2018 AACE ANNUAL SCIENTIFIC & CLINICAL CONGRESS ABSTRACTS

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ADRENAL DISORDERS

Abstract #100

ATYPICAL PRESENTATION OF CONGENITAL ADRENAL HYPERPLASIA

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Objective: Congenital adrenal hyperplasia (CAH) is characterized by dysregulation of adrenal steroid biosynthesis. The most frequent variant is caused by a 21-hydroxylase deficiency. A rarer form is caused by 3-beta-hydroxysteroid dehydrogenase (3ß-HSD) deficiency that is diagnosed in infancy with symptoms consistent with deficiencies of adrenal steroids. Patients with non-classical 3ß-HSD deficiency usually present for PCOS work-up as our patient who had irregular menses and hirsutism. This case report illustrates a rare form of non-classical CAH (3ß-HSD) deficiency.

Case Presentation: The patient is a 16-year-old female who presented with a two-year history of irregular menstrual cycles, acne and facial hair growth. She had menarche at age 10 with consistent menstrual cycles for the next four years. Past medical history is significant for a cystic pituitary micro-adenoma with no evidence of pituitary hormone overproduction. Physical examination revealed BMI of 23.9, extra hair on back, arms and face, and negative for acanthosis nigricans or areas of skin discoloration. The patient was negative for polycystic ovaries via pelvic ultrasonography. She had elevated 8 am 17OH pregnenolone. Cosyntropin stimulation test demonstrated elevated baseline and stimulated levels of pregnenolone (759 ng/dL), DHEAS (605 ng/dL) and stimulated 17-OH pregnenolone (1334 ng/dL), which confirmed the diagnosis of CAH 3ß-HSD. The patient did not experience salt-wasting symptoms, hypotension or skin changes. Her symptoms improved with eight months of low-dose steroid therapy.

Conclusion: CAH 3ß-HSD is a rare disease, causing impairment in all steroid hormones. Patients with classical salt wasting variant typically present in infancy with hypotension, hypoglycemia and salt-wasting symptoms. Our patient presented late with mild symptoms marked by hirsutism and menstrual irregularities, a presentation typically observed in PCOS. ACTH stimulation test demonstrated an elevation in necessary substrates for diagnosis. However, in order to be considered a diagnosis of classic 3ß-HSD, the patient should have elevated 17-OH pregnenolone levels greater than 10 standard deviations above normal the mean (i.e., > 4500 ng/dL). As this patient did not meet the laboratory criteria and clinically presented with late-onset and mild symptoms, she was diagnosed with non-classical 3ß-HSD. Medical practitioners should have a high level of suspicion for 3ß-HS CAH in PCOS patients. The prognosis is excellent with low-dose corticosteroids.

Abstract #101

EFFECT OF NORPLANT ON THE ADRENAL RESERVE CAPACITY USING A DYNAMIC STRESS TEST

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Alexandria University

Objective: To evaluate the response of the adrenals to the effect of stress among Norplant users

Methods: Fifty Norplant users for at least 6 months and fifty non-Norplant users matched for age and body mass index as a control. Each woman was subjected to the dynamic stress test of insulin hypoglycemia. Serum glucose and cortisol were measured before and 30, 45, 60, and 90 minutes after intravenous injection of crystalline aqueous insulin (0.15 u/kg)

Results: Cortisol measurements were significantly lower among Norplant users than the control at all times (before and after 30,45,60 and 90 minutes after intravenous insulin), with a trend towards a delayed response to reach a peak. In spite of the delayed response among Norplant users, no significant differences were found in the time intervals needed for cortisol to rise by 275nmol/L or to reach a peak

Discussion: The mechanism of suppressive effect of Norplant on suprarenal function and reserve capacity appears to be through a local mechanism affecting the pathway of suprarenal steroidogenesis. The observed minor adrenal inhibition was not enough to divert the results to abnormal ranges and there still remains the question about the response to more powerful or more prolonged stresses such as a major surgery

Conclusion: The adrenal response to stress by insulin hypoglycemia was significantly reduced at all times during the test among Norplant users. Future evaluation of a larger number of cases would confirm the present data. However, all cases were able to achieve the cortisol levels accepted as
the lower limit of a normal response. Further assessment of adrenal function may be required in Norplant users in situation of acute or prolonged stress.

**Abstract #102**

**A GIANT ADRENAL INCIDENTALOMA IN A 78 YEAR OLD: INCIDENCE, RADIOLOGIC AND MANAGEMENT ISSUES OF ADRENAL MYELOLIPOMA**

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**Objective:** Adrenal myelolipoma is a rare benign neoplasm composed of mature adipose and hematopoietic tissue. Most are small, unilateral and asymptomatic, discovered incidentally at autopsy or on imaging studies performed for other reasons. Accounting for 3–5% of all primary tumors of the adrenals, the true incidence of these tumors is not known, although it is thought to be 0.08%–0.4%. No similar diagnosis has been reported in our local setting. We report a rare case of a giant adrenal incidentaloma.

**Case Presentation:** This is a case of a 78-year-old male, who had a general check-up, in which Ultrasound and CT scan of the whole abdomen showed an incidental finding of right adrenal mass. He was completely asymptomatic except for an on and off vague right flank pain. Biochemical evaluation was consistent with a non-functioning adrenal tumor. MRI of the adrenal glands with contrast revealed a multilobulated mass lesion in the right suprarenal region measuring about 4.3 x 3.6 x 7.2 cm consistent with adrenal myelolipoma. Due to the relative large size of the tumor and the risk of retroperitoneal bleeding, an elective Laparoscopic Adrenalectomy was done. Postoperative course was uneventful.

**Discussion:** Adrenal Myelolipoma is a rare benign neoplasm composed of mature adipose tissue and on occasions a variable amount of haematopoietic elements. It is usually discovered incidentally on autopsy, surgery, or as an incidentalomas on imaging for other reasons with a reported incidence of from 0.08% to 0.4 %. They are mostly unilateral and do not undergo malignant transformation. Most lesions are small and nonfunctioning and therefore patients are always asymptomatic.

Our case was diagnosed based on MRI finding consistent with Myelolipoma. Histological examination is confirmatory that showed adipocytes with interspersed haematopoietic elements, consisting of myeloid and erythroid precursors, as well as, megakaryocytes.

The most well-recognised complication of adrenal myelolipoma is spontaneous retroperitoneal hemorrhage. With the advent of minimal invasive surgery, laparoscopic adrenalectomy is advised. The long-term prognosis of this case is very good and no long-term follow-up is needed.

**Conclusion:** We report a rare case of Adrenal Myelolipoma seen as adrenal incidentaloma on imaging. Due to its large size and the risk of retroperitoneal bleed, adrenalectomy was recommended.

Abstract #103

**PARANEOPLASTIC ECTOPIC ACTH SYNDROME: A CASE OF CUSHING’S SYNDROME ASSOCIATED WITH ADENOCARCINOMA OF THE PROSTATE TRANSITIONING TO A NEUROENDOCRINE TUMOR**

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**Objective:** We present a rare case of Cushing’s syndrome due to ectopic ACTH secretion in a patient initially diagnosed with prostate adenocarcinoma, but with subsequent neuroendocrine differentiation.

**Case Presentation:** A 63 year old male was hospitalized for hyperglycemia and an evaluation of his diabetes. The patient was diagnosed with prostate adenocarcinoma ten years prior, and subsequently progressed to end stage cancer with metastases. He received 3 months of prednisone and abiraterone acetate which was discontinued 3 weeks prior to his hospitalization due to hypokalemia and anasarca. He had presenting symptoms of polyuria, polydipsia, dry mouth, and decreased appetite. Physical exam showed a weight of 68 kg (BMI- 24.4 kg/m2) and blood pressure of 143/82 mmhg with bilateral lower-extremity swelling. No other findings of Cushing’s syndrome were observed. His initial laboratory findings showed a blood glucose level of 508 mg/dl (normal, 70 to 100 mg/dL). Upon endocrine consultation, further work up was ordered to clarify why the patient’s hyperglycemia had exacerbated weeks after discontinuing corticosteroids. Results showed adrenocorticotropic hormone (ACTH) of 1250 pg/mL (normal, 10-46 pg/ml); Am cortisol 92 mcg/dL (normal, 7-28 mcg/dL); 24 hour urine free cortisol levels of 3002 mcg (normal, 3.5-45 mcg/24h); calcitonin 1715 pg/ml (normal, <= 8.4 pg/ml); chromogranin A 1802 ng/ml (normal, <93). His am serum cortisol levels were 72.2 mcg/dl (normal, <1.8 mcg/dL) following 1 mg dexamethasone, therefore the diagnosis of Cushing syndrome was established. Magnetic resonance imaging of the pituitary showed no adenoma. Computed tomography (CT) of the chest and abdomen showed evidence of metastases and enlarged adrenal glands bilaterally. The patient had normal adrenals on CT imaging three months prior. Paraneoplastic
ectopic ACTH secretion was suspected, and a biopsy of the inguinal lymph node was performed. The pathology report was consistent with high-grade neuroendocrine cancer with immunohistochemistry staining positive for synaptophysin, chromogranin A CD56; negative staining for CDX2, PSA, CK20 and CA-19. The patient was started on ketoconazole. After discharge, the patient was unable to attend his follow up visit due to poor health. He was in comfort care and expired after a few weeks.

**Conclusion:** It is reported that neuroendocrine cells lack androgen receptors and proliferate after androgen blockade therapy. This may explain the neuroendocrine transition seen in our patient following abiraterone acetate treatment. Further research is needed in this area.

**Abstract #104**

SEVERE HYPERCORTISOLISM AND VIRILIZATION IN A 63-YEAR-OLD WOMAN WITH AN ABDOMINAL MASS

*Jose Paz-Ibarra, Cintya Andia Colque, Aurea Urquizo*

Hospital Rebagliati / Universidad Nacional Mayor de San Marcos

**Objective:** To present a rare case of functioning adrenocortical carcinoma.

**Methods:** Clinical and paraclinical data of the patient are presented

**Case Presentation:** A 63-year-old woman, with no significant pathological history, started 7 months ago with abdominal pain in the right flank, throbbing, associated with abdominal distension, later noted weight gain, and proximal weakness, 3 months ago note of lip hair increase superior and hair loss. On physical examination: Cushingoid phenotype, acne and hirsutism, androgynous alopecia, BP: 150/95mmHg and palpable mass on the right flank of hard and painful consistency. Analytical: Cr: 0.57mg / dl, Glucose: 90mg / dl, Sodium: 143mmol/L, Potassium: 3.0mmol/L, Cortisol 8 a.m: 31ug / dl, ACTH: <5pg / ml, Cortisol 4pm: 25 ug / dl, cortisol 12pm: 29.1ug / dl, UFC: 1117ug / 24h; Androstenedione:> 10 ng / ml (0.3-3), DHEAS: 496ug / ml (35-430), Aldosterone: not available. Adrenal TEM: Heterogeneous multilobed right adrenal mass of 12x8 cm, absolute wash: 18%. Body CT: no evidence of metastatic lesions. The patient was subjected to right adrenalectomy, removing a 10cm tumor, and liver segmentectomy was performed due to a 3cm liver tumor (segment VI). Pathology: Adrenocortical carcinoma, partially encapsulated 15x13mm (histological grade Fuhrman 3), hepatic metastasis of adrenocortical carcinoma. Currently without evidence of hypercortisolism or distant metastasis in the PET-CT study. Follow-up by endocrinology and oncology.

**Discussion:** Adrenocortical carcinoma has an incidence of 0.7-2 cases / million inhabitants per year, frequently producing adrenocortical hormones. The present case shows a patient with Cushing’s syndrome and virilization due to a malignant tumor as confirmed. The preoperative functional, detailed imaging study and an expert surgeon are key prerequisites for a complete resection that offers the best healing possibilities.

**Conclusion:** The early recognition of the symptoms and signs of adrenal hyperfunction and the suspicion of adrenal carcinoma is important for the early diagnosis and timely treatment of this entity with such a poor prognosis.

**Abstract #105**

BILATERAL ADRENAL INCIDENTALOMAS IN A 67 YEAR OLD MALE

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**Objective:** To report an interesting case of bilateral adrenal tumor.

**Methods:** The clinical and paraclinical data of the patient are presented

**Case Presentation:** A 67-year-old male from Lima, with a history of colonic diverticulosis, AIM in 03 opportunities, a pacemaker carrier for ventricular tachycardia, denies TBC. Brother with kidney disease. He came to Emergency due to severe abdominal pain, with an incidental finding in the abdominal CT of a 15 mm tumor in the right adrenal and 42x33mm in the left adrenal. At physical examination: BP: 130/80mmHg, no Cushingoid or Addisonian phenotype. Analytical: Glucose: 100mg%, Cr: 1.1mg%, Urea: 39.9mg%, Na+: 142mmol/L, K+: 4.38mmol/L, Cl: 106mmol/L; Leucocytes 6880, Serial BK and PPD (-); B2 microglobulin 3.55mg/L (VN: 0.61-2.16 mg / L), ACTH: 39.7 pg/ml, Cortisol 8AM: 18.6ug/dL, , Aldosterone: 3.2 ng/dL, DHEA-S: 55.4ug/dL, Metanephrines: 0.641mg/Urine 24h; Cr Clearance: 55 mL/min, Proteinuria: 68 mg/24h, UFC: 40ug/24h. Echocardiogram: Ischemic heart disease with moderate systolic dysfunction (Ejection fraction 37%), Adrenal CT: left adrenal focal lesion of 40x35.7mm, hypodense, with some punctate internal calcifications, whose internal density in the noncalcic portions varies between 23 HU, and after administration of contrast in venous phase, there are heterogeneous solid marginal portions with a density of 146 HU, with washout at 13 minutes, with a density of 87 HU. In the non-central collecting portion with fluid or necrotic content, the percentage of absolute
ABSTRACTS – Adrenal Disorders

Lavage corresponds to 46%. The patient underwent left adrenalectomy. The pathological study report: Cortical area with infiltration marked by proteinaceous material, congo red staining seen in polarized light (+): Adrenal amyloidosis. Studies to determine type of amyloid protein not available; currently under follow-up by nephrology and hematology.

**Discussion:** The most common type of familial amyloidosis is transthyretin amyloidosis, but we can recognize other types with proteins that include the fibrinogen A chain (AFib), lysozyme (ALys), apolipoproteins AI (AApo AI) and AII (AApo AII) and gelsolin (AGel). Recently, a new type of highly prevalent amyloidosis has been described in the Hispanic population derived from the chemotactic factor of leukocytes 2 (LECT2). The majority of reported cases have been described in patients of Mexican descent, for which reason a genetic role can be argued. The clinical manifestations related to ALECT2 have been largely limited to the kidney; however, there may be deposits in liver, splenic, colonic and adrenal tissue.

**Conclusion:** Adrenal amilolidosis should be considered within the differential diagnosis of adrenal tumors.

**Abstract #106**

MARKED IMPROVEMENT IN METABOLIC PARAMETERS IN A PATIENT WITH ACTH-INDEPENDENT HYpercortisolism WHILE ON MIFEpristONE

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**Objective:** Hypercortisolism is associated with metabolic disorders including diabetes, hypertension, and obesity. If left untreated, hypercortisolism can lead to significant morbidity and mortality. The following is a challenging case of a patient with a cortisol-secreting left adrenal adenoma treated with the glucocorticoid receptor antagonist, mifepristone (MIFE, Korlym®, Corcept Therapeutics) who then experienced improvement in glycemic and metabolic parameters. To the best of our knowledge, this is the first case report of a patient with only 1 adrenal gland and 1 kidney to be treated with MIFE.

**Case Presentation:** A 75 y/o woman presented after a recent move to the area with a history of poorly controlled diabetes for 22 years and treatment-resistant hypertension. The patient was initially diagnosed with a benign adrenal adenoma but experienced worsening metabolic derangements over 10 years. On a repeat CT scan 9 years after her initial scan, the adenoma was enlarged (2.9 x 2.8 cm HU=8). The patient previously had a right nephrectomy and adrenalectomy secondary to a renal carcinoma. On physical exam, her weight was 215 pounds and BMI was 32.8 kg/m2. Average fasting blood sugar levels were 198 mg/dL and HbA1c was 7.7%. She was on 5 antihypertensive medications and required a total daily dose 115 units of insulin. Cortisol response to DST was 4.64 mcg/dL before initiation of MIFE. ACTH levels were 12 pg/mL. The findings are consistent with the diagnosis of hypercortisolism.

A second adrenalectomy was considered but rejected because she would require lifelong corticosteroid and mineralocorticoid replacement, so medical therapy with mifepristone was initiated at 300mg and titrated to 600mg two weeks later. Clinical response with improvement in blood sugars and blood pressure was observed within the first month. The patient experienced cortisol withdrawal syndrome, including nausea and fatigue. Spironolactone was started 50mg PO BID. After MIFE treatment for 7 months, the patient lost 32 pounds. Her total daily dose of insulin decreased to 28 units with an HbA1c of 5.8%. She was also able to eliminate 2 antihypertensive medications.

**Conclusion:** Using the medical option of MIFE allowed for significant clinical improvements in glycemic parameters as evidenced by reduction of total daily dose of insulin by 75% and significant weight loss and reduction in antihypertensive medications. Earlier diagnosis of hypercortisolism might have prevented uncontrolled diabetes and other complications.

**Abstract #107**

PRIMARY HYPERALDOSTERONISM DUE TO UNILATERAL ADRENAL HYPERPLASIA WITH SURGICAL RESOLUTION

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**Objective:** To present a case of primary hyperaldosteronism (PHA) due to unilateral adrenal hyperplasia (UAH).

**Methods:** The patient’s clinical and paraclinical findings are presented

**Case Presentation:** Male, 50 yo, of chinese ascendancy. HTA from 30 years of age on treatment with irbesartan, nifedipine and hydrochlorothiazide. Since 2002, he has had hypokalemia that compensates with food. In 2008, he is suffering from AMI that requires placement of a stent in AD. In April 2016 he went to the ER after alteration of dietary habits, he presented muscular weakness in the lower limbs, BP: 180/100mmHg, alert, quadriplegia with predominance of symmetrical lower limbs, with hypotonia and hyporeflexia; associated with K+ levels of 1.8 mmol/L.
Analytical: Plasm Aldo: 790.46 pg/ml (VN 10-160), PRA: 0.2 ng/ml/hr (VN 1-5.2), RAR: 395.2. Adrenal CT: Left adrenal gland with mild thickening. Normal-appearing right adrenal gland. Adrenal vein catheterization resulted: Ratio: RAV/IVC: 8.3; LAV/IVC: 1; RAV: Aldo: 533.9 Cortisol: 35.9, Index A/C: 14.8; LAV: Aldo: 230.1 Cortisol: 4.28 Index A/C: 53; IVC: Aldo: 148.2 Cortisol: 4.28 index A/C: 34. He underwent laparoscopic left adrenalectomy, whose findings were: 7-cm specimen, and microscopy: adrenal characterized by the presence of multiple nodular areas consisting of predominantly acidophilic partially encapsulated cortical cells. The major lesion measures 9x6mm, with cortical areas of nodular appearance, non-encapsulated smaller size of 5 and 3 mm respectively. The preserved medullary area and the vascular structures in normal limits. Histological appearance consistent with nodular cortical hyperplasia. The definitive diagnosis is histopathological.

Discussion: The UAH is a rare presentation of PAH, with a reported prevalence, according to the different series, of between 0.1 and 2%. Its clinical and biochemical presentation is similar to that of the APA, and is a condition correctable by surgery. Its diagnosis should be suspected in patients with highly suggestive clinical and biochemical features, when it is not possible to clearly define an image suggestive of adrenal adenoma in the CT scan. In these cases, the sampling of the venous sinuses only defines the laterality of aldosterone hypersecretion. The definitive diagnosis is histopathological.

Conclusion: The UAH is a different entity and it is not an asymmetric variant of the bilateral adrenal hyperplasia. In the study of patients with PHA and imaging tests with absence of adenoma is a diagnosis that must be considered before cataloguing patients with BAH and start a medical treatment, because UAH would have a surgical resolution.

Abstract #108

LARGE TESTICULAR ADRENAL REST TUMORS IN A PATIENT WITH CONGENITAL ADRENAL HYPERPLASIA

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Case Presentation: Introduction: Testicular adrenal rest tumors (TART) are rare benign tumors that develop in young males with endocrine disorders. It is thought that excess ACTH secretion leads to growth of ectopic remnants of adrenal tissue in the testes. In most instances, patients present with symptoms of pain and palpable bilateral testicular masses or infertility. This entity classically presents on a background of congenital adrenal hyperplasia (CAH).

Clinical Case: A 23-year old man known to have CAH, the salt-wasting variety presented with increasing size of testicles. The testicular masses were painless but progressively increasing in size over past 10 years. He had been referred to an Urologist who arranged fine needle aspiration of testis. Biopsy revealed histopathological findings consistent with testicular tumor of the adrenogenital syndrome. The CAH was diagnosed at age 6 months when he presented with vomiting/dehydration. He was started on salt tablets and later fludrocortisone and hydrocortisone. At age 9-10, he had precocious puberty and was placed on leuprolide injections for a time. He also has history of primary hypothyroidism, ADHD and learning difficulty. His current medications are Fludrocortisone 0.1 mg daily, Hydrocortisone 25 mg in divided doses, and Levothyroxyne 88 mcg daily. This patient was known to be poorly compliant with medical therapy over the years. This was evidenced by elevated 17-hydroxyprogesterone levels at pediatric visits.

Discussion: This patient with CAH, salt wasting variety and poor compliance with medications presented with bilateral testicular masses. Testicular biopsy was reported as testicular adrenal rest tumor. Rest tumors are ACTH-dependent. Poor medication compliance would have resulted in high ACTH levels in this patient and stimulation of adrenal rests on his testes. Most patients present with pain although our patient had no testicular pain. Testicular adrenal rests, while benign in nature, may gradually expand and destroy normal testicular tissue causing infertility and low testosterone levels. Ensuring adequate medical management (glucocorticoid and mineralocorticoid) is the first-line therapy. Increasing glucocorticoid therapy may not lead to resolution of pain or mass. Surgical tumor enucleation may help with fertility. But orchiectomy may be needed in highly symptomatic masses.

