressure measured/reported at initial visits during COVID-19 was 86.5% compared to 2.5% pre COVID-19 ( $p < 0.0001$ ). In terms of blood-work ordered, there was no difference for most labs except urine microalbumin: creatinine ratio which was ordered less during COVID-19 (63.4% vs. 73.3%;  $p = 0.0122$ ). There were more changes made to insulin doses at follow-up visits pre COVID-19 (66.7%) compared to during COVID-19 (47.4%;  $p = 0.0245$ ). However, at initial visits pre COVID-19, there were less changes made to oral anti-hyperglycemic doses (23.4%) compared to during COVID-19 (50%;  $p = 0.00079$ ), and more changes made to anti-hypertensive doses (7.1%) compared to during COVID-19 (0%;  $p = 0.0152$ ). There was no difference in the amount of new insulin starts pre and during COVID-19 (7.8% vs 5.9%;  $p = 0.739$ ).

**Conclusion:** This study helps us understand how patterns of care for diabetes have changed as a result of virtual care and the COVID-19 pandemic.



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## CHARACTERIZING CLINICAL AND GERMLINE GENETIC VARIANTS OF PATIENTS WITH PHEOCHROMOCYTOMAS ASSOCIATED WITH NEUROFIBROMATOSIS TYPE 1

**Introduction:** Pheochromocytomas and paragangliomas (PPGLs) are the tumors with the highest heritability in adult patients, with identification of a germline mutation in more than 30% of cases. Up to 20 susceptibility genes for PPGLs are known including NF1. Neurofibromatosis type 1 (NF1) is an inherited disease affecting approximately 1 in 3000 people that predisposes to the development of tumors, such as pheochromocytomas (PHEO). Up to recently, the diagnosis of NF1 was mainly based on clinical manifestations and NF1 genetic characterization was not systematically performed.

**Objectives:** To investigate clinical characteristics and germline pathogenic variant mutations in the NF1 gene in patients with PHEO and NF1. **Methods:** In this retrospective study, we reviewed the charts of patients with a pathology-proven diagnosis of PHEOs that were investigated at Centre hospitalier de l'Université de Montréal (CHUM) between 2000 and May 2023. Genetic analysis included gene sequencing by Sanger method or multigene sequencing by NGS with a panel.

**Results:** In our cohort of 220 PHEOs, 15 patients (6.8%) had a diagnosis of NF1. Among these patients, 6 were male and 9 were females. Mean age at diagnosis of PHEO in NF1 patients was  $50 \pm 13$  years contrasting to the mean age of  $38.7 \pm 15.2$  years in patients carrying germline mutations in non-NF1 genes most likely reflecting lack of systematic biochemically screening of PHEO in NF1. Urinary metanephrines were elevated in 7/15 patients. 2/15 (13.3%) NF1 patients had bilateral PHEO and 1/15 (6.7%) metastatic disease. Mean tumour diameter was 3.5 cm (min-max 1.2–9.5 cm). Seven out of 15 NF1 patients underwent NF1 genetic analysis. NF1 germline pathogenic variants were found in all of them: 2 deletions, including one encompassing the entire gene, 4 premature stop codons leading to truncated proteins or loss of function, and 1 splicing defect.

**Conclusions:** We report a large cohort of patients with NF1 and PHEO. The older age at diagnosis of PHEO in NF1 is expected based on lack of systematic biochemical screening for PHEO in NF1 clinical guidelines. We report 7 germline NF1 mutations associated with PHEOs. Further studies are required to fully understand the impact of genetic pathogenic variants in this population and to unveil a possible genotype-phenotype correlation.



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## EVALUATION OF PERI-OPERATIVE PATIENT CARE AFTER IMPLEMENTATION OF A STANDARDIZED PITUITARY SURGERY ORDER SET: A QUALITY ASSURANCE STUDY

**Background:** Peri-operative pituitary surgery care varied greatly within our organization, leading to lack of standardized practices or optimization for endocrine outcomes, particularly regarding peri-operative steroid use. In 2018, a combined Endocrinology-Neurosurgery clinic was established for assessment and management of patients with pituitary tumors. Concurrently, a pituitary surgery admission order set was implemented to standardize and improve the detection and management of immediate post-operative endocrine complications.

### Objectives:

- To evaluate the use of the pituitary surgery order set on improving the appropriate use of steroids peri- and post-pituitary surgery.
- To evaluate screening and detection of endocrine complications post-pituitary surgery.

**Methods:** Retrospective chart review was conducted of all patients aged  $\geq 18$  years who underwent pituitary surgery at our centre between 2014–2022. Data collection included parameters such as baseline pituitary function; peri-operative steroid use; peri-operative lab testing; and post-operative complications [transient or permanent diabetes insipidus, SIADH, adrenal insufficiency (AI), and thyroid dysfunction]; as well as hormone replacement discharge prescriptions.