Conclusion: This case highlights the importance of medication compliance, regular follow-up, and periodic testicular examination and ultrasonography in male patients with CAH.
Abstract #109

PHEOCHROMOCYTOMA, 2 CLINICAL CASES PRESENTATIONS

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Objective: To document the first two pheochromocytomas diagnosed in English Guyana where previously there was no specialty of endocrinology

Methods: Pheochromocytoma is a rare tumor of chromaffin cells that produces catecholamines.

Case Presentation: Clinical cases (P#1, P#2): both female; age 44 and 65 years old with history of long-standing hypertension refractory to the use of multiple drugs. P#1: had several admissions because hypertensive crisis. P#2 complained of slight abdominal pain. The radiological (Fig. 1) and metabolic studies confirmed the diagnosis of adrenal localization pheochromocytoma in both cases. Fractionated catecholamines (FC): Dopamine 24 h Urine P#1: 2570, P#2: 794 (0-510ug). Norepinephrine Urine 24h: P#1: 2853 ,P#2: 156 (0-135 ug/L).P#1 received open abdominal surgery with no complications, Biopsy confirmed the diagnosis. After surgery, patient remained in apparent control, but recently had episodes of recurrent hypertension and chest pain. Computed tomography (CT) Abdomen pelvis contrasted showing lymphadenopathy and destructive masses in ribs and spine. P#2: no surgical intervention was possible.

Discussion: The presentation of high blood pressure resistant to treatment should orient towards a treatable secondary cause like pheochromocytoma. It develops between the fourth and sixth decades with predominance by the female sex (P#1, P#2). The elevation of FM in plasma or in 24-h urine are key for diagnosis. The symptoms corresponded to the degree of elevation FC (more in P#1). The clinical picture is usually very florid (paroxysmal) or asymptomatic in 20 % (headache, diaphoresis and palpitations). Some of them discovered upon interrogation only in P#1. Worldwide robotic and laparoscopic adrenalectomy are performed (not available in our environment). Another therapeutic alternative are chemotherapy and radiotherapy. The first surgical intervention was successfully achieved with P#1 (open surgery) and the biopsy did not show any apparent signs of malignancy. The P#2 was scheduled twice for exploratory laparotomy, but the tumor was very large adherent to the liver and the inferior vena cava and could not be extracted. In P #1, post-operative follow-up could not be performed in the most satisfactory way due to several factors. And, after the diagnosis of metastasis, reassessment is carried out to decide the best and most viable therapeutic decision, taking into account ours limitations of resources. The P#2 is maintained with symptomatic follow-up.

Conclusion: When faced with a young patient or not with arterial hypertension, it is imperative to rule out secondary causes such as pheochromocytoma. This type of patient is very difficult to treat effectively if resources are limited.

Abstract #110

COMPOSITE PHEOCHROMOCYTOMA-GANGLIONEUROMA IN A NEUROFIBROMATOSIS TYPE 1 PATIENT

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Objective: To describe an interesting case of composite adrenal tumor in a patient with NF1.

Methods: Biochemical lab data, imaging and pathology were analyzed.

Case Presentation: 74 year-old male with a history of NF1, hypertension, and spinal stenosis was referred to endocrinology for evaluation and management of incidentally found right adrenal mass. Patient was diagnosed with NF1 in his 20’s based on clinical phenotype with development of multiple skin neurofibromas, which progressively covered his entire body. His hypertension was well controlled on Losartan 50 mg daily. He denied headaches, palpitations but reported fatigue and weight loss of 20 lbs. in the last year.

Computed tomography (CT) showed a 2.1 x 1.8 cm right adrenal mass, that was heterogeneous and had high HU. Further laboratory evaluation was consistent with PCC: significantly elevated urine normetanephrines of 2036 ug/24 hr (normal <500), plasma fractionated metanephrines 1.01nmol/L (normal < 0.49) and normetanephrine 2.12 nmol/L (normal < 0.89). Other pertinent labs showed normal thyroid function, normal calcium and PTH, elevated hemoglobin A1c of 6.0%. Hemoglobin was 18 with negative JAK2 mutation.

On physical exam blood pressure was 118/82 mmHg and heart rate was 102 beats/min. He was obese (BMI 33.7 kg/m2) and had multiple soft, fleshy, sessile and pedunculated tumors diffuse over all skin (neurofibromas) as well as multiple café-au-lait lesions and axillary and inguinal freckling. He had decreased proximal muscle strength in both lower extremity and decreased ROM in spine and hips; His left ankle showed a 6 cm soft well circumscribed
mass (peripheral plexiform neurofibroma). Patient was started on phenoxybenzamine with good control of his BP preoperatively. Later on, metoprolol 12.5 mg twice daily was added. Patient underwent uneventful robot-assisted laparoscopic adrenalectomy. Pathology showed a 2.1 cm tumor composed predominantly of PCC and with a small ganglioneuroma (GN) component characterized by schwannian stroma and mature ganglion cells. The PCC component showed profound nuclear pleomorphism but with no aggressive features to suggest malignancy (no capsular or vascular invasion, necrosis, or tumor spindling).

**Discussion:** Composite PCC-GN are seen in approximately 6-8% in cohorts of PCC patients. Although not commonly seen, these composite PCC-GN tumors have been described in patients with known syndromes such as MEN2 as well as NF1 patients.

**Conclusion:** We present a case of PCC co-existing with GN in a patient with NF1 syndrome. While PCC is present in a minority of patients with NF1 (0.1-5.7%), composite adrenal tumors (with other components i.e neuroblastic type of tumor) are even more rare.

**Abstract #112**

**CAREFUL WITH THAT NEEDLE! TAKOTSUBO-LIKE CARDIOMYOPATHY PRESENTING WITH APPARENT STEMI FOLLOWING BIOPSY OF A PHEOCHROMOCYTOMA**

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**Case Presentation:** Pheochromocytomas are rare catecholamine-producing neuroendocrine tumors that have occasionally been reported in association with a Takotsubo-like catecholamine cardiomyopathy (TLC). TLC is characterized by transient hypokinesis of the LV apex. The reversible impairment of LV function is thought to represent myocardial stunning due to high levels of...
circulating catecholamines.
A 72-year-old female with stage IV squamous cell lung cancer who had been treated with chemotherapy and radiation underwent a restaging PET/CT. She had a past medical history significant for COPD, diabetes mellitus type 2, hypertension, coronary artery disease, and tobacco use. The restaging PET/CT showed improvement in malignant adenopathy, however, a hypermetabolic left adrenal mass measuring 4.8 cm, unchanged from prior imaging. To further characterize the adrenal mass, a CT-guided biopsy was performed at an outside facility. The day following the adrenal biopsy, our patient developed acute onset of substernal chest pressure and shortness of breath. ECG at the outside facility was concerning for ST-elevation MI with ST elevation in leads II, III, aVF, V3-V6 and she was transferred to our facility for emergent coronary angiogram. An echocardiogram following cardiac catheterization demonstrated a left ventricular ejection fraction of 42% and severe hypokinesis of the apex, consistent with Takotsubo-like cardiomyopathy.

During her hospitalization, her adrenal biopsy returned as a pheochromocytoma. Metanephrines were not obtained prior to biopsy at the outside facility. Serum metanephrines were obtained and were significant for elevated total metanephrines (8.62 nM/L), norepinephrine (5.32 nM/L), and chromogranin A (3,368 ng/mL). She was placed on doxazosin and her home carvedilol dose was later increased. Ejection fraction recovered to normal on repeat echocardiogram 3 months later. Given her comorbidities, surgery was deferred in favor of medical management for the pheochromocytoma.

**Conclusion:** Our case is a unique presentation of Takotsubo-like cardiomyopathy presenting just hours following biopsy of a pheochromocytoma. It is important to remember that adrenal biopsy is rarely indicated, except in cases of possible adrenal metastasis from an unknown primary. Pheochromocytoma should always be excluded prior to invasive procedures involving adrenal masses as manipulation or biopsy of a pheochromocytoma may have dire consequences. This case illustrates the necessity of maintaining a broad differential even when the diagnosis seems almost certain and to always perform biochemical testing prior to biopsy of adrenal masses to exclude catecholamine-secreting neoplasm.

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**Abstract #113**

**ACUTE PSYCHOSIS AS AN INITIAL PRESENTATION OF ADRENOCORTICAL CARCINOMA**

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Hamad Medical Corporation

**Objective:** Adrenocortical carcinoma (ACC) is a rare malignancy and its functional subtype has more predilection for females. We report a case of metastatic ACC who presented with acute psychosis and severe acne.

**Case Presentation:** A 17-year-old female presented to emergency room with features of acute psychosis with abnormal behavior, agitation, insomnia, and inability to concentrate for a week. In the prior 2 months, she visited a dermatologist for severe acne and hirsutism; however, no reason was identified and she was given symptomatic treatment to which she did not respond. On examination, she had cushingoid facies, severe generalized acne, hypertension, bilateral lower limbs edema, abdominal striae and Ferriman gallwey score of 32/36. Workup revealed dehydroepiandrosterone sulfate 56.4 umol/L (1.7-13.4), androstenedione 9.21 ng/ml (0.25-2.78), testosterone 3.6 nmol/L (0.69-2.78), morning cortisol 827 nmol/L (138-580) with no suppression (511 nmol/L) to 1mg dexamethasone, ACTH < 5 pg/ml (5-60), serum cortisol day curve [12 am: 519, 6 am: 560, 12 pm: 619, and 6 pm: 606 (normal evening cortisol 55-386)], normal aldosterone /renin ratio, and normal 24 h urinary (cortisol, metanephrine and normetanephrine). CT chest and abdomen showed 12 cm x 10.6 cm hypervascular right adrenal mass with metastases to the liver (largest 9.8 cm) and lungs with the possibility of inferior vena cava infiltration. Therefore, she was diagnosed with metastatic ACC with excess cortisol and androgens secretion. She received mitotane and metyrapone with no surgery because of her extensive disease. For hypertension, she was treated with spironolactone that assisted in blood pressure control and hypokalemia. She is still under treatment and is planned for cytotoxic chemotherapy. Genetic testing for possible underlying mutations e.g. Li-Fraumeni syndrome was negative.

**Discussion:** ACC is a very aggressive malignancy with a life expectancy of 2-2.5 years, dropping to few months in the presence of metastasis. Presentation varies, as 50% are hormone-secreting tumors (30% cortisol, 20% androgens, 10% estrogens, and 2% aldosterone) that present with features of hormone excess such as virilization in females, Cushing’s syndrome, and hypertension, or symptoms of mass effect with nonfunctioning masses. Cortisol excess can lead to various psychiatric symptoms as depression, mood disorders, cognitive deficits and even psychosis.
**Conclusion:** Acute psychosis is a very rare initial presentation of an ACC. ACC should be considered in the differential diagnosis of the organic causes of psychiatric illness especially if it is accompanied by other features such as new onset acne and hirsutism.

**Abstract #114**

**POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AS THE FIRST PRESENTATION OF RETROPERITONEAL PARAGANGLIOMA**

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**Objective:** We report a patient with a retroperitoneal catecholamine-secreting paraganglioma (CSP) who presented with posterior reversible encephalopathy syndrome (PRES).

**Case Presentation:** A 47-year-old woman, with hypertension for 1 year and type 2 diabetes, presented with a sudden onset severe headache and blurred vision. Her blood pressure was 225/107 mmHg and CT head ruled out hemorrhage. Her headache responded partially to morphine and fentanyl, so neurologist requested CT angiogram and venogram that was normal. Also, the cerebrospinal fluid analysis was unremarkable. MRI head showed subtle cortical-subcortical T2 and FLAIR hyper-intensities in both occipital lobes suggestive of PRES. In less than 48 hours of her hospital stay, she experienced a severe headache followed by generalized tonic-clonic seizures and blood pressure rose to 230/140 mmHg. Therefore, catecholamine excess was suspected and 24 h urine study was done for metanephrines: 1.52 umol (0–1.4), and normetanephrines: 21.95 umol (0–3.45). An MRI revealed a well-defined left retroperitoneal mass (3.0 x 2.7 x 3.7 cm) separated from the left adrenal gland with features of pheochromocytoma. Workup for other adrenal hormones excess including cortisol, aldosterone, and androgens was essentially normal. In preparation for surgical excision, the patient was started on prazosin (alpha-blocker), and then a beta-blocker was added to control her blood pressure adequately. The patient was put on a high salt diet with adequate hydration to avoid intravascular volume depletion. Thereafter, a robotic resection of the retroperitoneal mass was performed. Histopathology showed features of pheochromocytoma with capsular invasion. Repeated MRI head showed resolution of the PRES features. The patient was discharged in a stable condition, and her blood pressure was well controlled with significantly lower doses of anti-hypertension medications. Repeated 24 h urine investigations showed normal metanephrines: 0.18 umol, and normetanephrines: 0.6 umol.

**Discussion:** PRES is a clinico-radiological diagnosis that characterized by altered sensorium, headache, seizure, visual disturbance and a brain MRI showing hyperintensities on T2 weighed imaging. It has been described before as a complication of catecholamine producing tumors; however, this is the first case to be reported of PRES as an initial presentation of an adult patient with a retroperitoneal paraganglioma. CSPs are very rare neoplasms arising from chromaffin cells of sympathetic ganglia. The combined pheochromocytoma/paraganglioma incidence is 0.8 per million population.

**Conclusion:** Catecholamines excess needs to be considered in the differential diagnosis of patients presenting with PRES.

**Abstract #115**

**PRIMARY ALDOSTERNISM SECONDARY TO UNILATERAL ADRENAL HYPERSECRETION CONFOUNDED WITH A CONTRALATERAL NON-SECRETING ADRENAL ADENOMA.**

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**Objective:** Background: Primary hyperaldosteronism is an underdiagnosed cause of resistant hypertension. It should be suspected in individuals with the classic triad of resistant hypertension, hypokalemia and metabolic alkalosis. The most common causes of primary hyperaldosteronism include aldosterone-producing adenomas and bilateral hyperaldosteronism. However, it is important to recognize other less common causes such as unilateral adrenal hyperplasia, adrenocortical carcinomas, ectopic tumors and familial hyperaldosteronism.

**Case Presentation:** Case report: 53 years old male with medical history of hypertension diagnosed at age 33-year-old by his primary care physician. Since diagnosis he has been in multiple antihypertensive therapies including more than three antihypertensive agents at optimal doses and hydrochlorothiazide without successfully achieving blood pressure control. Fifteen years after the diagnosis of hypertension, hypokalemia was identified at 1.7 mEq/dl (nl, 3.5–5.0 mEq/dl) on routine blood testing. He was subsequently referred to a Nephrologist who ordered a screening workup for primary hyperaldosteronism. Screening results showed low plasma renin activity (PRA) at 0.28 ng/ml/hr (nl, 0.3–3.7 ng/ml/hr) and elevated plasma aldosterone concentration (PAC) at 36 ng/dl (nl, 9-16 ng/dl) with a PAC/PRA ratio of 128.57; which confirmed
the diagnosis. Aldosterone-antagonist was added to his therapy with normalization of potassium levels and systolic blood pressure levels around 130-150 millimeters of mercury. An adrenal CT scan was performed and revealed a right adrenal adenoma. Patient was then referred to an Endocrinologist for further evaluation. Laboratory tests to rule out Pheochromocytoma and Cushing’s syndrome were ordered and resulted negative. Adrenal Venous Sampling was done after withdrawal of the aldosterone-antagonist and hydralazine, showing a left-sided adrenal vein PAC of 7,279 ng/dl consistent with left-side lateralization. Therefore, surgery for left adrenalectomy is scheduled for next February 2018.

Conclusion: Based on the Endocrine Society clinical practice guideline from 2016, patients willing to undergo surgery, with age more than 40 years old, should have an adrenal venous sampling to confirm the diagnosis before surgery. This case illustrates the relevance of the adrenal venous sampling, despite the presence of an adenoma on adrenal CT scan, to prevent surgical excision of the non-affected adrenal gland.

Abstract #116
INCIDENTAL FINDING OF PHEOCHROMOCYTOMA IN PREGNANCY

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Case Presentation: Pheochromocytomas (PCT), catecholamine secreting tumors arising from chromaffin cells in the adrenal medulla, affect 50% of patients with MEN2 syndrome. The incidence of PCT in pregnancy is <0.2 per 10,000 pregnancies, but it is often mistaken for pre-eclampsia, and is associated with high morbidity & mortality. This case describes a pregnant female with hypertension (HTN) and proteinuria, who received emergent C-section for presumed pre-eclampsia, and was subsequently diagnosed with PCT. A 35 year old female was evaluated for IUI conception. She noted testing positive for a familial genetic mutation leading to prophylactic thyroidectomy at age 13. She successfully conceived, and apart from mild chronic HTN, her 1st trimester was uneventful. At 25wk3d gestation, she was hospitalized with abdominal pain and worsening HTN. Urine protein:creatinine was in the pre-eclampsia range, so she was treated with magnesium, betamethasone, and labetalol/hydralazine, and a live infant was delivered via Caesarian section 3 days later. Postpartum, she continued to have episodic HTN to 220 mmHg. Uncharacteristic of pre-eclampsia, this prompted consultation to our service to evaluate for secondary causes. A thorough chart review revealed that she has a RET gene mutation. Biochemical studies showed a 24 hr urine epinephrine 42 mcg (N<21), norepinephrine 1971 mcg (N 15-80), metanephrine* 864 mcg (N<400), and normetanephrine* 14310 mcg (N<900) in 5400 mL. CT-adrenals revealed a heterogeneously enhancing 5.4 cm left adrenal mass (HU precontrast 44, postcontrast 104; washout abs 66%, rel 38%) highly suggestive of a PCT. After 2 wks of alpha blockade with phenoxybenzamine, she had an uneventful laparoscopic left adrenalectomy, with confirmation of the diagnosis by surgical pathology. Unfortunately, the baby succumbed to complications of prematurity at 9 wks.

*hypertensive normal (N) values

Conclusion: Our case underscores the importance of thorough prenatal history taking and appropriate vigilance for MEN2-associated pathologies when a history of a familial syndrome is given, particularly one that results in a prophylactic thyroidectomy at a young age. Initiation of a multi-disciplinary approach in the pre-conception period would have been beneficial. Early case detection of PCT in pregnancy can lower maternal and fetal mortality to <5% and <15%, respectively. Although information on our patient’s specific RET codon is unavailable, due the remoteness of her testing, a low threshold for PCT screening would be advisable when given such a history. Our case also demonstrates that lifelong MEN2 surveillance with certain RET codon mutations is crucial, even lacking a history of MTC.

Abstract #117
NOT ANOTHER CASE OF VIRILIZATION

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Objective: To report a rare cause of a virilizing adrenal malignancy.

Methods: Case report and literature review.

Case Presentation: “I am turning into a dude” was the chief complaint of a 43 year old female patient seen for endocrine evaluation. She reported new acne, hair growth on the face, chest, oligomenorrhea, elevated blood pressure, deepening of voice and aggressive behavior. She was evaluated by her family physician and was started on anti-hypertensive medications. Her Gynecologist checked a Total Testosterone level, which was 70 (normal range 15-70 ng/dL). She had a normal pelvic exam and sonogram.
On history and exam it was evident that patient had recent onset and rapidly progressing hirsutism (Ferriman-Gallwey score of 22) and virilization (deep voice, male pattern baldness, clitoromegaly). Suspicion of an androgen-secreting tumor was high on the differential. Exogenous androgen administration was ruled out.

Evaluation of hormones revealed a significantly elevated androgens: Testosterone (261), Androstenedione 3464 (30-200ng/dL), DHEA-SO4 384 (18-244 mcg/dL). A CT scan of abdomen confirmed our suspicion. A large homogenous left adrenal mass (9cm) with central necrosis was seen on the contrast images. On the non-contrast images the tumor had a density of 35 Hounsfield units. Right adrenal gland was normal. There was no evidence of nodal, visceral or skeletal metastases. Testing was also negative for Pheochromocytoma, glucocorticoid and aldosterone excess. She was evaluated by endocrine surgery and had robotic-assisted transabdominal left adrenalectomy. She did well in the immediate postoperative days.

Pathology confirmed a large adrenocortical carcinoma confined to the capsule. The patient was positive for 2 major and 3 minor Lin-Weiss-Bisceglia (LWB) criteria for adrenocortical neoplasm, classifying it as malignant. Surprisingly the sections revealed oncocytic adrenal cortical carcinoma characterized by variably sized polygonal cells with granular, pink cytoplasm arranged in sheets, islands, nests and trabecular formations. The nuclei showed heterogeneity in size and shape with prominent nucleoli and high mitotic counts.

Discussion: Oncocytomas occur most frequently in the thyroid, kidney, salivary gland, and pituitary. A review of the literature shows fewer than 10 cases of oncocytic adrenocortical carcinomas and most of them were non-functioning.

Conclusion: This to our knowledge is one of the few reports of a virilizing oncocytic adrenal cortical carcinoma in an adult.

Abstract #118

RAPID ENLARGEMENT OF BILATERAL ADRENAL MASSES AND ACUTE SEVERE HYPERCALCEMIA AS INITIAL PRESENTATION OF DIFFUSE LARGE B CELL LYMPHOMA

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Case Presentation: A 68-years-old man with HCV, HTN and bilateral adrenal masses presented with sudden onset of acute renal failure and severe hypercalcemia in July 2014. Bilateral adrenal lesions were incidentally found during MRI abdomen for abdominal pain in July 2013. Those were homogenous masses measuring 3.8 cm x 2.9 cm on the right and 2.8 cm x 1.7 cm on left with uniform loss of signal on the opposed phase sequence suggesting bilateral adenomas. Repeat MRI in May 2014 showed enlarging adrenal masses measuring up to 9 cm with areas of central necrosis and a group of enlarged abdominal lymph nodes suggesting a malignant process. Biochemical work up for pheochromocytoma and hypercortisolism was negative and DHEAS level was suppressed. CBC revealed no anemia but did show mild leucopenia with normal differential count. While he was being evaluated for adrenalectomy, he presented with sudden onset of severe hypercalcemia and subsequent biopsy of left adrenal gland showed diffuse large B-cell lymphoma. As part of hypercalcemia workup, calcitriol was elevated with suppressed levels of PTH and PTH-rP. Patient completed 6 cycles of RCHOP with resolution of hypercalcemia and reduction of adrenal glands to normal sizes. Adrenal function remained intact and patient is still in remission 3 years after diagnosis.

Discussion: Lymphomas arising primarily in endocrine organs are rare and represent < 3% of extra-nodal lymphoma. Early diagnosis of PAL impacts the prognosis and, unlike thyroid lymphoma, it has poor survival rate ranging from 10 days to 24 months in literature review. Rapid enlargement of bilateral adrenal glands along with or without hypercalcemia or adrenal insufficiency should raise the possibility of PAL. The majority of cases (70%) are complicated by adrenal insufficiency as a consequence of > 90-95% destruction of the glands by tumor. Adrenal insufficiency at the time of diagnosis or during later stage is associated with poor prognosis. Hypercalcemia is a rare presentation in PAL and also corresponds to decreased survival rates. It is thought that tumor related rise in calcium is mediated through humoral, bone metastasis or adrenal insufficiency. In one report, 4 out of 100 PAL cases presented with hypercalcemia and those were due to PTH-rP. To date, there were only three other cases of calcitriol mediated hypercalcemia in this scenario.

Conclusion: Primary adrenal lymphomas are a rare entity which might present as rapid growing adrenal masses frequently accompanied by adrenal insufficiency. Hypercalcemia is sporadically associated with this condition and, when present, can be mediated by PTH-rP or, less commonly, increased calcitriol production.
INTRAVASCULAR LARGE CELL LYMPHOMA DIAGNOSED FROM BILATERAL ADRENAL INVOLVEMENT

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Case Presentation: A 56 year old woman was admitted to hospital for evaluation of expressive aphasia. Contrast-enhanced magnetic resonance imaging (MRI) of the brain revealed multiple T2/FLAIR hyperintense lesions of the white matter in both cerebral hemispheres. Cerebral spinal fluid (CSF) analysis was notable for a two-fold elevation of protein level and modestly elevated white blood cell count with lymphocyte predominance, but cytological evaluation failed to reveal malignant cells. Peripheral white blood cell count ranged from 4.0-6.3 k/mm3 (3.4-9.4). Left adrenal gland enlargement was found on whole body computed tomography (CT), and fluorodeoxyglucose positron emission tomography (FDG-PET) was notable for bilateral adrenal hypermetabolism (maximum standard uptake value 24.7 in the left adrenal, 8.8 in the right adrenal). An 8 AM cortisol level was 18.6 mg/dL, and both plasma normetanephrine (0.34 nM, 0.00-0.89) and metanephrine (< 0.10 nM, 0.00-0.49) were unremarkable. Needle biopsy of the left adrenal gland yielded a lymphoid infiltrate with morphological and immunophenotypic features diagnostic of intravascular large B-cell lymphoma. The patient was subsequently treated with six cycles of rituximab-based chemotherapy. FDG-PET after treatment showed resolution of hypermetabolism in both adrenal glands, and CNS MRI showed significant improvement of T2/FLAIR lesions. Neurological abnormalities also resolved after chemotherapy.

Discussion: Intravascular large cell lymphoma (ILCL) is a rare lymphoma subtype characterized by proliferation of lymphoma cells in small vessels but no discrete extravascular tumors or detectable cells in the peripheral circulation. Patients most commonly present with CNS and cutaneous involvement, but ILCL hematogenously disseminates to multiple organ systems and has an aggressive course. The prevalence of adrenal involvement in cases of ILCL has not been systematically reported, and spread to the adrenal glands appears to be typically diagnosed on postmortem examination. This patient’s case is unusual due to her type of lymphoma and adrenal involvement at time of initial presentation that ultimately led to the diagnosis of ILCL.

Conclusion: Adrenal glands are involved in up to 25% of advanced cases of non-Hodgkin lymphoma, and it is appropriate to consider lymphoma in the differential diagnosis of an adrenal mass or adrenal enlargement, particularly when clinical suspicion is high. After excluding pheochromocytoma, needle biopsy of the adrenal may yield a cytological diagnosis of lymphoma and avoid biopsy of more difficult sites such as the CNS when there are no easily accessible lymph nodes or there is no lymphadenopathy.
and CXCL5 6 weeks after treatment with Nivolumab which were considered possible biomarkers for impending ACTH insufficiency which were not checked in our patient. Mechanism responsible for endocrine side effects of anti PD1 therapy is unclear. However, autoimmune pathogenesis has been supported by the presence of antithyrotropin and anti-corticotrophin antibodies in some patients with Ipilimumab induced hypophysitis.

**Conclusion:** Isolated adrenal insufficiency is a rare but life threatening complication of anti-PD-1 therapy. There are no clear biomarkers for impending ACTH insufficiency nor clear guidelines regarding management of adverse events. Clinicians should be aware of this life threatening complication in patients on anti-PD-1 therapy presenting with nonspecific symptoms for prompt evaluation and treatment.

**Abstract #121**

**GIANT BILATERAL ADRENAL MASSES**

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Banner Medical Center University of Arizona

**Case Presentation:** A 46 year-old man was admitted to the hospital for severe anemia secondary to a gastrointestinal bleed and was found to have massive bilateral retroperitoneal masses. He unintentionally and gradually lost 40 lbs over the last few years but was otherwise asymptomatic with no cough, fever, night sweat, change in appetite, or fatigue. He reported being “a very sick child” with multiple childhood hospitalizations but did not recall being on glucocorticoid or mineralocorticoid therapy. He also had a history of arthritis for which he took ibuprofen. Otherwise, he denied taking any other medications. On physical exam his heart rate was 86 bpm, blood pressure was 94/54 mmHg, temperature 98.6 F. He was very cachectic with temporal wasting. He had non-tender, palpable bilateral abdominal masses and a normal genital exam.

Laboratory evaluation revealed:

- WBC 14.4
- Hb 2.9
- Plt 528
- Na 137
- K 3.1
- Cr 0.6 GFR >60
- Glucose 85
- TSH 3.98
- Aldosterone 3 (ref ≤ 28 ng/dL)
- Plasma renin activity 15.19 (ref 0.25-5.82 ng/mL/h)
- 17-OH progesterone 13,428 (ref 33-195 ng/dL)
- FSH 0.7 (ref 1.5-12.4 IU/L)
- LH < 0.1 (ref 1.7-8.6 IU/L)
- Total testosterone 67
- Free testosterone 8.7
- DHEA-S 13 (ref 95-530 ug/dL)
- Plasma metanephrines:
  - Epinephrine < 10 (ref 10-200 pg/mL)
  - Norepinephrine 728 (80-520 pg/mL)
  - Dopamine 32 (0-20 pg/mL)
- Free Metanephrine < 25 (ref ≤ 57 pg/mL)
- ACTH 132 (ref 6-50 pg/mL)
- ACTH stimulation test: cortisol levels 5.2 (0 minutes), 5.0 (30 minutes), and 5.4 (60 minutes)
- MRI chest, abdomen, and pelvis without contrast: bilateral large retroperitoneal fatty masses measuring 25 cm on the right and 20 cm on the left, respectively, as well as a 2.3 cm opacity in the lower lobe of the right lung.
- MRI brain without contrast: No gross acute intracranial abnormality.

**Discussion:** Diagnostic data suggest congenital adrenal hyperplasia (CAH) with the markedly elevated 17-OH progesterone level of greater than 10,000 ng/mL. Radiographic imaging suggests giant bilateral adrenal myelolipomas, which are rare, benign, and typically non-functional neoplasms. The presence of large amounts of macroscopic fat on imaging is diagnostic of a myelolipoma. However, malignancy cannot be completely excluded. He also has primary adrenal insufficiency and hypoadosteronism. The patient was prescribed hydrocortisone 15 mg daily in two divided doses and fludrocortisone 0.05 mg daily will be added. These large adrenal myelolipomas may spontaneously rupture or hemorrhage when the size exceeds 5 cm. Therefore, surgical excision should be considered.

**Conclusion:** It is important to recognize CAH in an adult patient that present with bilateral adrenal myelolipomas as well as the radiographic features of such adrenal masses.

**Abstract #122**

**A CASE OF REVERSIBLE ADRENAL SUPPRESSION INDUCED BY FLUCONAZOLE IN AN HIV-INFECTED PATIENT**

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University of Cincinnati

**Objective:** To describe a case of reversible adrenal suppression induced by fluconazole in an HIV-infected patient

**Case Presentation:** A 50-year-old man with Hepatitis C infection and HIV/AIDS with CD4 count of 97 cells/mm3 was admitted to the hospital with group A streptococcus septic arthritis affecting the left knee, right hip and right subclavian joints with progression to septic
shock. He required pressor support and intubation for five days. On day 6 patient was extubated and weaned off pressor support with stable BP. He had received multiple intravenous antibiotics until culture and sensitivities were available and was switched to cefazolin. Other medications included Darunavir 600 mg etravirine 200 mg, Ritonavir 100 mg, Tenofovir 25 mg. On hospital day 7, laboratory tests showed sodium at 138 mEq/L. On hospital day 8 patient was given fluconazole 200 mg for one dose then 100 mg daily for oral candidiasis. On hospital day 9 sodium was at 130 mEq/L and gradually fell to 125 mEq/L by hospital day 12. An ACTH stimulation test was performed and showed relatively flat cortisol levels of 13.4, 14.9 and 17.9 µg/dL at 0, 30, 60 minutes respectively, indicating adrenal insufficiency; however, ACTH level prior to the stimulation was not obtained. He was started on hydrocortisone 15 mg in the morning and 10 mg in the afternoon. Fluconazole was discontinued on hospital day 14 and a repeat ACTH stimulation test was repeated on hospital day 18. The baseline ACTH was 12.1 pg/ml and cortisol were 14.7, 18.4 and 21.6 µg/dl at 0, 30, 60 minutes respectively.

Discussion: Adrenal dysfunction is frequently involved in patients with HIV. Causes include opportunistic infections such as CMV, tuberculosis, disseminated fungal infections, neoplasms and medications. Some case reports suggested a role of fluconazole in the suppression of steroidogenesis, although it remains debatable if fluconazole can cause adrenal insufficiency. There are rare clinical case reports of adrenal insufficiency with the use of Fluconazole. In our case, the ACTH stimulation test was attenuated, which has been reported in HIV patients. Upon stopping Fluconazole, the cortisol response to ACTH stimulation improved (though was not robust). We suspect that Fluconazole was an additional cause of the blunted cortisol response to ACTH stimulation. Clinicians should be aware of this potential effect of Fluconazole especially as it is widely used in the HIV patient group who are already prone to developing adrenal insufficiency from other causes.

Conclusion: Abnormal ACTH stimulation test in HIV patients can occur when receiving Fluconazole and this can be reversible after stopping this medication.

Abstract #123

IMMUNE CHECKPOINT INHIBITOR COMBINATION VERSUS ECTOPIC ACTH-SECRETING NEUROENDOCRINE TUMOR CAUSING CUSHING’S SYNDROME: A CASE REPORT

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Case Presentation: We present a case of a 49-year-old woman with history of advanced neuroendocrine carcinoma of unknown primary, recently initiated on combined therapy with nivolumab and ipilimumab, who presented with loose stools and persistent hypokalemia. The patient was found to have an elevated morning cortisol level of 79 mcg/DL in the setting of a 30lb weight gain and worsening bilateral lower extremity swelling. Physical exam was notable for morbid obesity, facial plethora, and significant bilateral lower extremity edema. Subsequent laboratory data confirmed elevated morning cortisol level of 107 mcg/DL and elevated adrenocorticotropic hormone (ACTH) level of 198.6 pg/mL. Following low-dose Dexamethasone suppression test, cortisol level remained elevated at 142.8 mcg/DL. A 24-hour urinary cortisol confirmed hypercortisolism at 3210 ug/24 hour. Aldosterone and renin levels were within normal range at 4.6 and 0.2, respectively. Laboratory studies otherwise revealed persistent hypokalemia ranging 2.3 to 3.2 mmol/L. A CT of the abdomen and pelvis demonstrated diffuse liver metastases, anasarca, and normal adrenal gland morphology. Further evaluation with MRI of the pituitary and inferior petrosal sinus sampling are pending.

Discussion: The present case describes ACTH-dependent Cushing’s syndrome arising from two rare potential sources. Transient pituitary ACTH-dependent Cushing’s disease has been described in association with combination checkpoint inhibitors in one recent study. Our patient is further susceptible to Cushing’s syndrome due to ectopic ACTH production by a neuroendocrine carcinoma with hepatic metastases. It is therefore important for clinicians to maintain a high index of suspicion for Cushing’s syndrome in both patients with neuroendocrine carcinoma and combination checkpoint inhibitor therapy, and to differentiate the source of ACTH production. Importantly, Cushing’s syndrome associated with checkpoint inhibitors may regress without intervention, whereas ectopic ACTH production from a neuroendocrine tumor may be more likely to warrant therapy

Conclusion: Immune checkpoint inhibitor therapy is a new, rare potential cause of Cushing’s syndrome. It is important for physicians to recognize potential endocrinopathies associated with these novel agents, particularly given the potentially different progression of disease.
Abstract #124

ADRENAL MEDULLARY HYPERPLASIA AS A CAUSE OF SECONDARY HYPERTENSION AND METANEPHRINES EXCESS.

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Objective: Diffuse adrenal medullary hyperplasia (AMH) is a rare condition that clinically and biochemically can resemble pheochromocytoma. We reported a challenging case of resistant hypertension caused by bilateral AMH.

Case Presentation: A 48-year-old female with a history of uncontrolled hypertension was referred to endocrinology clinic for further investigation. The patient complained of having episodes of hypertension with a headache, sweating, palpitations, and chest pain for fourth years. She was on Carvedilol, Nifedipine, Hydrochlorothiazide, and Lisinopril. She had no family history of the endocrine disorders. She had a left breast cancer treated with mastectomy and tamoxifen, and thyroid adenoma treated with hemithyroidectomy. On physical examination, she had elevated blood pressure of 156/107 mmHg. She had no cushingoid features. Screening for primary hyperaldosteronism was negative. An abdominal CT scan angiography did not show evidence of renal arteries stenosis. Mild elevated metanephrines level in 24-hrs urine and blood samples were noticed twice. Serum and 24-hrs urinary catecholamines were normal. A CT scan of the abdomen showed a 7 mm nodule in the left adrenal gland with a density of 12.5 HU. A 123I-MIBG scintigraphy and SPECT/CT scan showed increased diffuse activity in both adrenal glands. She underwent left adrenalectomy and pathology report revealed adrenal cortical nodular hyperplasia and adrenal medullary hyperplasia. Postoperatively, her blood pressure was easier to control.

Discussion: Bilateral AMH is an uncommon, frequently unrecognized condition causing secondary hypertension. The etiology of AMH remains unknown. Moreover, currently, there are no standard guidelines, treatment, and work-up for this disease. Its presentation can resemble a pheochromocytoma except that the degree of catecholamines and metanephrines elevation is usually milder. AMH often demonstrates by increased uptake of either I-123 MIBG or I-131 MIBG. However, the definite diagnosis is histopathology after adrenal gland resection.

Conclusion: This clinical presentation of AMH is a real challenge to clinicians who encounter the case. AMH should be considered in the differential diagnosis of endocrine causes of hypertension. Special consideration should be given to patients with borderline elevated urinary and serum metanephrines and with increased uptake of MIBG without morphological evidence of pheochromocytoma.

Abstract #125

HYPERCORTISOLISM IN A PATIENT WITH A MEDIASTINAL MASS AND PITUITARY MACROADENOMA: A CASE REPORT

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Objective: Many diagnostic laboratory and imaging tests have been investigated for the purpose of differentiating Cushing’s Syndrome (CS) secondary to Cushing’s Disease (CD) vs. Ectopic ACTH Secretion (EAS). However, no gold standard testing exists for distinguishing the two entities. Herein, we report a rare occurrence of hypercortisolism in a patient with a pituitary macroadenoma and mediastinal mass. We discuss our diagnostic and therapeutic algorithm in the setting of overt confliction in the diagnostic work-up.

Case Presentation: A 61-year-old man with well-controlled hypertension was admitted for new-onset heart failure. His hospital stay was complicated by uncontrolled hypertension despite six anti-hypertensive agents. Evaluation for secondary causes of hypertension revealed evidence of excess, intrinsic cortisol production. A 1-mg overnight dexamethasone suppression test (DST) revealed a cortisol of 31 µg/dL (3.4-26.9 µg/dL), ACTH of 63 pg/mL (8-42 pg/mL) with a dexamethasone level of 498 ng/dL (140-295 ng/dL). Further work up revealed elevated 24-hour urinary free cortisol level of 259.5 µg/day (< 60 µg/day), and 2 elevated midnight salivary cortisol levels of 413 ng/dL and 1270 ng/dL (<100 ng/dL). In evaluation of ACTH-dependent CS, pituitary MRI revealed a 1.4x1.3x1.5 cm heterogeneous right sellar mass with no involvement of the optic chiasm. Meanwhile, CT imaging investigating his shortness of breath revealed a 3.0x3.8 cm anterior mediastinal mass with mild indium-111 uptake on a subsequent Octreotide scan. Further work up was obtained to delineate the source of his ACTH production. Patient failed to suppress to a high dose DST with a cortisol of 35.8 µg/dL, ACTH of 103 pg/mL, dexamethasone of 6060 ng/dL, supporting a diagnosis of EAS. On the other hand, post a CRH stimulation test, patient’s ACTH increased by 95% alongside an increase of 66% in cortisol levels supporting a diagnosis of CD.
Given concern for EAS and the high morbidity associated with such cases, a multidisciplinary decision was made to resect the mediastinal mass first. Post-resection, ACTH and cortisol levels remained elevated. Pathology of the mediastinal mass showed thymic tissue without evidence of ACTH staining. Subsequently, patient underwent a transphenoidal resection of his pituitary macroadenoma resulting in cure of his CD.

**Conclusion:** A myriad of diagnostic lab tests and imaging modalities are available to distinguish between CD and EAS. It is vital that these tests be used within the context of clinical judgment. It is important to consider the results of dynamic endocrine testing and imaging in totality while evaluating hypercortisolism.

**Abstract #126**

**PHEOCHROMOCYTOMA CAUSING ECTOPIC CUSHING’S SYNDROME**

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**Objective:** The coexistence of pheochromocytoma and Cushing’s syndrome (CS) has rarely been reported. We present a case of ACTH-producing pheochromocytoma.

**Case Presentation:** A 77 yo male with a past medical history of HTN and HLD presented to the ER with acute onset of altered mental status, nausea and vomiting and was found to have a right frontal intracranial hemorrhage. On admission BP was 200/97, pulse 94, BMI 21. Hospital course was complicated by hypertension requiring three agents (amlodipine 10mg daily, labetalol 200mg TID, and lisinopril 40mg daily) as well as persistent hypokalemia despite adequate repletion. On exam, patient had left hemiparesis, some central obesity but no other signs of cortisol excess. He underwent CT abdomen/pelvis w/out contrast for planning of gastrostomy tube placement and was found to have a 5.8 cm left adrenal mass. Given his presentation there was concern for secondary causes of hypertension, and given size of adrenal mass our differential included pheochromocytoma vs. adrenal cortical carcinoma. On laboratory evaluation serum sodium was 145 meq/L, potassium was 2.9 meq/L, HgA1c 6.1%. Biological testing revealed serum metanephrines of 9.45 (ref range 0.00-0.49 nmol/L), normetanephrines 11.49 (0.0-0.89 nmol/L), aldosterone < 3.0 (4.0 - 31.0 ng/dL), renin 0.1 (0.2-1.6 ng/mL/hr), 24hr urine norepinephrine 603 (11 - 60 ug/d), ACTH 10 (7 - 69 pg/mL), cortisol 15 (6.7 - 22.6 mcg/dL). The persistent hypokalemia and suppressed renin on ACE inhibitor prompted evaluation for elevated cortisol. Urinary free cortisol was 160 (ref range < 60 ug/d). After 1mg dex-suppression test ACTH was 7 pg/mL, cortisol 9 mcg/dl, dexamethasone level 199 (140-295 ng/dL). Patient was started on alpha-blockade and underwent left adrenalectomy. He received stress dose steroids prior to surgery and was discharged on hydrocortisone. Pathology confirmed a pheochromocytoma with positive ACTH staining. Serum metanephrines and normetanephrines were within normal range one month after surgery.

**Conclusion:** We present a case of a pheochromocytoma co-secreting ACTH and inducing CS. As pheochromocytomas are neuroendocrine tumors, they can rarely secrete other neuroendocrine peptides, notably ACTH and even CRH, and may be an unsuspected cause of ectopic CS. There have been about 40 cases in the literature to date of this syndrome. Most patients with ectopic CS present with some evidence of excess cortisol with hypokalemia in 70% of cases and diabetes mellitus in 90% of cases. In our patient the persistent hypokalemia suggested an excess cortisol state. Care should be taken to identify these cases pre-operatively so as to avoid hypocortisolism post-operatively.
ml and 2 ng/dl, respectively. Cortisol to cortisone ratio was elevated (10.4) and transtubular potassium gradient was elevated to 6.84 in the setting of hypokalemia. Joint decision was made at this time to stop posaconazole. Twenty-one days following cessation of posaconazole, the patient’s blood pressure returned to normal, as did his labs (potassium 4.9mmol/L, aldosterone 4n g/dl, renin 1.34ng/ml/h, 11-deoxycortisol 36 ng/dl, estradiol 35 pg/ml). He was then restarted on posaconazole, at a lower dose of 100 mg daily. After 4 weeks, blood pressure and labs (aldosterone, renin activity, 11-deoxycortisol, and estradiol levels) remained normal.

Discussion: 11B-HSD2 is a critical enzyme in the pathogenesis of AME. While posaconazole and itraconazole were recently shown to cause inhibition of 11B-HSD2 in vitro, our case is the first to demonstrate that posaconazole can lead to clinically significant inhibition of 11B-HSD2, resulting in AME. Furthermore, this inhibition occurred in a dose dependent manner, and was reversed by decreasing the dosage of the offending agent. More cases will need to be examined to confirm this observed effect.

Conclusion: Clinicians should have a low index of suspicion for AME in patients who develop hypertension and hypokalemia following initiation of posaconazole.

Abstract #128

WHAT IS THE SOURCE OF ACTH? IS 68-GALLIUM DOTATE SCANNING AS SENSITIVE AS WE THINK?