**Results:** 79 patients underwent pituitary surgery during 2014–2022, 46 of whom underwent surgery prior to the implementation of the standardized

order set. Patient demographics including age, gender, baseline pituitary function or surgical method did not significantly differ (all  $p > 0.05$ ) between groups. Following implementation, there was increased appropriate peri-operative steroid use, defined as peri-operative steroids only used in patients who had established AI ( $p = 0.022$ ) and improved frequency of appropriate discharge steroid prescriptions, defined as prescription only to patients who had established pre- or post-operative AI ( $p = 0.019$ ). Secondly, rates of post-operative complications did not significantly differ between groups (all  $p > 0.05$ ). Length of hospital stay, and readmission did not significantly differ between groups ( $p > 0.05$ ). After order set implementation, there was also increased frequency of complete pre-operative pituitary hormone testing (all  $p < 0.05$ ), increased frequency of standardized post-operative fluid balance monitoring ( $p < 0.001$ ), and blood work (all  $p < 0.05$ ), and improved frequency of complete post-operative pituitary hormone assessment (all  $p < 0.05$ ).

**Conclusions:** Prior to implementation of the pituitary surgery order set, there were high rates of incomplete peri-operative endocrine investigations and inappropriate short- and long-term post-operative steroid use in patients with intact hypothalamic-pituitary-adrenal axis. Following implementation, we observed improved resource stewardship in terms of endocrine hormone testing and increased standardization of peri- and post-operative steroid use. Results of this work may support implementation of standardized order sets for peri-operative pituitary surgery care at other centers.





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## PATTERNS AND RESULTS OF DYSGLYCEMIA SCREENING FOLLOWING A HYPERTENSIVE DISORDER OF PREGNANCY

**Background:** The relationship between dysglycemia and the hypertensive disorders of pregnancy (HDP) (i.e., gestational hypertension, preeclampsia, and eclampsia) is multifaceted. Women with pre-pregnancy dysglycemia or gestational diabetes have an increased risk of HDP. Further, those with HDP have  $\geq 2$  times higher risk of developing dysglycemias (type 2 diabetes, impaired fasting glucose and/or impaired glucose tolerance) within 10 years after delivery. At present, no Canadian guideline provides clear recommendations on screening for dysglycemia in this high-risk population after HDP. The objective of this study was to describe patterns and results of dysglycemia screening for women after HDP compared to normotensive pregnancies over a 10-year period as a foundational step towards a provincial postpartum cardiometabolic disease prevention pathway.

**Methods:** The Discharge Abstract Database (DAD) was used to identify singleton liveborn deliveries between 2010–2020 ( $n = 491\,850$ ). The first delivery for each participant was included and those with pre-pregnancy diabetes, cardiovascular or kidney disease were excluded resulting in 314 022 participants (291 558 without HDP and 22 464 with any HDP using ICD-10CA codes). The DAD was linked to a provincial lab database. Descriptive statistics were used to summarize testing and chi-square tests were used for comparisons between groups.  $P$ -value  $< 0.05$  was considered significant.

**Results Screening Patterns:** Each year from delivery to 8 years post-partum, the proportion of participants screened for dysglycemia was significantly higher in people with HDP, whereas after 8 years the proportion screened was higher in those without HDP ( $p < 0.05$ ). A1c was the most used screening test in both groups followed by fasting glucose, and lastly 2-hour OGTT.

**Dysglycemia:** Mean A1c (mmol/L) was higher in HDP versus non-HDP and trended upwards annually for both groups over a mean 5.66 years (standard deviation [SD] 2.88 years) of follow-up to 5.7% (SD 1.1) in HDP and 5.3% (SD 0.75) in non-HDP at 10 years ( $p < 0.05$ ). Based upon A1c levels, 2.7% ( $n = 614$ ) of those with HDP compared with 1.2% ( $n = 3574$ ) without HDP ( $p < 0.001$ ) were classified with diabetes ( $A1c > 6.5\%$ ); and 4.5% ( $n = 1012$ ) with HDP versus 2.9% ( $n = 8507$ ) ( $p < 0.001$ ) without HDP were classified with pre-diabetes ( $A1c$  6.0–6.4%).

**Conclusions:** Current clinical practice in our province demonstrates that compared with normotensive pregnancies, women with HDP have more laboratory screening tests for dysglycemia and a higher incidence of dysglycemia up to 10 years post-partum. A1c was the most used screening test. Next steps include determining optimal glycemic screening test, timing, and cut-offs to inform screening strategies for women after HDP.



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