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Objective: We present two cases of patients with ACTH dependent Cushing’s syndrome, illustrating the challenges of diagnosis and management even with advances in imaging for neuroendocrine tumors.

Case Presentation: Case 1: A previously healthy 65 year old woman was found to have an A1c of 6.5%, serum K+ of 1.8mmol/L and lower extremity ecchymoses. She had a cortisol level of 63.4 mcg/dL with an ACTH of 296.4 pg/mL. A 24 hr urinary free cortisol (UFC) was 13,607 mcg/24hr (4.50mcg). MRI showed a 4mm pituitary lesion. On Inferior petrosal sinus sampling (IPSS), the ratio of ACTH in the sinuses to the periphery was 1, with no increase in pituitary ACTH after corticotropin releasing hormone (CRH). A CT chest/abdomen showed a 1cm nodule in the lungs and a 1.6cm cystic lesion in the pancreas. Octreotide scan was negative, but PET/CT showed a hypermetabolic 1.8cm nodule in the lung. Her condition deteriorated and she was admitted with perforated diverticulitis and acute respiratory failure. FNA aspiration of the pulmonary nodule revealed Aspergillus fumigates and that of the pancreatic cyst was unrevealing. She failed treatment with ketoconazole, etomidate, and metyrapone and underwent adrenalectomy which showed hypertrophied adrenal glands with nodules up to 7cm and scattered extramedullary hematopoesis. A 68-Gallium Dotatate PET/CT was negative. Despite the aggressive nature of disease and extensive work up, the source of ACTH is occult.

Case 2: A 36 year old man presented with a history of Cushing’s disease treated with transphenoidal resection (TSR) in the past. He had a recurrence 14 years after initial treatment, and underwent a second TSR with biochemical remission. Pathology revealed hyperplasia or adenoma with diffuse ATCH staining in one region. He had a second recurrence 5 years later and was treated with radiotherapy to the sella. After a third recurrence he was briefly managed with medications (ketoconazole, mifepristone and cabergoline) without control. A 68-Gallium Dotatate PET/CT scan showed a lesion in the pancreas. He had a pancreatectomy of a 0.5cm neuroendocrine tumor, but staining for ACTH was negative. A possible explanation for his recurrent Cushing’s is ectopic CRH production from the pancreatic tumor. CRH staining is not currently available at our center. Following surgery, however, his symptoms are recurring, and thus the source of ACTH is occult.

Conclusion: These cases exemplify the challenge of finding a culprit lesion in patients with ACTH-dependent Cushing’s syndrome. Even with the advent of 68-Gallium Dotatate scanning, quoted to have >94% sensitivity in detection of neuroendocrine tumors, the source of ectopic ACTH in the most aggressive Cushing’s cases can be elusive.

Abstract #129

ADRENAL INSUFFICIENCY IN A PREGNANT WOMAN WITH POLYGLANDULAR AUTOIMMUNE SYNDROME TYPE 2 AND STEROID INSUFFICIENCY

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Objective: During pregnancy, activation of the HPA axis results in a physiologic state of hypercortisolism without clinical manifestations of elevated cortisol. Free cortisol levels rise from week 22 of gestation onwards. We describe a case of a woman with polyglandular autoimmune syndrome (PGAS) type 2 and suboptimal response to steroids presenting with the symptoms of adrenal insufficiency during the third trimester of pregnancy.

Case Presentation: A 33 year old woman with history of PGAS type 2 manifested by autoimmune adrenalitis, celiac disease, and positive anti thyroperoxidase antibodies presented at 33 weeks gestation for worsening
fatigue and lightheadedness. She reported a feeling of near syncope that persisted while lying, sitting or standing. She had a history of asthma and eosinophilic gastroenteritis for which she was treated intermittently with prednisone. On physical exam, the only pertinent findings were: tachycardia with a heart rate of 117, without orthostatic hypotension. Two years prior, she was found to have autoimmune adrenalitis based on: AM cortisol of 4.6 µg/dl, ACTH of 8 pg/ml and positive 21-hydroxylase antibodies. She was maintained on prednisone 5 mg daily and fludrocortisone 0.1 mg daily. At an endocrinology follow up visit, the patient complained of lightheadedness and fatigue and was switched to hydrocortisone 20 mg in the morning and 10 mg in the afternoon. However, the patient’s fatigue and lightheadedness persisted while on hydrocortisone. Her PCP referred her for a glucocorticoid lymphocyte proliferation assay and patient was found to have a diminished response to prednisolone. A prednisone pharmacokinetic study was also performed which showed incomplete or delayed prednisone absorption and rapid clearance of prednisolone. As a result, she was transitioned to methylprednisolone (MTP) by her PCP. The patient was maintained on MTP 20mg daily for about two years and through the first trimester of pregnancy. She began experiencing increased fatigue during second trimester and the dose was increased to 40mg daily. In the third trimester, her PCP attempted to taper her MTP dose but she was unable to tolerate a dose less than 32mg. At 35 weeks, the patient had a successful delivery via caesarean section during which she received stress dose dosing with IV hydrocortisone. On discharge, she was continued on MTP 32 mg daily and fludrocortisone 0.1mg daily.

**Conclusion:** Patients with adrenal insufficiency who have persistent symptoms while on steroid replacement should be evaluated for steroid insensitivity. Gravid addisonian women may warrant increased doses of corticosteroids and mineralocorticoids particularly during the latter stages of pregnancy.

**Abstract #130**

**A CASE OF PHEOCHROMOCYTOMA ASSOCIATED WITH NEVER REPORTED RARE NEW MUTATION OF VHL GENE**

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**Objective:** To report a case of rare and never reported mutation in VHL gene presenting with pheochromocytoma with no other evident tumors

**Case Presentation:** A 37 year old Caucasian male with past medical history of HTN who presented with complaints of episodic spells of excessive sweating, mood swing, hypertension, abdominal pain. He also had significant family history in grandmother who had adrenalecmey and his son diagnosed with Hypertension. His urine studies were negative for metanephrines and normetanephrines. CT scan showed 5.5 cm tumor on right adrenal gland and underwent successful right adrenalectomy. Pathology revealed pheochromocytoma. He was followed with biochemical test which were normal. Due to his diagnosis of pheochromocytoma at early age, genetic testing was ordered. Genetic testing showed positive for VHL gene mutation, with variant of p.Glu32Gly, Heterozygous, autosomal dominant considered to be unknown significance by the laboratory. This mutation has not been previously reported in HGMD database, nor in the Broad ExAc dataset indicating it is rare and not well-characterized. He later underwent MRI with contrast of brain, spine, abdomen and pelvis which showed no evidence of other tumors.

**Discussion:** Von Hippel-Lindau (VHL) disease is an inherited, autosomal dominant syndrome manifested by a variety of benign and malignant tumors including clear cell renal cell carcinoma, hemangioblastomas, pheochromocytomas, and other rare tumors. Various kind of VHL mutations have been reported so far. The type of mutation in the VHL gene impacts the disease phenotype. Autosomal Dominant pathogenic variants in VHL gene are associated with VHL syndrome and pheochromocytoma. Our case with pathologically proven pheochromocytoma is associated with never reported, very rare kind of VHL gene mutation. It is a heterozygous variant in VHL gene, NM_000551.3:c.95A>G(p.Glu32Gly), autosomal dominant with unknown significance. This variant has not been previously reported. Clinically our case has proven pheochromocytoma and we can confirm this mutation has important significance and is associated with pheochromocytoma indicating type 2a-c type of VHL.

**Conclusion:** This case again shows importance of genetic testing in a case of pheochromocytoma even if it looks like a sporadic case. This case again proves that there are so many yet unidentified genetic mutation associated with VHL and pheochromocytoma and we should be open for genetic analysis, especially if it involves a young patient. This case proves a rare mutation in VHL gene which is considered as clinically significant and needs further investigation to classify mutations involved in pheochromocytoma
Abstract #131

SALVAGING AN OLD MEDICATION FOR NEW USES – WITH CAVEATS

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Objective: ACTH-independent macro-nodular adrenal hyperplasia (AIMAH) is a rare cause of Cushing’s syndrome, characterized by autonomous production of cortisol from benign macro-nodular enlargement of the adrenal glands. Our patient was treated with unilateral adrenalectomy and mifepristone, developed life-threatening toxicity.

Case Presentation: A 57-year-old woman was incidentally found to have bilateral adrenal enlargement on imaging performed for elevated liver enzymes. She had a 10 year history of type 2 diabetes mellitus, with progressively worsening glycemic control and weight gain without cushingoid features, despite metformin and insulin glargine. Hormonal studies showed an elevated 8 AM cortisol which was non-suppressible after 1 mg of dexamethasone. She had low dehydroepiandrosterone sulfate (DHEAS) and ACTH levels, which was consistent with autonomous production of cortisol from the adrenal(s). A 24-hour urinary free cortisol and midnight salivary cortisol were normal. Adrenal venous sampling revealed elevated bilateral cortisol production; with significantly higher levels in the left adrenal vein compared to the right, diagnosing AIMAH leading to subclinical Cushing’s syndrome. She underwent a unilateral left adrenalectomy followed by significant reduction in insulin requirement, and her A1C fell from 8.2% to 6.3%. Her serum cortisol, DHEAS and ACTH also normalized.

A few months after surgery, she resumed gaining weight, associated with a rise in HbA1C and non-suppressible cortisol levels. Mifepristone was started for hypercortisolemia. A few weeks later, she required ICU admission for hypernatremia, severe hypokalemia, and fluid overload. Mifepristone toxicity was diagnosed, and she improved with discontinuation of mifepristone, aggressive diuresis and dexamethasone.

Discussion: Mifepristone is an approved non-surgical treatment for endogenous Cushing syndrome associated with hyperglycemia. Mifepristone dosage is titrated based on clinical improvement. Hypokalemia due to overstimulation of mineralocorticoid receptors from high cortisol levels resulting from blockage of glucocorticoid receptors can potentially result in life threatening arrhythmias, rhabdomyolysis, and diaphragmatic weakness. Our patient’s presentation was consistent with mifepristone toxicity.

Conclusion: Patients on therapy with mifepristone must comply with close follow ups and biochemical testing. Our patient missed her follow up and laboratory testing following dose escalation. Given the long half-life of mifepristone, it took approximately 3 weeks to recover from toxicity. Furthermore, the long term effect of unopposed mineralocorticoid receptors, especially on the cardiovascular system, remains unknown.

Abstract #132

A NOVEL TMEM127 GENE MUTATION ASSOCIATED WITH BILATERAL PHEOCHROMOCYTOMAS AND ATYPICAL SYMPTOMS

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Cleveland Clinic Foundation

Objective: Transmembrane protein 127 (TMEM127) gene mutations are associated with nonsyndromic pheochromocytomas (PCCs) and usually present with unilateral benign PCCs. We present a patient with atypical symptoms of PCC and bilateral adrenal involvement who was found to have a novel TMEM127 mutation.

Case Presentation: A 48-year old female was referred for evaluation of incidental bilateral adrenal masses noted on abdominal CT scan for renal calculi. The adrenal masses were also seen on imaging seven years ago but were not followed subsequently and had increased in size from 2.4 to 3.4 cm on the right with a non-contrast attenuation of 39 Hounsfield units (HU) and absolute washout (AW) of 55%, and 2.7 to 3.2 cm on the left with a non-contrast attenuation of 32 HU and AW of 48%. She complained of nausea, vomiting, hiccupping, sneezing and headaches only while lying on her left side. She had no history of thyroid disease and no family history of endocrine disorders. Vitals and physical exam were normal. Plasma blood work revealed elevated metanephrines 1390 pg/ml (12-67) and normetanephrines 601 pg/ml (18-101); ACTH 7 pg/nl (8-42) with baseline cortisol of 6.6 ug/dl that peaked to 14.2 ug/dl at 60 minutes after 250 mcg injection of co-syntropin. The rest of her blood work was normal with aldosterone 9.4 ng/dl (3.1-35.4), direct renin 13 pg/ml, aldosterone/renin activity ratio 1 (<4), TSH 0.636 uU/ml (0.4-5.5) and calcitonin < 2 pg/ml (0-5.1). 24-hour urine collection showed elevated metanephrines at 6037 ug/24 hour (52-341) and normetanephrines 1494 ug/24 hours (88-444) with normal sodium 54 mmol/24 hr (40-220) and potassium 136 mmol/24 hr (30-99). She was started on phenoxybenzamine and hydrocortisone with subsequent bilateral partial adrenalectomy that was uneventful and resolved her symptoms. Bilateral PCCs were noted on pathology. She was found to have a heterozygous
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substitution mutation of G for A at the initiator codon of Exon 2 of the TMEM127 gene on genetic testing.

**Conclusion:** We describe a novel TMEM127 mutation associated with bilateral PCCs. Mutations involving the initiator codon of Exon 2 in the TMEM127 gene are known to be pathogenic. Individuals with these mutations are usually asymptomatic or present with typical adrenocortical symptoms which was not the case with our patient. Bilateral PCCs are less commonly seen with TMEM127 gene mutations and the risk of malignancy is low (< 5%). Affected individuals are usually diagnosed at a mean age of 42 years. First degree relatives of an affected individual have a 50% chance of having the genetic mutation and should be screened. Long term follow up is essential in these patients.

**Abstract #133**

**ELEVATED DHEAS DUE TO FUNCTIONAL ADRENAL HYPERANDROGENISM OF PCOS.**

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SUNY Upstate Medical University

**Objective:** Introduction: Dihydroepiandrosterone (DHEA) and Dihydroepiandrosterone sulfate (DHEAS) are steroid hormones mainly produced by the adrenals. Elevated DHEAS can be caused by various conditions such as adrenal tumor, congenital adrenal hyperplasia (CAH), Adrenocorticotropic hormone (ACTH) dependent Cushing’s syndrome, glucocorticoid resistance, hyperprolactinemia and polycystic ovary syndrome (PCOS). We report a case of elevated DHEAS likely due to primary functional adrenal hyperandrogenism (FAH) of PCOS.

**Case Presentation:** Case: A 21-year-old female of Italian/Greek origin was sent for evaluation of elevated DHEAS. She had a history of regular menses since age 12 and cystic acne. Physical exam was significant for obesity (BMI 32.5) without hirsutism or virilization and normal blood pressure. Nine AM labs: total testosterone 20.1 (9-55 ng/dL), DHEAS 735 (63-380 ug/dL) and 17 hydroxyprogesterone 15.9 (17OHP, <206 ng/dL). Repeat labs (11 AM): DHEAS 626 ug/dL, cortisol 25.3 (4.3-22.4 ug/dL), androstenedione 1.01 (0.26- 2.14 ng/mL). Eight AM labs: DHEAS 556 (148-407 ug/dL), 17OHP pregnenolone 843 (53-357 ng/dL) and cortisol 35 ug/dL. Overnight 1mg dexamethasone suppression test (DST) showed a cortisol of <1.5 ug/dL. CT abdomen with contrast showed a 9 x 6 mm nodule in the medial limb of the left adrenal gland consistent with adrenal adenoma. Trans-vaginal ultrasound showed no ovarian enlargement. Thyroid, prolactin, ACTH, aldosterone: renin ratio, metanephrines and catecholamines were unremarkable. Long DST showed adequate suppression of DHEAS, testosterone and 17OHP. ACTH stimulation test ruled out non-classic congenital adrenal hyperplasia, but did show mildly elevated DHEAS and 17OHP levels suggestive of FAH. She was started on oral contraceptives. Repeat imaging with MRI did not visualize an adrenal nodule.

**Discussion:** Discussion: PCOS is a common endocrine disorder characterized by hyperandrogenism, anovulation and polycystic ovaries. Diagnosis can be challenging. 40-70% of women may have increased DHEAS; the mechanism of this is unknown. Our patient did not present with the typical features of PCOS. Testing ruled out many causes of elevated DHEAS and was consistent with FAH. Other differentials could be pseudo-PCOS of obesity or a mild form of 3 beta hydroxysteroid dehydrogenase deficiency. Mild adrenal hyperplasia is seen in CAH and FAH of PCOS.

**Conclusion:** Further studies are needed to find the correlation between DHEAS level in obese and non-obese women with and without PCOS and to investigate the underlying mechanism of hyperandrogenism in PCOS.

**Abstract #134**

**ASYMPTOMATIC CONGENITAL ADRENAL HYPERPLASIA - DIAGNOSIS IN PREGNANCY**

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California Pacific Medical Center

**Objective:** Highlight the increasing frequency that asymptomatic genetic diseases will be diagnosed due to increased use of genetic screening.

**Case Presentation:** A 38 year-old Italian-American woman with newly diagnosed nonclassic congenital adrenal hyperplasia (NCAH) due to 21-hydroxylase deficiency (21-OHD) presented to hospital for pre-eclampsia at 30 weeks of her first pregnancy with male twins. Patient is healthy at baseline except for infertility of unknown cause. She previously failed two rounds of in vitro fertilization before conceiving this pregnancy without assistance. Only through carrier genetic screening in pregnancy was patient found to be homozygous for CYP21A2 (V282L or V281L) mutation consistent with NCAH. Patient is asymptomatic and without clinical features or history of hyperandrogenism or menstrual disorders. There is no family history of congenital adrenal hyperplasia (CAH) and no fertility issues in her sisters. Laboratory testing was significant for 17-hydroxyprogesterone (17-OHP) level of 1856 ng/dL, which is in normal range for third trimester pregnancy but also consistent with levels in NCAH screening. Given her high-risk pregnancy, patient declined ACTH stimulation test to support genetic diagnosis and to evaluate degree of enzymatic deficiency.
She underwent scheduled cesarean delivery at 34 weeks with no complications.

**Discussion:** CAH due to 21-OHD is the most frequent autosomal recessive genetic disease with over 100 CYP21A2 mutations known. 21-OHD CAH is divided into three categories: classic salt-wasting, classic simple-virilizing, and nonclassic late-onset. The hallmark of NCCAH is post-natal hyperandrogenism of variable degree and possible impaired fertility but may also be completely asymptomatic. This discordance between genotype and phenotype has been observed in prior studies and may result in undiagnosed disease or delayed diagnosis. Most asymptomatic CAH patients were previously identified in family members of probands through genetic screening. In this patient's case, if she had not received carrier genetic screening in pregnancy, she likely would not have been diagnosed since she was asymptomatic except for her impaired fertility and she lacked family history of CAH.

**Conclusion:** As genetic screening tests are more commonly used, we will be seeing more patients with asymptomatic or minimally symptomatic genetic diseases and asked to comment on them. In cases like this, I propose that management should focus on counseling and educating patients and their families, while evaluating phenotypic expression through history, laboratory testing, and/or imaging studies.

Abstract #135

**A MALIGNANT PHEOCHROMOCYTOMA TREATED WITH AGGRESSIVE MEDICAL AND SURGICAL INTERVENTIONS**

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Medical University of South Carolina

**Case Presentation:** Introduction: Pheochromocytomas are rare catecholamine-secreting tumors arising from chromatin cells of the adrenal medulla, of which approximately 10% are malignant. The prognosis is variable with 5-year survival rates between 12 - 84%. There is sparse data on the available treatment options, most of which are palliative. We present a case of a metastatic pheochromocytoma for which aggressive therapy was initiated including medications, debulking surgery, and I-123 MIBG-therapy.

Case: 36 year old man with history of hypertension presented with facial swelling and hypertensive emergency. Review of systems was positive for night sweats, palpitations, flank pain, weight loss, and headaches for the last several months. Physical exam was unremarkable except for blood pressure of 241/131. Plasma and 24 hour urine catecholamines were markedly elevated with a predominance in plasma normetanephrines (50-fold) and urine normetanephrines (110-fold). Cortisol, DHEA, 17OH-progesterone, electrolytes were normal. CT abdomen showed a 9.3 cm left adrenal tumor with tumor thrombus extending from the left renal vein to the inferior vena cava. PET scan showed multiple hypermetabolic hepatic and para-aortic lymph node metastases. MIBG scan showed avid disease in the upper abdomen and liver. After a multidisciplinary meeting and discussion with the patient, the decision was made to undergo surgery and subsequent MIBG therapy.

The patient required alpha blockade with doxazosin 14 mg BID and beta blockade with metoprolol 75 mg BID before surgery. He underwent a left adrenalectomy, nephrectomy, splenectomy, lymph node resection, IVC thrombectomy and ablation of liver metastases. He required vasopressors for 24 hours post-op and then restarted doxazosin and metoprolol. Post op, there was a 94% decrease in plasma normetanephrines, although still elevated. He was discharged on terazosin 2 mg daily and metoprolol 50 mg BID.

**Discussion:** Deciding on treatment for our patient required evidence review, input from multiple subspecialties, and consideration of our patient’s wishes. Our goal was to prolong life while preserving functionality. Mortality is associated with tumor burden, so debulking surgery was the priority. Our patient was a candidate for MIBG therapy, which can prevent further tumor growth and decrease catecholamines in 50% without the toxic side effects of chemotherapy.

**Conclusion:** Treatment options for malignant pheochromocytomas consist mostly of palliative measures with limited long term evidence. Given our patient’s age and good performance status, our treatment strategy consisted of aggressive measures aimed at decreasing tumor burden surgically followed by targeted radiotherapy.

Abstract #136

**UNUSUAL CASE OF AUTOIMMUNE DIABETES IN THE SETTING OF EXTRA-ADRENAL PARA-GANGLIOMA WITH SUCCINATE DEHYDROGENASE DEFICIENCY**

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Virginia Commonwealth University School of Medicine

**Objective:** To report a case of a catecholamine-secreting aortic paraganglioma associated with a succinate dehydrogenase (SDH) deficiency and tumor-burden-dependent autoimmune diabetes mellitus.

**Methods:** We present the imaging, laboratory, and pathologic findings and describe the clinical course
of a patient with a catecholamine-secreting aortic paraganglioma with SDH deficiency who was concomitantly diagnosed with latent autoimmune diabetes of adults (LADA) at the time of paraganglioma diagnosis. 

**Case Presentation:** A 55-year-old man presented with new onset right flank pain at an outside institution. Subsequent imaging studies, biopsy results, hypertension on clinical exam, and laboratory findings were consistent with an extra-adrenal, retroperitoneal, norepinephrine-secreting paraganglioma. He was also found to have elevated serum glucose levels and positive anti-glutamic acid decarboxylase (GAD) and anti-insulin antibodies at that time, consistent with LADA, and was started on a basal-bolus insulin regimen. Surgical removal of the tumor resulted in positive surgical margins, and immunostaining demonstrated loss of succinate dehydrogenase subunit B (SDHB) expression in the paraganglioma cells, with normal, retained fumarate hydratase (FH) expression. His hypertension resolved and glycemic control rapidly improved, eliminating the need for any insulin therapy six months post-surgery. Approximately 18 months after surgery, he presented with worsening glycemic control, unintentional weight loss, and resumption of anti-hypertensive therapy to control his blood pressure. Compared to the initial presentation, his anti-GAD antibody titer increased dramatically from 97.9 to >5,000 U/mL. Imaging studies and lab results were consistent with recurrence of the paraganglioma with metastatic spread to the retroperitoneal lymph nodes. His diabetes is currently well-controlled on basal-bolus insulin therapy. 

**Conclusion:** Usually, hyperglycemia related to paraganglioma is the result of catecholamine-driven insulin resistance, inhibition of insulin release, and stimulation of glucagon secretion. We present a unique case of autoimmune diabetes in the setting of a paraganglioma with SDH deficiency, whose course of therapy and autoimmune antibody titers follow the timeline of paraganglioma treatment and recurrence.

**Abstract #137**

**A CASE OF CUSHING’S SYNDROME DIAGNOSED AS CARNEY COMPLEX SYNDROME IN AN OLDER FEMALE**

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**Case Presentation:** Carney Complex (CNC) is a rare multiple neoplasia syndrome inherited in an autosomal-dominant manner or occurring sporadically. The disease is caused by inactivating mutations or large deletions of the *PRKAR1A* gene, which encodes the regulatory subunit of protein kinase A.

We report a case of a 61-year-old Caucasian female with low back pain and hypertension on lisinopril, hydrochlorothiazide, and amlopidine. She was referred for evaluation of bilaterally enlarged adrenal glands discovered during MRI of the lumbar spine without contrast to evaluate back pain. On detailed physical exam her blood pressure was 150/100 mmHg, weight was 100 kg, and body mass index was 40. She had a round face with plethora, a firm nodule on her forehead, a café au lait spot on her face, and a blue nevus on her neck. Other physical findings included weight gain (primarily central), thick purple abdominal striae, proximal muscle weakness, and easy bruising. Laboratory testing revealed an elevated 24-hour urinary free cortisol excretion of 94.6 mcg/24hr, an elevated midnight salivary cortisol of 0.22 mcg/dL, a nonsuppressible blood cortisol level after 1 mg overnight dexamethasone administration with total serum cortisol of 21.4 mcg/dL, and baseline morning plasma corticotrophin (ACTH) level of less than 5 pg/mL. Other laboratory testing included plasma renin activity level of 4.57 ng/mL/h, plasma aldosterone concentration of 2 ng/dL, fractionated free metanephrines of 32 pg/mL, and fasting blood glucose of 180 mg/dL. MRI of the brain with and without contrast did not show a pituitary adenoma. The patient underwent bilateral adrenalectomy, and surgical pathology showed bilateral diffuse nodular cortical hyperplasia. After surgery, clinical improvement was achieved and she was started on hormone replacement therapy with hydrocortisone and fludrocortisone.

**Discussion:** Primary pigmented nodular adrenocortical disease (PPNAD) constitutes a histological benign form of bilateral adrenal hyperplasia. It can occur in an isolated form or as the main component of CNC. CNC has a diverse clinical course and is characterized by pigmented skin lesions including lentigines and blue nevi, cardiac and cutaneous myxomas, breast fibroadenoma, testicular and ovarian tumors, endocrine tumors including thyroid, pituitary and adrenal tumors. The diagnosis of CNC is presumptive if two features are present and definite when three or more occur. Most CNC patients with PPNAD present before the age of 30.

**Conclusion:** To date there have only been two cases reported in patients over the age of 60. Our case highlights the importance of including CNC as a differential cause of ACTH-independent Cushings Syndrome.
Abstract #138

BILATERAL MACRONODULAR ADRENAL HYPERPLASIA WITH SUBCLINICAL CUSHING’S AND ARMC 5 MUTATION

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Objective: Primary bilateral macronodular adrenal hyperplasia (PBMAH) is associated with variable levels of cortisol excess, large adrenal nodules, and frequently mutation in the armadillo repeat containing 5 (ARMC5) tumor suppressor gene.(1) PBMAH can present with overt Cushing’s syndrome (CS), however, as in this case, subjects also present with indolent subclinical CS.

Case Presentation: 73 year old African American male with incidentally discovered bilateral macronodular hyperplasia on CT of abdomen done for increased abdominal girth in the ED. He was asymptomatic and showed no signs of CS. Review of a prior abdominal CT performed 5 years earlier revealed identical adrenal findings. Dexamethasone suppression test was positive with adequate dexamethasone level (post-cortisol 16.9mcg/dl and post-dexamethasone 320ng/dl). Further workup showed suppressed ACTH <5 pg/ml, elevated 24hr urine free cortisol (136.1 mcg/dl), midnight salivary cortisol of 0.65 mcg/dl (<0.09 mcg/dl), and 17-hydroxyprogesterone 16 ng/dl (37-129ng/dl ). Complete mineralocorticoid and adrenal medullary evaluation was normal. His HbA1C was 5.8%, BP was well controlled on two anti HTN meds, DXA scan at L2-L4 showed a T-score of 1.6 , LFN T-score was 1.4, and RFN T-score was 1.4. Germ cell gene mutation analysis revealed a heterozygous variant (c.2485T>C, p. Cys829Arg) in the ARMC5 gene (NM_001288767.1).

Conclusion: This patient presented with subclinical CS due to PBMAH which was discovered to have been present for several years prior. PBMAH is an uncommon cause (<2 percent) of endogenous Cushing’s syndrome. (2) ARMC5 germline mutations are common in PBMAH, although this patients variant have not been previously described and is of unknown significance.

Abstract #139

A SUBTLE PRESENTATION OF AN AGGRESSIVE DISEASE

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Objective: Given the variable spectrum of clinical presentation, diagnosis of hypercortisolism is often delayed and requires a high degree of clinical suspicion. We present an initially subtle case of hypercortisolism which progressed aggressively.

Case Presentation: A 51-year-old female with a metastatic pancreatic neuroendocrine tumor (PNET), currently on a programmed cell death protein 1 (PD-1) inhibitor, presented with polyuria and polydipsia. She was found to have hyperglycemia to 540 mg/dL which was attributed to a side effect of immunotherapy. She was started on insulin as her glycosylated hemoglobin was 9.1%. C-peptide was within normal limits. Labs revealed a slightly elevated ACTH to 47 pg/mL (normal 0-46) and elevated random cortisol to 36 ug/dL (normal 4.3-22.4), but no further workup was pursued given acute illness and symptomatic improvement with glycemic control. At this time, she had no weakness, confusion, or electrolyte abnormalities.

Three weeks later, she presented with confusion, weakness, and fatigue. Physical exam revealed tachycardia, muscle wasting, proximal muscle weakness, and disorientation. There was no dorsocervical fat pad, abdominal striae, or facial plethora. She was found to be hypokalemic to 2.5 mEq/L with markedly increased ACTH to 215 pg/mL and morning cortisol to 157 ug/dL.

Given her unstable clinical status and substantial evidence of hypercortisolism, formal diagnostic testing was not pursued. The patient was diagnosed with ectopic ACTH from her underlying PNET and was treated with mifepristone. However, her hospital course was complicated by sepsis, pulmonary embolism, gastrointestinal bleeding, and eventual multi-organ failure, and she was transitioned to comfort care.

Conclusion: In the appropriate clinical setting, such as active malignancy, new hyperglycemia should prompt investigation for hypercortisolism. Though our patient’s hyperglycemia was initially attributed to immunotherapy, she had evidence of beta cell function, making an immune-mediated side effect of her PD-1 inhibitor therapy less likely. However, she initially appeared well and lacked any other manifestations of hypercortisolism, which made the diagnosis more challenging.

This case also demonstrates the challenge in management and aggressive nature of ectopic ACTH syndrome. In a period of three weeks, our patient progressed from isolated
hyperglycemia to medically refractory hypercortisolism. In such refractory cases, bilateral adrenalectomy should be considered if the patient is able to tolerate surgery.

Abstract #140

STAGING OF PATIENTS WITH MALIGNANT PHEOCHROMOCYTOMA AND PARAGANGLIOMA

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Objective: 15-17% of individuals diagnosed with Pheochromocytoma (P) and Paragangliomas (PG) will have a malignant tumor. Primary tumor size greater than 5 cm, primary tumor location (adrenal vs. extra-adrenal), and germline mutations of Succinate Dehydrogenase B (SDHB) gene are well-recognized clinical predictors of metastasis. The American Joint Committe on Cancer (AJCC) recently established guidelines for TNM staging for patients with PPG based on some of these clinical predictors. The purpose of the study is to validate TNM staging.

Methods: This is a retrospective study. Using the MD Anderson Cancer Center PPG database, a review of radiographic and pathologic reports was performed. Clinical characteristics and survival rates of patients with diagnosis of malignant PPG were assessed using statistical analysis in SPSS Statistics 22 software. Survival time was calculated as the time between the first tumor diagnosis and the last follow up date or the date of death.

Results: This study includes 123 patients with diagnosis of metastatic PPG seen between 2000 and 2017. 103 (84%) had complete information for staging. 57 (55.3%) were males, 25 (24.3%) had SDHB mutations, 58 (56.3%) had Pheochromocytomas, and 45 (43.7%) had Paragangliomas. 2(1.9%) were diagnosed with Stage I, 36 (35.0%) with Stage II, 24 (23.3%) with Stage III, and 41(39.8%) with Stage IV disease. Median Overall Survival (OS) for Stage I was 94.2(62.4-125.9), Stage II 103.9(17.4-304.5), Stage III 64.1(2.33-179.58), and Stage IV 37.3(0.23-258.20) months (P = 0.002). Of the patients with Stage III disease, 1(4.2%) was diagnosed with T1N1M0, 9(37.3%) with T2N1M0, and 14(58.3%) with T3N0M0 status. Median OS for T2N1M0 was 67.0 (2.33-132.9) and T3N0M0 (47.8-115.8) was 58.8 months (P= 0.698).

Discussion: Our study suggests that patients with stage I disease rarely develop metastasis. Approximately 63% of patients with malignant PPG do not present with distant metastasis at the time of initial diagnosis. Regional nodal metastasis and tumor invasion into adjacent tissues (pancreas, liver, kidney, etc) is associated with similar risk for distant metastasis and decreased OS.

Conclusion: Our preliminary results seem to validate the current AJCC TNM staging for PPG. Further data collection will include patients diagnosed with non-metastatic disease with a follow up period of ten years for comparison.

Abstract #141

X-LINKED ADRENOLEUKODYSTROPHY UNMASKED BY TRAUMATIC BRAIN INJURY

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Objective: X-linked Adrenoleukodystrophy (X-ALD) is an inborn error of metabolism from accumulation of very long chain fatty acids (VLCA) manifesting as neuromuscular disease or primary adrenal insufficiency (PAI)1,2. We present a case of X-ALD with refractory hypotension following severe head trauma.

Case Presentation: A 29-year-old male was admitted with severe traumatic brain injury after an assault. Hospital course was complicated by recurrent hyperkalemia, hyponatremia, and hypotension requiring pressor support. Physical exam was notable for palmar hyperpigmentation. CT trauma scan showed small adrenal glands without calcifications. History revealed previous hospitalization complicated by hyponatremia and maternal uncle with X-ALD. Cosyntropin stimulation test (ACTH 3294 pg/ml; cortisol 60 min 3.1 mcg/dL), negative 21-hydroxylase antibodies and elevated C26:0, C24/22, C26/22 levels confirmed diagnosis of X-ALD. Stress dose steroids resulted in clinical improvement. He was discharged on hydrocortisone and fludrocortisone.

Conclusion: X-ALD is an inborn error of metabolism that leads to accumulation of VLCA with destruction of nervous system white matter and adrenal cortex 1,2. It presents in early childhood with cognitive and behavioral impairment, early adulthood with progressive paresis, or as PAI only2. Studies have estimated prevalence in young adult males with idiopathic PAI as 35%3. Endocrine Society recommends screening males with PAI and negative 21-hydroxylase antibodies for VLCA. Treatment consists of steroid replacement if adrenal glands are affected2. Hematopoietic stem cell transplantation may be considered with early brain involvement2. This case highlights the importance of careful physical exam and history to elicit the diagnosis of X-ALD.

References:
Abstract #142

A PHASE 2 STUDY TO EVALUATE THE EFFECTS OF CABOZANTINIB IN PATIENTS WITH UNRESECTABLE METASTATIC PHEOCHROMOCYTOMAS AND PARAGANGLIOMAS

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Objective: Malignant pheochromocytomas and paragangliomas (MPPG) are frequently hypervascular and associated with bone metastases. Cabozantinib is a potent anti-angiogenic tyrosine kinase inhibitor that also targets the c-met receptor. C-met mutations have been found in patients with MPPG. Cabozantinib could be an effective treatment for MPPG.

Methods: This is an investigator initiative phase 2 clinical trial. The trial has two branches: 1. Patients with measurable disease (n=14); 2. Patients with predominant/exclusive bone metastases (n=8). Patients require histological confirmation and demonstration of disease progression over one year. Patients receive Cabozantinib at initial dose of 60 mg daily with dose reduction to 40-20 mg depending on tolerability. Primary endpoint: objective response rate; secondary endpoints: progression free-survival (PFS), blood pressure control, quality of life, and safety.

Results: 15 patients have been enrolled. Median age=53 years, (range 37– 79); median number of previous systemic therapy=1 (range 0 – 2). 5 patients carry germline mutations of the SDHB gene. Six patients with measurable disease achieved a partial response (>30% reduction) and three patients achieved moderate responses (15-30% reduction). 5 patients with predominant bone metastases exhibited disease stabilization (as per FDG-PET) and no skeletal related events. One patient had disease progression. Tumor shrinkage has been observed in lymph nodes, liver, and lung metastases and has been associated with blood pressure improvement, disappearance of diabetes mellitus, and improvement of performance status. PFS=12.1 months (range 0.9-28). PFS before treatment=3.2 months. Toxicity has led to a reduction of the dose of Cabozantinib from a starting dose of 60 mg to 40-20 mg daily in 13 patients. Most common toxicities have been grade 1-2 fatigue, dysgeusia, and hand and foot syndrome. No grade 4 or 5 adverse events related to Cabozantinib have been reported. Genomic analysis has not found mutations or amplification of the c-met gene. All patients with SDHB mutations and most patients with apparently sporadic MPPG have responded to Cabozantinib.

Discussion: Cabozantinib causes tumor shrinkage in patients with measurable disease and disease stabilization in patients with bone metastases. Cabozantinib seems a safe medication for patients with MPPG.

Conclusion: Cabozantinib may be an effective treatment for patients with MPPG
PREDIABETES/DIABETES MELLITUS

Abstract #200

A REAL-WORLD, OBSERVATIONAL STUDY OF WEEKLY EXENATIDE ADDED TO BASAL INSULIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (NCT02895672)

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Objective: Glucose-lowering agents frequently prescribed for the management of type 2 diabetes mellitus (T2DM), including insulin and sulfonylureas, are associated with an increased risk for weight gain and hypoglycemia; two adverse effects clinicians work to mitigate. Glucagon-like peptide-1 (GLP-1) receptor agonists are effective anti-diabetic agents which are not only associated with appreciable reductions in HbA1c, but also weight loss and a placebo-like risk for hypoglycemia. Recently, use of liraglutide was found to be associated with cardiovascular benefit. This is a pre-post observational study from an endocrinology ambulatory care practice that assessed the effectiveness and safety following the addition of the GLP-1 receptor agonist, weekly exenatide, to basal insulin therapy in patients with T2DM. Liraglutide plus basal insulin served as a comparison group.

Methods: A data collection form was utilized to collect study-related information. The primary study outcome was change in HbA1c from baseline to 12 months after GLP-1 receptor agonist therapy was added to basal insulin. Secondary outcomes were change in weight, percentage of patients achieving an HbA1c of less than 7% (53 mmol/mol) or less than or equal to 6.5% (48 mmol/mol), changes in blood pressure and lipid parameters. Safety was assessed by a collection of reported adverse events.

Results: One-hundred and fifty patients met inclusion criteria (seventy-five per treatment arm). After one year of therapy, HbA1c decreased by 0.7% in the entire cohort (once-weekly exenatide: -0.7%; once-daily liraglutide: -0.8%; no significant between-group difference). More subjects in the weekly exenatide arm achieved an HbA1c < 7% (53 mmol/mol) [p = 0.03], but a comparable number achieved an HbA1c ≤ 6.5% (48 mmol/mol). Of note, the baseline HbA1c was lower in the weekly exenatide arm (7.9%) compared to the liraglutide arm (8.4%). No significant differences were observed between groups for other secondary outcomes; however, weight decreased by five pounds in each arm. A similar number of subjects discontinued therapy, primarily due to gastrointestinal-ill effects, and the incidence of hypoglycemia was similar compared to the previous year.

Discussion: These real-world data reflect the benefits associated with GLP-1 receptor agonist therapy – appreciable reductions in HbA1c, weight loss and a placebo-like risk for hypoglycemia. Select guidelines currently recommend this class as the preferred add-on therapy for patients with an entry HbA1c greater than or equal to 7.5% (58 mmol/mol).

Conclusion: The addition of once-weekly exenatide to basal insulin was associated with appreciable reductions in HbA1c and weight without an increase in hypoglycemia at one year.

Abstract #201

UNDERSTANDING PUBLIC AWARENESS REGARDING THE ASSOCIATION BETWEEN TYPE 2 DIABETES AND CARDIOVASCULAR DISEASE: FINDINGS FROM THE “FOR YOUR SWEETHEART™” SURVEY

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Objective: While clinicians are aware of the association between type 2 diabetes (T2D) and cardiovascular disease, it is less clear whether individuals with T2D and their loved ones (as potential health-seeking motivators) understand the importance of cardiovascular disease as the major cause of morbidity and mortality in T2D.

Methods: KRC Research conducted an online survey (Oct. 24 – Nov. 1, 2016) among US adults (≥18 years) to evaluate the degree of awareness regarding the link between T2D and cardiovascular disease. The survey administration process was validated. Participants were identified online based on demographic information and received an email invitation. Quality checks of the data received ensured that duplicate or fraudulent respondents were excluded. Incomplete surveys were excluded.

Results: Of 13 027 participants recruited, 1505 completed the survey (12% response rate); 501 with T2D, and 1004 consumers, of whom 364 knew someone with T2D (eg, spouse/partner, friend, relative, colleague; ‘SweetHearts’). Of those with T2D, 52% (n=262) were unaware that patients with T2D are at increased risk of cardiovascular disease and related macrovascular events. People with T2D were more likely to be aware of the increased risk of microvascular disease (retinopathy [57%; n=287], nephropathy [57%; n=287], neuropathy [64%; n=321]) and diabetes than macrovascular disease (myocardial infarction [41%; n=208], stroke [43%; n=216]) and diabetes. Despite cardiovascular disease being the leading cause of death in T2D, 67% (n=336) of those with T2D and 69% (n=252) of SweetHearts were unaware of this, which were similar figures to those of all consumers (74%; n=740). People with T2D indicated that they would take preventive measures if they were aware
of their increased risk of cardiovascular disease: 88% (n=440) would modify their diet, and 81% (n=408) would talk to their healthcare provider. Of respondents with T2D, 73% (n=366) indicated that a desire to live longer/spend more time with family would motivate them to decrease their risk of cardiovascular disease.

Discussion: Results from this analysis indicate a lack of awareness of the association between T2D and cardiovascular disease in those most likely to be affected.

Conclusion: Results also highlight an interest in learning and changing behavior that is motivated, in part, by social bonds.

Abstract #202

THE INFLUENCE OF METFORMIN ON SERUM CARBOHYDRATE ANTIGEN 19-9 (CA 19-9) LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS

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Objective: Diabetes mellitus has been claimed to be a risk factor for the development of pancreatic carcinoma. CA 19-9 has a great sensitivity in detection of pancreatic adenocarcinoma. Metformin exhibits a strong and consistent antiproliferative action on several cancer cell lines including pancreatic cancer. We aim to determine the influence of metformin on CA 19-9 levels in type 2 diabetes mellitus patients.

Methods: Total 193 patients with type 2 diabetes mellitus were registered for a single centre, cross-sectional study. On the basis of treatment modalities, patients were divided into metformin group (93 patients) and non-metformin group (100 patients). Detailed history, clinical examination, anthropometric measurements, serum CA 19-9 level, glucose and lipid metabolic profiles were determined. Results were presented as mean±SD. Association between CA 19-9 level and other variables were assessed with Pearson correlation and multiple stepwise regression analysis.

Results: Mean CA 19-9 level was 18.99±4.30 U/ml in the metformin group as compared to 30.49±5.61 U/ml in non-metformin group (p<0.001). Mean value of CA 19-9 was found highest among all i.e. 37.05±4.94 U/ml in patients taking insulin. Patients having lifestyle modification for the management of diabetes had their mean CA 19-9 level of 21.39±5.62 U/ml. CA 19-9 level is positively correlated with age, duration of diabetes, BMI, 2-hour Plasma Glucose level, HbA1C, VLDL cholesterol, triglyceride, total cholesterol, LDL cholesterol (p<0.005) and negatively correlated with HDL cholesterol (p<0.001).

Conclusion: Metformin is associated with lower level of CA 19-9 in type 2 diabetes mellitus patients. It may have a protective role in preventing pancreatic damage and pancreatic cancer in diabetic individuals. CA 19-9 level could be an effective indicator of glycemic control, disease progression and lipid metabolism in patients with type 2 diabetes mellitus.

Abstract #203

THE REAL LIFE EFFECTIVENESS, METABOLIC EFFECTS AND TOLERABILITY OF HYDROXYCHLOROQUINE ONCE DAILY IN THE TREATMENT OF TYPE-2 DIABETES MELLITUS

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Objective: There are limited therapeutic alternatives to treat patients with type 2 diabetes mellitus (T2DM) recalcitrant to conventional combination of oral hypoglycemic agents and unwilling to take insulin. Aim of this study was to evaluate the efficacy and safety of hydroxychloroquine in patients with uncontrolled T2DM on a combination of two oral hypoglycemic drugs.

Methods: A prospective, investigator initiated, observational, single-centred study was conducted where 49 patients with age between 18-65 years, with uncontrolled T2DM on a combination of two oral hypoglycemic drugs with HbA1c ≥7.5%, fasting plasma glucose of ≥126 mg/dL or 2-hour plasma glucose ≥200 mg/dL and body weight ≥60 kg were prescribed hydroxychloroquine sulphate 400 mg once daily for 24 weeks. Mean change in HbA1c, blood glucose, serum creatinine and lipid parameters at baseline, week 12 and 24 were assessed using paired t-test. Results: Nearly 15% reduction in fasting glucose, 23% reduction in postprandial glucose and 12.5% reduction in HbA1c levels was observed after 24 weeks of treatment (<0.0001). None of the patients discontinued the drug during the course of the treatment owing to side effects.

Discussion: According to the International Diabetes Federation’s (IDF) estimates, there were 415 million people with diabetes aged 20–79 years in 2015 and 5.0 million deaths attributable to diabetes. Most patients with T2DM initially respond to sulfonylurea and/or metformin, and later these agents lose their effectiveness with time. For the patients uncontrolled on a two-drug combination therapy, the option left is either addition of third oral drug or insulin.
High cost and poor compliance limits the use of insulin. The newer patented therapies like gliptins and SGLT-2 inhibitors are comparatively costly. Hydroxychloroquine is a generic, inexpensive and relatively well tolerated drug. In this study, hydroxychloroquine has been used as an add-on to the combination of two oral antidiabetic drugs resulting in significant reduction of fasting glucose, postprandial glucose and HbA1c levels at the end of 24 weeks. It was well tolerated with no discontinuation. Conclusion: Hydroxychloroquin was seen to be a potent third agent in the above population for better control. With favorable effects on clinical parameters of T2DM, and widely reported pleiotropic benefits, hydroxychloroquine could emerge as a valuable therapeutic option for the treatment of T2DM. Being relatively cheaper it becomes a viable fallback, especially in developing countries.

Abstract #204

GLP1 AGONIST DULAGLUTIDE AND PROTEINURIA REDUCTION IN OBSESE DIABETES PATIENT WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS

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Objective: In patients with type 2 diabetes, GLP1 agonists have been shown to reduce new onset macroalbuminuria in clinical trials (liralutide, semaglutide) and to reduce degree of proteinuria in smaller studies. We report a case of dulaglutide’s significant reduction of nephrotic range proteinuria in kidney disease due to biopsy proven focal segmental glomerulosclerosis superimposed on mild diabetic nephropathy. This finding suggests that GLP-1 agonists may play a role in non-diabetic proteinuric kidney disease.

Case Presentation: A 41 year old obese male was diagnosed with Type 2 Diabetes in September 2016 with a hemoglobin A1C of 6.5%. The patient opted for dietary management alone and declined Metformin. In April 2017, A1C was 6.9%, urine protein/creatinine ratio 6.8 (nl 0.1-0.15) and creatinine 1.6 mg/dL (eGFR 48 mL/min). The patient’s weight was 267 lbs (BMI 39.41). He was started on Dulaglutide 0.75mg once weekly as monotherapy in April 2017 onward. 6 months may be related to the weight loss induced by the Dulaglutide and possibly direct renal protective effects of dulaglutide unrelated to glucose lowering.

Conclusion: GLP-1 agonists have been shown to reduce onset and progression of diabetic nephropathy. We report a case of improvement in proteinuria using GLP-1 agonists in nephrotic renal disease due to FSGS in a severely obese man. GLP-1 agonists may be beneficial in proteinuric kidney disease due to etiologies other than diabetes. The mechanism by which proteinuria decreased by 75% over 6 months may be related to the weight loss induced by the Dulaglutide and possibly direct renal protective effects of dulaglutide unrelated to glucose lowering.

Abstract #205

CAN CYSTIC FIBROSIS RELATED DIABETES IMPROVE AFTER LUNG TRANSPLANT?

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Case Presentation: Cystic fibrosis related diabetes (CFRD) has features of both type 1 and type 2 diabetes mellitus; insulin insufficiency due to chronic obstructions of pancreatic ducts and insulin resistance peripherally due to chronic infections. More than 50% of patients over age 30 have CFRD, prevalence increases with age. Lung transplant (LT) is the current modality used to increased survival of patients with CF. Generally, CFRD is known to worsen post LT postulated due to chronic daily steroid use, immunosuppressants that increase insulin resistance in the setting of a higher BMI post LT. Here we present a patient who not only has decrease in insulin requirements post LT despite weight gain but now has a high c-peptide compared to minimal c-peptide pre LT.

Conclusion: A 35yo woman with history of CF and CFRD, underwent double LT; diagnosed with CFRD 3 years prior to LT. She was treated with basal-bolus insulin regimen of Glargine 15units daily, a carbohydrate ratio (CHO) of 1:15 with correction factor (CF) of 1:30 above 130. Immediately post-transplant she had a low c-peptide level of 0.5ng/ml (0.2 -2.7ng/ml) with a concurrent blood glucose (BG) of 133mg/dl. However, post LT she began to require less insulin despite gaining weight, daily steroid (Predisone 10mg) and double immunosuppressants (Tacrolimus and Sirolimus) that worsen insulin resistance. Interestingly at four years after LT she was noted to have a high c-peptide level of 2.8mg/ml (0.2-2.7mg/ml) with a concurrent BG of 88mg/dl. She is not requiring meal time insulin; basal dose of Glargine has decreased to 10units and CF of 50 above 150mg/dl.

It is not uncommon that post LT, patients with CF have worsening of CFRD or develop diabetes mellitus however
to our knowledge, very limited data is reported in the literature for improvement of diabetes post LT. The literature search supports this phenomenon of worsening or development of CFRD post LT. However, some data in the literature supported improvement of CFRD or resolution in select patients with CF post LT. The patient presented has an improvement of diabetes post LT. This may be in part due to recovery of insulin release post transplant as indicated by increase in c-peptide levels 4 years post-LT. The pathophysiology of this change is unclear. In discussion with the transplant lung transplant colleagues, they also have noticed cases with improvement in diabetes post lung transplant. Due to this emerging opposing data, the area of CFRD evolution post LT needs further characterization especially with use of specific markers such as c-peptide to be able to understand this disease process better.

Abstract #206

CANAGLIFLOZIN AND SITAGLIPTIN INDUCED ACUTE PANCREATITIS

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Objective: Acute pancreatitis induced by drugs used to treat diabetes mellitus (DM) is a rare but clinically significant entity. Though sitagliptin has been recognized to be associated with varying degrees of pancreatitis in multiple studies, there is limited data on the association of pancreatitis with canagliflozin use. Here, we present a case of acute pancreatitis associated with taking canagliflozin and sitagliptin.

Case Presentation: A 54-year-old woman with type 2 DM, dyslipidemia, and hypertension presented to our hospital complaining of epigastric pain for two weeks duration. She described the pain as 4/10 in intensity (with 10 indicating most severe pain), constant, radiating to the mid-back, without known aggravating or alleviating factors. She denied having fever, nausea, vomiting, constipation, or diarrhea. She was otherwise asymptomatic. Her home medications included canagliflozin, which she began taking 1 month before presentation; sitagliptin, taken for the past year; metformin; glimeperide; simvastatin; and lisinopril daily. She noted that her last alcoholic drink was 15 years ago. She denied having a history of pancreatitis, gallstones, hypercalcemia, chronic infections, abdominal trauma, autoimmune conditions, or history of malignancy. On examination, she had normal vital signs. Her BMI was 34.7 kg/m2. There was tenderness and guarding in the epigastric region. The rest of the physical exam was unremarkable. Laboratory investigations disclosed a serum lipase of 511 IU/L (normal 10-60 IU/L). A complete metabolic panel, lipid profile, complete blood count, and urinalysis were within normal limits, as was an electrocardiogram. Abdominal computed tomography showed mild to moderate inflammatory changes and small amount of fluid surrounding the pancreatic head, consistent with acute pancreatitis. There was no evidence of gallstones, biliary dilation, or gallbladder disease. The patient’s symptoms resolved within 2 days of stopping canagliflozin and sitagliptin, in addition to standard supportive care.

Discussion: Drug-induced pancreatitis is commonly overlooked, partly due to its rarity. A meta-analysis in the Trial Evaluating Cardiovascular Outcomes with Sitagliptin suggested a small increased risk of pancreatitis. In the current literature, four cases of canagliflozin induced pancreatitis have been published, with one case of necrotizing pancreatitis occurring in a patient taking sitagliptin plus canagliflozin. Larger studies are needed to evaluate the risk of pancreatitis with use of canagliflozin.

Conclusion: In this case report, we highlight the importance of awareness regarding the potential increase in risk of acute pancreatitis with use of canagliflozin alone, or when added to sitagliptin.

Abstract #207

IMPORTANCE OF FURTHER EVALUATION FOR NON ALCOHOLIC FATTY LIVER DISEASE IN DIABETES PATIENTS WITH ELEVATED ALANINE TRANSAMINASE

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Objective: To determine the need for further evaluation of nonalcoholic fatty liver disease (NAFLD) in patients with diabetes and elevated alanine transaminase (ALT)

Methods: Electronic medical records from 2007 to 2014 of 1550 patients, age > 18 years, with diabetes were reviewed for elevated ALT. Patients with alcohol use and hepatitis were excluded. Among the patients with elevated ALT, records were reviewed for the presence of abdominal ultrasounds with features of NAFLD. Patients with elevated ALT and abnormal ultrasounds were divided into 3 groups: 1) HbA1c >7%; 2) BMI >30; 3) BMI >30 plus HbA1c >7%.

Results: Of the 1550 charts reviewed, 484 (31.2%) had elevated ALT (cut off values for male >45 U/L, female
After excluding alcohol use and hepatitis, 390 (80.5%) had elevated ALT. Of the 3 groups, 251 (64.3%) had HbA1c >7%, 223 (57.1%) had BMI >30 and 146 (37.4%) had both HbA1c >7% plus BMI >30. Out of 390 patients, 73 had abdominal ultrasounds. Among which 43 (59%) showed the features of NAFLD. Of the 3 groups, 58% had HbA1c >7%, 37% had BMI >30 and 14% had BMI >30 plus HbA1c >7%.

Discussion: NAFLD, a spectrum of liver disorders, has 57-80% prevalence in patients with diabetes depending on the diagnostic method. Noninvasive methods lead to delay or under diagnosis of NAFLD. It is associated with increased cardiovascular events, liver fibrosis, and metabolic consequences in diabetes. To improve the prognosis, high level of suspicion is necessary to diagnose NAFLD. We reviewed the association of abdominal ultrasounds in patients with diabetes and elevated ALT. In our study ALT was elevated in 38% of patients with diabetes. ALT is not the best marker for diagnosing NAFLD; however, of the patients with elevated ALT, more than 50% of abdominal ultrasounds showed features of NAFLD.

Conclusion: As endocrinologists, screening for NAFLD in diabetes patients with ALT and subsequent imaging may serve as an initial evaluation. Early intervention with lifestyle modification and pharmacologic agents may modify the disease progression.

Abstract #208

DIABETIC KETOACIDOSIS WITH PEMBROLIZUMAB THERAPY FOR MERKEL CELL CARCINOMA.

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Objective: Pembrolizumab therapy is associated with endocrine immune related adverse events including thyroid, pituitary, and adrenal disorders and, less commonly, type 1 diabetes mellitus with ketoacidosis. There have been 10 case reports of diabetes associated with pembrolizumab therapy. Of the reported cases of diabetic ketoacidosis (DKA) with pembrolizumab, five of the 10 cases have positive autoimmune diabetes markers. In four of the 5 cases of DKA with negative autoimmune diabetes markers, the c-peptide levels are very low or undetectable. We report a case of a patient on pembrolizumab therapy for Merkel Cell Carcinoma presenting with DKA with negative autoimmune diabetes markers and normal c-peptide level.

Case Presentation: 71-year-old man with Merkel Cell Carcinoma (T2, N1) of the right lower extremity being treated with pembrolizumab for 6 months presented to his Urologist’s office with complaints of polyuria and polydipsia. He had past medical history of hypothyroidism diagnosed 3 months prior and thought to be associated with pembrolizumab therapy, hyperlipidemia, hypertension, gout, and obesity. Although he had no history of diabetes, his father had diabetes. He had an A1C of 5.8% nine years before this visit and a serum glucose level of 378 mg/dL without anion gap thirteen days prior to this visit. Blood testing was ordered at the visit showing a blood glucose of 992 mg/dL with anion gap of 19. The patient was directed to the emergency room. Physical examination on admission was remarkable for blood pressure of 119/96 and BMI of 33.47 kg/m2. The admission labs showed sodium 122 mM (136-144), chloride 81 mM (101-111), bicarbonate 23 mM (22-32), beta hydroxybutyric acid 3.99 mM (0.00-0.27), triglycerides of 448 mg/dL(25-150), lactic acid 2.5 mM (0.4-2.8), A1C 11.8% and normal lipase. Urinalysis was positive for glucose >500 and ketones. Two days after admission, his c-peptide was 1.2 ng/mL (1.1-1.4). Autoimmune diabetes markers (Gad-Abs, Insulin Abs, Islet cell Abs) were all negative. The DKA resolved with insulin drip treatment. He was discharged on daily insulin glargine and aspart.

Conclusion: DKA is a potentially life threatening endocrine immune related adverse event associated with pembrolizumab treatment. This case demonstrates a patient who had risk factors for type 2 diabetes (obesity, abnormal A1C in the past, and family history) and presented with DKA after 6 months of therapy with pembrolizumab. While he did not have autoimmune markers for type 1 diabetes or a low c-peptide, he had significant DKA. This is the first case that we are aware of a patient with Merkel Cell Carcinoma being treated with pembrolizumab that developed DKA with a normal serum C-peptide level.

Abstract #209

PHASE 4 STUDY OF SAFETY AND EFFICACY OF THE FIRST ANTI-INFLAMMATORY DRUG APPROVED IN INDIA IN TYPE 2 DIABETES MELLITUS (HYDROXYCHLOROQUINE) - A PRELIMINARY EVALUATION

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Objective: Type 2 Diabetes Mellitus (T2DM) is increasingly recognized as an inflammatory condition and hydroxychloroquine (HCQ) is the first anti-inflammatory agent approved in India for management of T2DM in patients...
uncontrolled on sulfonylurea and metformin combination. This phase 4 study evaluated safety, efficacy and effect of HCQ on various inflammatory parameters in T2DM.

**Methods:** This open-label multicentric study recruited uncontrolled (A1c ≥7%) T2DM patients receiving stable doses of metformin and sulfonylurea for at least 3 months prior enrolment. Eligible patients received HCQ 400mg/day in addition to existing therapy for 52 weeks. Efficacy was assessed by changes in glycemic and lipid parameters from baseline. Changes in systemic inflammatory markers like hsCRP, WBC and ESR were also assessed.

**Results:** Of the 600 planned subjects, results of 208 (females 60%, mean age 49 years, median diabetes duration 4 years, mean hsCRP 5.14mg/l) who have completed at least 24 weeks follow-up are discussed herein. Patients were divided into 2 groups based on baseline hsCRP (≤3 and >3 mg/l). 65% females and 37% males had hsCRP >3. Both groups were comparable at baseline with respect to mean A1c, FBG, PPG and lipids. Adding HCQ led to significant fall in inflammatory parameters in both groups with numerically higher fall in hsCRP >3 arm: A1c (-1.42 vs -1.19%), FBG (-22 vs -15mg/dl) and PPG (-43 vs -33mg/dl). Significant reduction in inflammatory markers was seen only in the hsCRP >3 arm. Lipids (total-, LDL-, nonHDL-cholesterol and triglycerides) were reduced significantly in both groups. Interestingly, %change in LDL-C was significantly more in hsCRP >3 group (p=0.035). Non-responders (no change or rise in A1c) were significantly lesser in hsCRP >3 group (5.7% vs 14.6%, p=0.037). HCQ was well tolerated with common treatment-related adverse events being mild-moderate and included GI symptoms (3.5%) and hypoglycaemia (2%).

**Discussion:** A critical component of T2DM is chronic, low-grade inflammation, recently referred to as ‘metaflammation’. Our study also reports 88% subjects having moderate to high hsCRP levels (>1 mg/l). Enrolled population had more females and they had higher inflammatory load. Addition of HCQ led to significant reduction in A1c (1.3%) and other glycemic parameters which is comparable to existing oral anti-diabetic agents. Besides this, HCQ also significantly reduced lipid and inflammatory parameters which are typically deranged in T2DM. Benefits of HCQ were more pronounced in patients with higher inflammatory load.

**Conclusion:** T2DM patients have high inflammatory load and HCQ provides effective and well-tolerated option with beneficial effects on lipid and inflammatory markers.

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Abstract #210

**WHEN TRANSLATIONAL MEDICINE HITS REALITY: THE HYBRID CLOSED-LOOP INSULIN DELIVERY SYSTEM IN REAL-LIFE PATIENT EXPERIENCE**

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**Objective:** Patients with Type 1 DM struggle with their disease management. In 2016, pivotal trial results regarding efficacy of a hybrid closed-loop (HCL) insulin delivery system led to FDA approval of this linked automated insulin delivery and continuous glucose sensor system (CGM). The objective of our study was to review experience of this HCL system in practice, as compared to published trial data.

**Methods:** Data was reviewed from 26 patients with type 1 DM started on the Medtronic Minimed 670G insulin pump/CGM between April and August 2017. Blood glucose and insulin delivery data was uploaded to a centralized system prior to November 21, 2017. Several parameters were evaluated before and after initiation of HCL start and compared to a previously published trial.

**Results:** Demographics: Six (23.1%) male, age 44.9±11.0 yr, duration of diabetes 25.48±11.0 yr. Total daily dose (TDD) insulin, time in range (TIR), active insulin time (AIT), sensor average glucose (SG), hemoglobin A1C, and weight were compared before and after HCL initiation and with prior trial results (table). Percentage of time hyperglycemia (SG>180 mg/dL) decreased with intervention and was less than pivotal trial, time in range (SG 70-180 mg/dL) increased. One patient had severe hypoglycemia, but hypoglycemia rates were rare prior to initiation of the HCL system and after HCL start. Change in TDD insulin was less in our cohort, pivotal trial data showed a daily insulin increase of 3U compared to our cohort’s 0.5U. Measured hemoglobin A1C showed only trend toward improvement. Pump setting of AIT required adjustment from 2.3 hours used in the pivotal trial.

**Discussion:** In this single-center analysis, patient response to a new combined insulin delivery/CGM system was reviewed and compared to published trial results. Important differences were noted. Our cohort had less hypoglycemia at baseline but one severe episode when starting HCL. Trial AIT setting was used in the first patients in our group but, due to hypoglycemia, required increase for subsequent patients. TIR improved in both studies but the improvement in our cohort was due solely to the reduction in hyperglycemia. Hypoglycemia was low...
at entry onto HCL, perhaps due to participant’s prior use
of the pump feature “suspend-before-low”. In our cohort,
improvement in SG did not translate to early decreased
hemoglobin A1C (data not available in 9 patients).
Conclusion: This analysis offers preliminary data from
experience with a new HCL system. Results differ
significantly from published trial data. We offer practical
experience with a novel technology.

Abstract #211
ANALYSIS OF A COMMUNITY HOSPITAL’S DIA-
BETIC KETOACIDOSIS MANAGEMENT PROTOCOL
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Objective: Diabetic ketoacidosis (DKA) is an acute
complication of diabetes characterized by a serum glucose
>250mg/dl, presence of serum ketones, blood pH <7.3,
and an anion gap metabolic acidosis. DKA has about
1%-5% in-hospital mortality. Management involves
fluid resuscitation, electrolyte replacement, intravenous
insulin therapy, and careful monitoring of blood glucose,
electrolytes, and pH levels until resolution. Our hospital
developed a treatment algorithm based on the latest
American Diabetes Association Guidelines for the
treatment of Hyperglycemia and Hyperglycemic Crisis
in adults. The PowerPlan includes a step-wise treatment
algorithm from diagnosis to resolution. The PowerPlan
is to be initiated in the Emergency Department (ED) on
diagnosis of DKA and requires basic metabolic panel
(BMP) and venous blood gas (VBG) every two hours.
The objective of this project was to assess the outcomes
of patients treated for DKA according to the PowerPlan.

Methods: This study analyzed medical records data from
patients treated for DKA according to the PowerPlan
from April 1, 2016 to January 31, 2017 (N=189). Patients
were included in the study if they met the criteria for
DKA diagnosis and had the DKA PowerPlan initiated
on admission. Patients were excluded from the study if
the DKA PowerPlan was not initiated on admission. Data
from the chart reviews included triage time, diagnosis
time, PowerPlan initiation time, insulin dosage, timing of
BMP and VBG, length of stay (LOS), and mortality.

Results: Of the 184 eligible patients treated for DKA
during the study period, 52% had the PowerPlan initiated
in the ED. About 75% of the patients had insulin therapy
initiated in the ED and of those, only 52% had the
appropriate insulin dosage. Incorrect insulin dosing was
associated with a 1.9 days increase in LOS (4.9 days in
correct insulin dosing compared to 6.8 days in incorrect
insulin dosing). There was variability in the timing of BMP
and VBG with average time of 3.1 hours in the ICU and
3.7 hours in the PCU. Cost of therapy was higher among
those with incorrect insulin dosing ($10,624) compared
to those with correct insulin dosing ($5,673). Incorrect
insulin dosing resulted in an increased LOS costing $2.1
million and resulted in a net loss of $1.15 million after
average Medicare reimbursement. There was no mortality
observed during the study period.

Discussion: The standardization of DKA management
with an easy-to-use PowerPlan decreases physician and
nursing variability in treatment and is credited for the
DKA mortality reduction observed in our study.

Conclusion: Education of all providers on the DKA
PowerPlan ensures prompt treatment of DKA, reduction
in LOS and mortality, and cost-effective high value care.

Abstract #212
ASSOCIATION OF SERUM INSULIN AND
URINARY ALBUMIN WITH OCCULT CORONARY
ARTERY DISEASE IN PATIENTS WITH TYPE-2
DIABETES MELLITUS
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Objective: To determine the severity of occult CAD in
type 2 diabetes patients with Fasting insulin level and
Albuminuria

Methods: The study was hospital based observational
cumulative study. It was conducted in outpatient or
inpatients department of tertiary care hospital of north
India. A total of 120 type II DM patients with no history
of IHD were enrolled. These patients were divided into
two groups as per insulin levels, Higher insulin level and
Normal insulin level. These two groups were further divided into three
subgroups as per duration of type II DM to access the
ongoing atherosclerosis and risk of CAD.

Group I 20 patients type II DM with ≤5years duration.
Group II 20 patients type II DM with >5 years to ≤10 years
duration.
Group III 20 patients type II DM >10 years duration.

Each enrolled patient was subjected to detailed medical
history, demography and physical examination. Blood
samples were obtained for testing of blood sugar (fasting
and PP), lipid profile, liver and renal function. Urine
samples were obtained for testing of Microalbuminuria, 24
hrs urinary albumin and urine complete. ECG, X-ray, USG,
CTMT, 2D echo, and CT angiography was also performed.

**Results:** In group 1 the incidence of CAD with normal insulin levels was single vessel disease 25, double vessel disease 10 and triple vessel disease 10, while in high insulin group single vessel disease was 60, double vessel disease 5 and triple vessel disease 10.

In group 2 the incidence of CAD with normal insulin levels was single vessel disease 35, double vessel disease 10 and triple vessel disease 5, while in high insulin group single vessel disease was 25, double vessel disease 35 and triple vessel disease 15.

In group 3 the incidence of CAD with normal insulin levels was single vessel disease 30, double vessel disease 20 and triple vessel disease 25, while in high insulin group single vessel disease was 35, double vessel disease 20 and triple vessel disease 35.

**Discussion:** In type II DM, CAD generally is detected in an advance stage with an extensive atherosclerosis and poor outcome. Diabetes is an important risk factor for development of CAD. It has been estimated that 75 of the deaths in diabetic patients may be attributed to CAD.

The detection of silent CAD in patients with diabetes will assume even greater importance as a health issue in the future as the number of people with diabetes increases.

**Conclusion:** Higher incidence of silent CAD in patients with diabetes is reasonably correlated with hyperinsulinemia which is strong marker for atherogenesis as well as with Microalbuminuria. This observational study is much more relevant in developing country every asymptomatic diabetic should be screen for occult CAD by means of simple test like CT angio.

Abstract #213

**INSULIN HYPERSENSITIVITY – A CHALLENGING PROBLEM**

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**Case Presentation:** Introduction: Hypersensitivity reactions to insulins have been described. Reactions to insulin itself are rare (0.1-3%) but may have a significant impact on the management of diabetes.

A 72-year old man with Type 2 Diabetes was managed with metformin alone for 12 years. He was placed on Prednisone for suspected Polymyalgia Rheumatica and developed hyperglycemia. Insulin Glargine was started at night and later Insulin Gulisine was added at meal times. On this regimen, glycemic control improved. He was tapered off the Prednisone but continued to require multiple insulin injections for glycemic control.

Unfortunately, after four months of insulin therapy, the patient began to notice redness, swelling, pruritus, and burning pain at insulin injection sites. Reaction described was delayed in onset, with discomfort occurring 4 to 6 hours after injection. His insulins were changed to Insulin Detemir and Insulin Aspart. Skin preparation and pen needles were changed. He continued to have localized symptoms. Rotations to NPH insulin and Novolin Regular insulin, then Humulin N and Insulin Lispro insulins were unsuccessful in eliminating his symptoms. No relief was found with oral antihistamines. With improvement in diet, the insulin requirement reduced from 180 units down to 110 units daily. Glycemic control remained adequate with blood sugar readings in the 5-9 mmol range and HbA1C of 6.8%. Serum insulin antibody was found to be elevated at 3.2 kU/L (RR <0.4 kU/L). Diabetes medications were reviewed: meal time Insulin Lispro was stopped. Instead Repaglinide with meals and Metformin/Sitagliptin were started and Insulin Glargine was given at night. While the patient continued to have injection site reactions to Insulin Glargine, the reactions were milder and this once daily injection was better tolerated that multiple insulin injections. Ultimately, the patient achieved glycemic control with combination of Repaglinide 2-3 mg with meals, Metformin/Sitagliptin 1000/50 mg twice daily, Insulin Glargine 60 units at night and dietary modifications.

**Discussion:** The injection site reactions were delayed often by 4-6 hours. No other systemic symptoms were present. There was redness and some induration at the site. There was no eczematous changes. Insulin antibody levels were elevated. No relief was found with oral antihistamines. Considering the redness and induration, possible Type 3 reaction was possible. Trial of other insulins were not helpful. Eventually, meal time insulins needed to be stopped and patient had to be managed with oral agents instead.

**Conclusion:** The patient described had persistent delayed injection site reactions with no response to antihistamines. Considering the redness and induration, possible Type 3 reaction was possible. Trial of other insulins were not helpful. Eventually, meal time insulins needed to be stopped and patient had to be managed with oral agents instead.
Abstract #214

IMPROVEMENT OF GLYCEMIC CONTROL AND INSULIN RESISTANCE IN HYPOGONADAL MEN WITH TYPE 2 DIABETES (T2DM) RECEIVING UP TO 10 YEARS OF TESTOSTERONE TREATMENT IN A REAL-LIFE REGISTRY

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Objective: To assess long-term effectiveness and safety of testosterone undecanoate injections (TU) in hypogonadal men with T2DM from a registry.

Methods: Registry of hypogonadal men (T ≤12.1 nmol/L) in a single urologist’s office. Of 776 patients, 286 (37%) had T2DM. 133 received TTh with TU 1000 mg/12 weeks (T-group). 153 opted against TTh and were controls (CTRL). Measurements were performed 1-4 times a year. Mean changes over time between groups were compared by mixed effects model for repeated measures with random effect for intercept and fixed effects for time, group and their interaction, and adjusted for age, weight, waist circumference, fasting glucose, blood pressure and lipids to account for baseline differences between groups. Mean (median) follow-up was 6.9 (7) years in the T-group and 7.3 (8) years in CTRL.

Results: Mean age: 61.8±5.4 (T-group), 64.2±4.6 years (CTRL). HbA1c progressively decreased from 8.8±0.9 to 5.9±0.3% after 10 years (T-group) and increased from 7.3±0.6 to 9.5±0.9% in CTRL, estimated adjusted difference between groups: 4.6% (p<0.0001 for all). Fasting glucose decreased from 7.6±1.1 to 5.3±0.1 mmol/L (T-group) and increased from 6.2±0.6 to 6.9±1.0 mmol/L in CTRL, between-group difference: 2.2 mmol/L (p<0.0001 for all). HOMA-IR decreased from 10.2±2.0 to 3.6±1.2 (T-group) and increased from 7.4±1.4 to 11.4 in CTRL, between-group difference: 9.4 mmol/L (p<0.0001 for all). Fasting insulin decreased from 29.6±4.2 to 15±4.8 µU/mL (T-group) and increased from 26.5±2.6 to 37 µU/mL in CTRL, between-group difference: 23.1 µU/mL (p<0.0001 for all).

At baseline, 54 patients in the T-group received insulin, mean dose: 32.4±12.1 U/d. Dose requirement declined to 20.6±11.3 U/d. In CTRL, 55 patients received insulin at baseline, mean dose: 29.4±5 U/d. Dose requirement increased to 39.5±7.2 U/d, between-group difference: 25.7 U/d (p<0.0001 for all).

T-group: 106 (80%) achieved HbA1c <6.5%, 116 (87%) achieved HbA1c <7% at last measurement. In CTRL, no patient achieved either HbA1c <6.5% or HbA1c <7.0%. All but 1 man had an increase in HbA1c.

T-group: 4 patients (3%) died of non-cardiovascular events. CTRL: 24 patients (15.7%) died, 26 had a non-fatal MI, 24 stroke.

Discussion: The study was not randomized nor designed to investigate effects of TTh on T2DM. Adherence to TTh was 100% as all injections were given in the office and documented.

Conclusion: Long-term TTh in hypogonadal men improved T2DM. Measuring testosterone in men with T2DM and correcting hypogonadism, as recommended in the AACE obesity guidelines, supports standard T2DM treatment.

Abstract #215

ASSOCIATION OF CORNEAL SENSITIVITY WITH CAROTID INTIMAL MEDIAL THICKNESS (IMT) IN ASIAN INDIAN TYPE 2 DIABETIC SUBJECTS THE CHENNAI URBAN RURAL EPIDEMIOLOGY STUDY (CURES)


MDRF

Objective: Loss of corneal sensation has been reported in people with diabetes and relates to the severity of retinopathy and neuropathy but no data exist on association of corneal sensitivity with carotid intimal thickness, a marker, strongly associated with cardiovascular disease. This paper deals with the relationship between loss of corneal sensitivity and carotid intimal thickness.

Methods: 944 type 2 diabetic patients were recruited from the Chennai Urban Rural Epidemiology Study, an ongoing epidemiological study in South India. Corneal sensitivity was measured using a Cochet Bonnet aesthesiometer (C-BA (model II; Luneau Ophthalmologie, Chartres, France) and grading was done on the basis of corneal sensation felt at the aesthesiometer filament length. It was graded as normal (60 mm), moderately reduced (55 mm) and significantly reduced (≤ 50 mm). Carotid IMT was measured as per standard protocol already published.

Results: Corneal sensitivity was normal in 670 (70.9%), moderately reduced in 197 (20.9 %) and significantly reduced in 77 (8.2%) type 2 diabetic subjects. The mean carotid IMT was highest (0.93 mm) in significantly reduced corneal sensitivity group, moderately higher (0.89 mm) in moderately reduced corneal sensitivity group and minimum (0.84 mm) in normal corneal sensitivity group. There was a significant difference in carotid intimal thickness with in the groups (p < 0.001). Significant differences in carotid...
IMT was also observed in normal to significantly reduced corneal sensitivity group (p < 0.005) and moderately to significantly reduced corneal sensitivity group (p = 0.016). Corneal sensitivity was also found to be associated with neuropathy (as measured by Vibration perception threshold at right great toe) and with duration of diabetes. **Conclusion:** This study shows that loss of corneal sensation is associated with carotid intimal medial thickness in type 2 diabetic subjects

**Abstract #216**

**ABSENCE OF CHANGES IN GALECTIN-3 WITH INSULIN SENSITIZATION AND ANTI-INFLAMMATION**

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**Objective:** Galectin-3 (gal-3) has recently been shown to mediate insulin resistance in mice. Its deletion leads to insulin sensitization while its excess is associated with insulin resistance.

**Results:** We undertook an investigation into its role in the reversal of insulin resistance in three human models of insulin sensitization: (1) 6 months following bariatric surgery (RYGB) and weight loss in patients with morbid obesity; there was a reduction in BMI from 52.1±4.8 to 40.4±4.0 kg/m2 (p<0.001) and HOMA-IR fell from 7.1±1.1 to 2.1±0.3 (p<0.001); (2) 12 weeks of pioglitazone (45mg/day) treatment in obese patients with type 2 diabetes, when HOMA-IR fell from 3.5±0.7 to 2.1±0.4; and (3) following 6 months of testosterone replacement in obese patients with type 2 diabetes and hypogonadotropic hypogonadism, when HOMA-IR fell from 4.2±0.9 to 2.7±0.4. Gal-3 levels at baseline were 7.6±1.1, 5.7±0.9 and 4.4±0.7ng/ml, respectively in the 3 groups. In all three models, there was no significant change plasma concentrations of gal-3 (8.0±1.2, 5.9±0.9 and 5.8±0.9ng/ml, respectively) following interventions.

**Conclusion:** There was no change in the expression of gal-3 in peripheral blood mononuclear cells either. Thus, insulin sensitization in all three human models is not associated with any significant alteration in either plasma concentrations or cellular expression of gal-3. Our data do not support a key role for gal-3 in the pathogenesis of insulin resistance or its reversal.

**Abstract #217**

**INTERACTION ANALYSIS OF CAPN10 AND PGC-1A GENES WITH TYPE 2 DIABETES IN THREE UNRELATED ENDOGAMOUS GROUPS OF NORTH-WEST INDIA: A CASE-CONTROL AND META-ANALYSIS STUDY**

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**Objective:** Calpain 10 (CAPN10) gene regulates the pancreatic β-cell function and uptake of insulin-stimulated glucose. The present study is aimed to study the association of CAPN10 SNP-43 (rs3792267), SNP-19 (rs3842570) and SNP-63 (rs5030952) polymorphisms in T2D among ethnically diverse populations from Punjab (North-west India).

**Methods:** A total of 1125 samples including 554 T2D patients and 571 controls belonging to three endogamous groups from North-West India (202 cases and 207 controls from Banias, 151 cases and 158 controls from Brahmans, 201 cases and 206 controls from Jat Sikhs) were included.

**Results:** The allele and genotype frequencies of studied SNPs between cases and controls showed variable pattern of association with T2D among studied endogamous groups. The A allele of SNP-43 provided 1.5-2 fold risk for T2D development in Brahmin and Jat Sikh cohort. Intriguingly, the D-allele of CAPN10 SNP-19 played protective role against T2D in Brahmins whereas; it provided 1.4-fold T2D risk in Jat Sikh group, thereby, highlighting the importance of ethnicity in case-control studies. The T allele of SNP-63 posed 1.6 fold T2D risk in Bania and Jat Sikh groups.

**Discussion:** Minor allele (A-allele) of CAPN10 SNP-43 polymorphism was validated to confer increased risk by 1.33-fold towards T2D predisposition when various studies were complied and analyzed which is consistent to the risk causing effect of A-allele in all groups of present study except Bania population. Interestingly, the D-allele of CAPN10 SNP-19 polymorphism played protective role against T2D in Brahmns whereas; it provided 1.4-fold T2D risk in Jat Sikh group, thereby, highlighting the importance of ethnicity in case-control studies. The T allele of SNP-63 posed 1.6 fold T2D risk in Bania and Jat Singh groups.

**Conclusion:** Minor allele (A-allele) of CAPN10 SNP-43 polymorphism was validated to confer increased risk by 1.33-fold towards T2D predisposition when various studies were complied and analyzed which is consistent to the risk causing effect of A-allele in all groups of present study except Bania population. Interestingly, the D-allele of CAPN10 SNP-19 polymorphism played protective role against T2D in Brahmns whereas; it provided 1.4-fold T2D risk in Jat Sikh group, thereby, highlighting the importance of ethnicity in case-control studies. The T allele of SNP-63 posed 1.6 fold T2D risk in Bania and Jat Singh groups.
in Indian populations for better diagnosis and prognosis.

**Conclusion:** The CAPN10 emerged as a genetic risk factor for T2D among different ethnic groups of North-West India emphasizing the role of ethnicity in the etiology of complex disease like T2D.

**Abstract #218**

**PREDICTORS OF ANTEPARTUM ADMISSION IN DIABETES**

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**Objective:** Diabetes is associated with increased healthcare utilization and cost in pregnant women. We therefore sought to investigate the predictors of antepartum hospitalization in pregnant women with diabetes.

**Methods:** We performed a retrospective review of women with pregestational diabetes who received care in a multidisciplinary diabetes in pregnancy program from 2006-2011. We collected data on demographic and socioeconomic factors, medical comorbidities and glycemic control. Our primary outcome was antepartum hospitalization, with a secondary measure of length of stay. We modeled the multivariate odds of hospitalization prior to delivery using logistic regression.

**Results:** We identified 244 women during the study period of whom 103 (42.2%) required antepartum hospitalization. The median length of stay was 5 days (interquartile range of 14 days). The most common indications for hospitalization were glycemic control (53, 51.4%) and hypertensive disorders of pregnancy (43, 41.7%). The distribution of age, race and body mass index (BMI) was similar among both groups (Table). A similar proportion of women had type 2 diabetes (63.6% among women not hospitalized vs 63.1% of women hospitalized, p=1). Women who were admitted were more likely to have public insurance (59.2% vs 44.6, p=0.048) and had a higher first HbA1c on average (mean of 8 + 1.94 vs mean of 6.84 + 1.34) (table). In a multivariate model, chronic hypertension was associated with increased odds of antepartum admission (odds ratio 1.5, 95% CI 1.24-1.81). Type of diabetes, initial HbA1c, race or insurance were not significantly predictive of length of stay.

**Discussion:** Pregnant women with diabetes incur high health care costs. However, current data on predictors of hospitalization are limited. We found that initial HbA1c during pregnancy and chronic hypertension were associated with increased hospitalization in pregnant women with diabetes. Hyperglycemia prior to pregnancy is a modifiable risk factor which if optimized might prevent hospitalizations and decrease heath care costs.

**Conclusion:** In our population of women with diabetes, health prior to pregnancy was strongly predictive of need for antepartum admission, suggesting the importance of a renewed emphasis on preconception health for reproductive-aged women with diabetes.

**Abstract #219**

**WHAT? I’M DIABETIC? A CASE OF PEMBROLIZUMAB INDUCED DIABETES PRESENTING AS DKA**

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**Objective:** Immune checkpoint inhibitors have been increasingly used in immunotherapy. Pembrolizumab is a monoclonal antibody that inhibits PD-1, used in treatment of advanced / metastatic malignancies. It blocks the inhibitory ligand of the PD-1 (programmed cell death 1) receptor. It has been shown to precipitate type 1 diabetes in non-obese diabetic mice models and recently more cases are being reported of occurrences in humans. We report a case of antibody negative acute diabetic ketoacidosis warranting hospitalization in a patient with no prior history of diabetes on pembrolizumab for metastatic angiosarcoma.

**Case Presentation:** A 70-year-old caucasian male with significant history of metastatic angiosarcoma of the spleen s/p splenectomy and no history of diabetes presented to the emergency department with polydipsia, polyuria, and hyperglycemia when checked at home. There was no history of flu, fever, URI, or other infection. Patient’s paternal grandmother had diabetes. He was being treated for his angiosarcoma, and was on a protocol using pembrolizumab 200mg IV q3 weeks which was started 25 days earlier. The patient was not on steroids or other diabetogenic medication. Patient was dehydrated, tachycardic, glucose was 569, urinary ketones present, HCO3 was 16, and AGAP 23. GAD antibodies, insulin antibodies, and islet cell antibodies were all negative. Insulin level was in normal range. C-peptide was low at .5 ng/mL (.9 - 7.1). Hemoglobin A1c was 6%. Thyroid function and baseline cortisol were within normal range. Pt was treated for diabetic ketoacidosis appropriately and patient was started on insulin. A month later, he had an A1c of 7.5% and c-peptide was undetectable. Pembrolizumab was still continued for angiosarcoma.
**Discussion:** The action of PD-1 is down regulation of the immune system. In normal individuals, programmed cell death allows tolerance to self-antigens and limits normal tissue auto-immunity and destruction. Tumor cells may over express the PD-1 ligand, thereby binding to T-cells and deactivating them. Pembrolizumab is an IgG-4 monoclonal antibody, an immune checkpoint inhibitor, preventing the interaction of PD1-PDL1. By decreasing programmed cell death, it removes negative regulation for T-cell activity, increases immune function, thereby risking autoimmunity as well. PD-1 ligand is expressed on pancreatic islet cells, thus lending proclivity for auto-immune diabetes, though he was antibody negative. The only therapy known is insulin. It is unknown if discontinuing pembrolizumab would allow pancreatic function to return.

**Conclusion:** Due to the increasing use of various immunotherapies, physicians should be aware of this rare side effect of T1DM, and consider screening as appropriate.

**Abstract #220**

**24-HOUR WEARABLE BASAL-BOLUS INSULIN DELIVERY DEVICE IMPROVES TIME IN RANGE AND TREATMENT SATISFACTION OVER MULTIPLE DAILY INJECTIONS- A PILOT STUDY**

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**Objective:** To evaluate the change in percent time in range (80 to 140 mg/dl) and treatment satisfaction when switched to a 24-hour wearable insulin delivery device (V-Go) from multiple daily injections (MDI).

**Methods:** This is a single center, prospective, pilot study conducted in a real-world practice setting under usual standard of care. Patients diagnosed with type 2 diabetes on stable doses of ≥ 3 insulin injections had sensors placed to monitor 24-hour glucose levels for ≥ 7 days using a blinded continuous glucose monitoring (CGM) system (Freestyle Libre Pro). Following the CGM evaluation for MDI, patients were switched to V-Go and CGM was conducted after 1 month of V-Go use. Self-monitored blood glucose (SMBG) logs, insulin dosing, weight and use of concomitant agents were also evaluated. A patient questionnaire measured treatment satisfaction.

**Results:** Ten patients were recruited of which 9 eligible patients switched to V-Go with 7 completing the study. Bruising and not staying adhered to skin (both V-Go and CGM sensor) were reported reasons for discontinuation. The mean age was 64 yrs, weight 226 lbs, and insulin total daily dose (TDD) 97 U/day (n=1 premix, n=6 basalbolus) at baseline. Known insulin duration ranged from 2 to 17 yrs. After 1 month on V-Go, mean time in range increased by 35% and TDD with V-Go decreased from 97 to 59 U/day (p=0.029). On a patient basis, 6 out of 7 patients experienced improvement in time in range (49% increase) and a decrease in TDD from 83 to 56 U/day (p=0.020). Concomitant agents were not adjusted during the study. Across all patients, ease of use and treatment satisfaction favored V-Go with reported scores of 9 out of 10 for both measurements compared to MDI therapy scores of 5 and 4 out of 10, respectively. Patients ranked their overall experience with V-Go as 8 compared to 5 out of 10 with MDI therapy. Further, patients reported they were less likely to miss mealtime insulin doses with V-Go. No significant change to weight was observed.

**Discussion:** Glucose profiles were improved in most patients when switched from MDI therapy to V-Go. These findings are impressive considering, first, V-Go CGM occurred the week of Thanksgiving in 5 out of 7 patients, secondly the targeted time in range in this study was narrow (80 to 140 mg/dl) and lastly insulin dosing was not maximized with V-Go.

**Conclusion:** Glucose time in range was increased and total insulin dose decreased with V-Go compared to MDI therapy in this pilot study. Higher treatment satisfaction and better adherence were also reported with V-Go. Larger trials are warranted to further evaluate.

**Abstract #221**

**COMBINATION THERAPY WITH ONCE WEEKLY GLP 1 RECEPTOR AGONIST DULAGLUTIDE AND SGLT2 INHIBITORS IN ASIAN INDIANS WITH TYPE 2 DIABETES**

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**MDRF**

**Objective:** Obesity and diabetes pose a global challenge. Drugs used in the management of type 2 diabetes tend to increase body weight. Dulaglutide and SGLT 2 inhibitors have shown a potential of weight loss with better glycaemic control. This paper deals with the effect of combination of Dulaglutide and SGLT 2 inhibitors on obesity and glycaemic control in Asian Indians with type 2 diabetes.

**Methods:** We performed a retrospective study to look into the effects of SGLT2 inhibitors and Dulaglutide in patients with type 2 diabetes mellitus (in addition to their existing antidiabetic regimen) from the diabetes electronic medical records of a tertiary care hospital for diabetes at Chennai in South India.183 patients on SGLT2 inhibitors and Dulaglutide combination, who came for their first follow-up visit between 3 to 6 months, were included in
Objective: The prevalence of obesity, pre-diabetes and diabetes is increasing at an alarming rate, especially in the Southeastern United States. It is estimated that more than 85 million Americans now have pre-diabetes and 9 out of 10 are unaware. Without intervention, 15-30% of people with pre-diabetes will develop type 2 diabetes within 5 years. Point of care (POC) hemoglobin A1c (HbA1c) testing allows for immediate access to HbA1c values during a medical visit.

Methods: New patients at the university-based obesity clinic have POC HbA1c values tested at each patient’s initial visit unless a recent HbA1c is available within last 3 months. Patients are instructed to arrive to the clinic having fasted for at least 4 hours prior to the visit. A Siemens DCA Vantage POC HbA1c machine is used for all testing. HbA1c reference range, as defined by the American Diabetes Association, was used.

Results: Over an approximate 30 months, a total of 968 new patients had POC HbA1c values tested. Of those, 31.5% were found to have HbA1c value in the normal range; 44.4% had HbA1c in pre-diabetes range; and, 24.0% had HbA1c in diabetes range. The age range for the total population was 18 - 81 with a median age of 49; no difference in the 3 HbA1c categories. The majority of the population were women, 79.3%, with no significant difference between groups. BMI did not differ between groups.

Discussion: POC HbA1c assays are a time-efficient tool for identifying persons with or at-risk of diabetes during a medical visit. Identifying pre-diabetes or diabetes at the initial visit at a weight loss clinic could help patients progress through the stages of change necessary for weight loss success and reversal of the pre-diabetes or diabetes. Traditional methods for diabetes diagnosis include evaluation of glucose on multiple occasions or use of oral glucose tolerance testing, which are time consuming and could delay diagnosis. Limitations of this analysis include a possible under-detection of diabetes as these patients were more likely to have had a HbA1c checked in the 3 months prior to their visit. Additionally, without conclusive evidence of hyperglycemia, HbA1c results should be confirmed with additional testing but this was not available for this analysis.

Conclusion: POC HbA1c testing is a useful tool for identifying people with pre-diabetes in a weight loss clinic at an academic medical center who are at risk of progressing to diabetes and identifying otherwise undiagnosed diabetes.

Abstract #223

A CASE OF DIABETIC KETOACIDOSIS IN PREGNANCY

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Objective: Diabetes has affected people worldwide across different ethnicity, gender, including the obstetric population. We report a case of a 28 year-old, multi-gravid, who has not been previously diagnosed with diabetes in her 1st and 2nd pregnancy, with no family history of diabetes, but developed severe Diabetic Ketoacidosis (DKA) in her third pregnancy.

Case Presentation: A 28 year old, Filipino, on her 24th week age of gestation presented with dyspnea and vomiting. On admission, she was received lethargic and hypotensive with a blood pressure of 80/50mmhg, a heart rate of 120-130 beats per min, and tachypneic. She had muscle weakness and significant premature uterine contractions. Her random blood glucose was only 357 mg/dl but was severely acidotic. Arterial Blood Gas revealed a ph of 7.036, HCO3 of 2.6 mmol/L and PCO2 of 9.5 mmHg, with serum ketones of 4.9mmol/L and an anion gap of 34mmol/L. An ultrasound

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of the abdomen revealed a single live, 24 weeks by fetal biometry with good cardiac and somatic activity, but with sonographic consideration of hydrops fetalis with cardiac enlargement. She was advised to have a complete prenatal diagnostic work up for which she did not comply, and came in with a critical presentation that has lead to maternal and fetal complications.

**Discussion:** Pregnancy is a physiologic state that can lead to a significant change in metabolism. Understanding the biochemical feedback compared to the non-pregnant state is important in the diagnosis of diabetes. A serious but rare metabolic complication is DKA in Pregnancy. Our case is a rare complication of diabetes in pregnancy in the era of approved insulin analogue use. The incidence of DKA in Pregnancy varies from 0.5%, the lowest reported rate in western countries to 8.9% in a study conducted in China. The degree of hyperglycemia in pregnancy complicated by DKA does not present with significant elevation as it may be blunted due to several maternal and fetal adaptive mechanisms. Therefore, it is a diagnostic challenge because the glucose levels are either near normal or not as elevated as the non-pregnant DKA state due to the biochemical feedback.

**Conclusion:** This case illustrates a rare but preventable complication of pregnancy. If diagnosed right away and managed properly, maternal complications can be minimized. Review of hospital records did not show any similar reported case in the files of Cebu Doctors’ University Hospital. Our case illustrates vigilance in diagnosis as it may have long term complications both for the mother and the unborn child.

**Abstract #224**

**MEAL INTAKE IS SUPPRESSIVE OF KETOGENESIS IN PATIENTS WITH TYPE 1 DIABETES**

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**Objective:** To investigate whether the intake of a meal suppresses ketogenesis in patients with type 1 diabetes

**Methods:** 30 patients with type 1 diabetes with no C-peptide, fasted overnight, were divided into 3 groups of 10 patients each. The first (group 1) continued the fast for 5 hours after arrival in our clinical research unit while the second (group 2) was administered a high fat high calorie (HFHC) meal without preprandial insulin and the third (group 3) was administered the meal with preprandial insulin. Blood samples were obtained prior to and after the meal at hourly intervals for 5 hours.

**Results:** In group 1, glucose and glucagon concentrations remained unchanged while FFA concentrations increased (by 74±16%) as did acetacetate (AcAc) and beta-hydroxybutyrate (BHB) concentrations (by 52±13% and 64±16%, respectively). In group 2, the intake of the meal without preprandial insulin induced marked increase in glucose, glucagon and FFAs (by 235±32%, 81±18% and 75±17%, respectively) concentrations. However, the meal induced significantly lower increase in AcAc or BHB concentrations (increased by 29±9% and 35±11%, respectively) compared to group 1. In group 3, given preprandial insulin before the meal, there was a significant reduction in glucose and glucagon concentrations as compared to group 2 and a fall in FFA concentrations (by 41±12%) below baseline levels. There was no significant increase in AcAc and BHB

**Discussion:** While a prolonged fast was associated with maintenance of glucose and increases in FFA, AcAc and BHB concentrations, the intake of the meal prevented increases in AcAc and BHB in spite of increases in glucose, glucagon and FFA concentrations.

**Conclusion:** These actions are consistent with an anti-ketogenic effect of the meal intake even in type 1 diabetes with an absence of β cell function
20 µg between 6-7 pm or placebo (P group) subcutaneous daily and prospectively evaluated at baseline, 3 and 12 months with bone turnover markers (BTM) (P1NP and CTX, ng/ml), foot radiographs, F18-PET/CT (Discovery) and DXA scan (Hologic) at region of interest (ROI). The primary outcome measures were the changes in BTM, Standardized Uptake Value (SUVMAX)on F18-PET scan, bone mineral density (BMD) and progression of deformities as measured by talar-declination (TDA), talocalcaneal (TCA) and calcaneal-inclination (CIA) angle on plain radiographs from baseline.

Results: Final analysis was done for 20 patients (ten patients in each arm). Mean age was 55±7.8 and 52.3 ± 8.83 years and duration of diabetes 15.8± 7.45 and 13.7± 6.56 years within group P and T, respectively. Midfoot was the most common region involved in both the groups. There was a significant increase in SUVMAX at ROI in group T contrary to decrease in group P at 3 and 12 months (Fig. 1). Both P1NP (14.21±3.9, p<0.01) and CTx (0.035±0.030, p<0.01) increased within group T compared to decrease in P1NP in group P (-0.67±2.26, p<0.01) at 3 and 12 months, respectively, from baseline. There was increase in BMD at ROI within group T (+0.06±0.04 g/cm2) compared to a decrease in group P (-0.058± 0.08 g/cm2) (p= 0.10) at 12 months. There were no change in angles of the foot.

Discussion: This is the first ever study to evaluate the efficacy of Teriparatide in diabetic chronic CN of foot. The study showed a significant increase in osteoblastic activity and foot bone remodeling with Teriparatide as suggested by increase in F18 tracer uptake, a trend to increase in BMD (ROI), and increase in BTM. There was no progression of deformities over one year of follow-up. The outcome measures in the present study are unique and pertinent to chronic CN.

Conclusion: Teriparatide, an osteo-anabolic agent increases foot bone remodeling, bone density and prevents progression of deformities in chronic diabetic CN.

Abstract #226

DEVELOPMENT OF AN ANTI-AP2 MONOCLONAL ANTIBODY TO TREAT OBESITY RELATED DIABETES AND FATTY LIVER DISEASE

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Objective: The lipid chaperone aP2/FABP4 has been implicated in the pathology of many immunometabolic diseases, such as diabetes and atherosclerosis. While multiple lines of evidence also supports its involvement in human disease, targeting aP2 for therapeutic applications have not yet been accomplished. Recent studies in our laboratory have shown that aP2 is not simply an intracellular protein binding lipids but an active adipokine that contributes to hyperglycemia by promoting hepatic gluconeogenesis and interfering with peripheral insulin action. Multiple groups have now demonstrated that serum aP2 levels are markedly elevated in mouse models of obesity, and human serum aP2 levels strongly correlate with BMI, insulin resistance, dyslipidemia, and cardiovascular risk. Importantly, blocking aP2 in preclinical models showed strong anti-diabetic activity. These observations raised an exciting new strategy for targeting serum aP2 to treat metabolic disease with a monoclonal anti-aP2 antibody. Here, we report the identification of a highly effective, anti-aP2 mAb, CA33, and the characterization of its effects in vivo.

Methods: We examined the properties of CA33 antibody by structural and biochemical studies including crystallography, identified its target epitopes, and demonstrated its target specificity. In hyperinsulinemic-euglycemic clamp studies, we found that the anti-diabetic effect of CA33 was predominantly linked to the regulation of hepatic glucose output and peripheral glucose utilization. We confirmed molecular effects of CA33 on hepatic glucose output with decreased gluconeogenic gene expressions and actual enzymatic activities. We investigated further effects of CA33 in energy expenditure by metabolic cage respiratory analysis.

Results: Treatment of mice with dietary or genetic obesity with CA33 lowered fasting blood glucose levels, improved glucose metabolism, increased systemic insulin sensitivity and reduced fat mass (including both white and brown adipose tissue) and liver steatosis. Furthermore CA33 successfully humanized for translational studies.

Discussion: Adipose derived molecules (adipokines) play important roles in the pathogenesis of obesity related immunometabolic disease clusters such as diabetes and fatty liver disease. Most of the time, consequences of obesity related metabolic alterations follow each other and co-morbidly sequentially. Adipose tissue centric therapeutic approaches could be utilized to ameliorate obesity related metabolic diseases.

Conclusion: We conclude that development of an anti-aP2 monoclonal antibody-mediated therapeutic is a feasible approach and would constitute a strong candidate for the treatment of diabetes and fatty liver disease.
Abstract #227

OCCURRENCE OF COMMON PATHOGEN AMONG DIABETIC FOOT ULCER PATIENTS IN SAUDI ARABIA

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Objective: To find out the occurrence of pathogens among diabetic foot ulcer patients in Saudi Arabia.

Methods: From February, 2015 to October, 2017, a retrospective analysis was performed among 126 patients aged 40-70 years at tertiary hospital, Saudi Arabia. Tissue culture method was used for the microbiological evaluation. Demographic variable such as age, gender, year of diagnosis, body mass index, education, family history of diabetes, ulcer site, peripheral vascular disease and penetration of ulcer (Wagner classification) were collected from medical records of the patients.

Results: Pseudomonas aeruginosa was the most common gram negative pathogen followed by Klebsiella spp (7.1%). Among the gram positive bacteria Staphylococcus aureus (37.3%) was the most common pathogen followed by (9%) Streptococcus. Gentamycin was the most common antibiotic sensitive among gram negative bacteria followed by ciprofloxacin (26.2%). Erythromycin (26.2%) was the most common antibiotic sensitive followed by (17.5%) augmentin. Further, the most common sensitivity antibiotic in the forefoot was erythromycin (13.6%), midfoot was erythromycin and gentamycin (3.2%), rare foot was erythromycin and gentamycin (2.4%), and dorsum area was septrin (4%). P.Sudomonous bacteria was the most common pathogen on the forefoot, midfoot, rare foot and E.coli was the most common pathogen on the dorsum of the foot. Further, the most common sensitivity antibiotic in the forefoot was ciprofloxacin and gentamycin (8.8%), midfoot was ciprofloxacin and ceftazidime (2.4%), rare foot was ciprofloxacin, gentamycin and ceftazidime (2.4%), and dorsum area was ciprofloxacin and clindamycin (0.8%). Majority of the pathogens were found on forefoot area.

Discussion: Research shows that Pseudomonas aeruginosa frequently causes severe tissue damage in diabetic foot ulcers. In the present study we found that Pseudomonas aeruginosa (16.7%) was the most common gram negative pathogen followed by Klebsiella spp (7.1%). Among the gram positive bacteria Staphylococcus aureus (37.3%) was the most common pathogen followed by (9.5%) Streptococcus. However, up to our knowledge there is no study found the sensitivity of anti-biotic based on the ulcer site/ulcer location. In this study we reported that majority of the pathogens were found on forefoot area. There were no studies discussed the frequency of pathogens and ulcer sites as per Wagner classification.

Conclusion: P. aeruginosa, Klebsiella spp, Staphylococcus aureus and Streptococcus were the most common causes of diabetic foot infections. Erythromycin and gentamycin/ augmentin could be the drug of choice before tissue culture sample collected.

Abstract #228

DAPAGLIFLOZIN SUPPRESSES PLASMA HEP-CIDIN CONCENTRATIONS

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Objective: Dapagliflozin and other SGLT2 inhibitors are known to increase hematocrit. One possible mechanism is glycosuria and polyuria and the loss of fluid from the vascular compartment. However, since type 2 diabetes is a pro-inflammatory state and since hepcidin, a known suppressor of erythropoiesis, is increased in pro-inflammatory states, we investigated the possibility that dapagliflozin suppresses hepcidin concentrations and thus increases erythropoiesis.

Methods: Twenty-two patients with type 2 diabetes and normal renal function (mean age: 62.1±1.7 years) were randomly treated with placebo or dapagliflozin 10 mg daily for 12 weeks.

Results: In the dapagliflozin group, there was a fall in HbA1c from 7.1±0.2% to 6.7±0.2% (p<0.05), increase in hemoglobin concentration from 13.2±0.8g/L to 13.8±0.4g/L (p<0.05) and in Hct from 40.2±1.3% to 41.9±1.8% (p<0.05). Plasma concentration of hepcidin fell from 265±26ng/mL to 215±24ng/mL (p<0.05). There was no significant change in any of these indices in the placebo group. Since one of the mechanisms through which hepcidin inhibits erythropoiesis is the suppression of the expression of ferroportin, which transports iron from iron storage cells into plasma, we also measured ferroportin expression in peripheral blood mononuclear cells. The expression of this transporter was not altered.

Discussion: We conclude that dapagliflozin suppresses hepcidin concentrations significantly but by a mechanism not involving ferroportin expression.

Conclusion: The decrease in hepcidin may contribute to the increase Hct and hemoglobin levels followin SGLT-2 inhibitor treatment.
Abstract #229

LOW FREE T3 IS ASSOCIATED WITH POOR GLYCEMIC CONTROL IN TYPE 2 DIABETES

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Objective: Clinical significance of low free T3 (FT3) has not been well explained in patients with type 2 diabetes mellitus (T2DM); FT3 level may be associated with diabetes control and complications. This study was carried out to explore the frequency of low FT3 syndrome in patients with type T2DM and to correlate the FT3 status with glycemic control (ie. HbA1c).

Methods: This cross-sectional study was carried out in the Endocrinology outpatient department of Mymensingh Medical College Hospital, Bangladesh from July-December 2016. Non-pregnant adults with type 2 diabetes with unknown thyroid function status were included in the sample. Patients with previously diagnosed thyroid disease or getting medications that can affect thyroid function and those who were acutely ill, non-ambulatory, having mental incapacity were excluded. HbA1c <7% was considered as well controlled diabetes and HbA1c ≥7% was considered as uncontrolled. Serum TSH, free T4 and free T3 were measured in all patients by radioimmunoassay (RIA). Low FT3 syndrome was defined as presence of low FT3 with normal TSH and normal FT4. Statistical analysis was done using SPSS version 23.0 software and P value ≤0.05 was considered to be statistically significant.

Results: This study included 153 (mean age 46.8±12 years; female 68%, mean duration of diabetes 5.5±0.53 years, 63.4% either overweight or obese) patients. The mean HbA1c was 8.3±1.7%, mean serum TSH 2.24±0.34 μIU/mL, mean FT4 16.5±6.56 fmol/mL and mean FT3 was 5.36±1.74 fmol/mL. 9.15% of the patients were found to have low FT3 syndrome. There was no statistical difference of FT3 level between male and female patients (5.87±1.50 vs. 5.99±1.85 fmol/mL, mean±SD; p=0.165) and among different BMI groups (p=0.179). But serum FT3 level was lower in patients with uncontrolled diabetes than in patients whose diabetes was controlled (5.91±1.83 vs. 6.15±1.21 fmol/mL, mean±SD) and the difference was statistically significant (p=0.024). FT3 level showed significant direct correlation with the duration of diabetes (r= 0.296, p=0.002) and FT4 level (r= 0.490, p=0.000) only in female subjects.

Conclusion: A large number of otherwise stable patients with type 2 diabetes had low free T3. Patients with uncontrolled diabetes had lower free T3 than those with controlled diabetes.

Abstract #230

UNRELIABLE HEMOGLOBIN A1C (HBA1C) IN A PATIENT WITH NEW ONSET DIABETES AFTER TRANSPLANT (NODAT)

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Objective: NODAT has an incidence at of 24% at 36 months and Autosomal Dominant Adult Polycystic Kidney Disease (ADPKD) is a known risk. HbA1c is usually the test of choice to monitor glycemic status in patients with diabetes. Whenever HbA1c is not reliable, Fructosamine levels can be monitored. Proper and reliable daily glucose logs are also a major factor when monitoring patient’s glycemic status which ideally should be match with HbA1c or Fructosamine levels.

Case Presentation: Forty seven year old male was referred due to elevated HbA1c 2 years after renal transplantation for ADPKD. HbA1c 1 month prior to initial consult was 8.1%. Prior HbA1c values had been < 6%. Patient had phlebotomy done 3 months prior, due to history of Polycythemia. Hemoglobin was 16.5 g/dL. Albumin and Total Protein were within normal limits and Ferritin was 10. He was chronically on Prednisone 5 mg daily. Daily blood glucose logs were not available at that time and he denied polyuria or polydipsia. Due to concern for unreliable HbA1c, Fructosamine level was ordered and was 406 (HbA1c 10-11%), blood glucose ranged from 200-400. Metformin was maximized and Glipizide was added. Follow up HbA1c after 3 months increased to 9.7%, but Fructosamine levels improved to 315 (HbA1c 7-8%) and his blood glucose average was mid-100s. Patient also did significant lifestyle changes and lost 7 lbs.

Discussion: Patient was diagnosed with NODAT based on persistent hyperglycemia and due the fact that he had no previous diagnosis of diabetes before kidney transplant. Solely based on HbA1c levels, his glycemia did seem to progress but blood glucose logs and Fructosamine levels did not reflect the degree of glycemia which the HbA1c seemed to have suggested. Initial and post treatment blood glucose measurements correlated with Fructosamine levels rather than with HbA1c, making Fructosamine more reliable indicator of overall glycemic control.

Conclusion: NODAT has to be considered in patients with persistent hyperglycemia after transplant. HbA1c levels are typically used to monitor and modify therapy in Diabetes.
Mellitus. Although HbA1c levels seem to be reliable in the majority of cases, re-consideration of reliability has to be considered when patients have other comorbid conditions that could influence the degree of glycation. In this particular case, the HbA1c was suggesting a higher degree of glyemia, likely influenced by a hematologic condition. This case also shows the importance of having patient measure blood glucose levels at home in order to pair with HbA1c and Fructosamine.

Abstract #231

CORRELATES OF PERIPHERAL NEUROPATHY IN TYPE 2 DIABETES IN SOUTH WESTERN NIGERIA: A PRELIMINARY REPORT

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Objective: Peripheral neuropathy is one of the common chronic complications of type 2 diabetes. Symptoms can be very distressing to patients. Prevalence increases with long duration of diabetes and poor glycemic control amongst other things. It increases the risk of diabetes foot ulcer and/or lower limb amputation in patients.

This study set out to determine the prevalence and correlates of peripheral neuropathy in type 2 diabetes patients attending an outpatient clinic.

Methods: This was a cross sectional study. Consecutive consenting subjects with type 2 diabetes attending the diabetes clinic of a tertiary hospital in Owo, South western Nigeria were recruited for the study. A structured questionnaire was used to obtain demographic data and clinical history, anthropometric parameters including weight, height, waist circumference and hip circumference were measured. Blood samples were taken for FBS, glycated hemoglobin and fasting lipid profile.

Results: A total of 41 subjects were assessed. The mean age of subjects was 59.7 + 12.8yrs. There were more females than males with a male to female ratio of approximately 1:1.6. Mean duration of diabetes was 6.9±4.2yrs, while mean BMI, FBS and HbA1C for the subjects were 25.7±4.4kg/m2, 6.4±2.7mmol/l and 8.8±2.2% respectively. Three (7.3%) of the subjects takes alcohol while only 1(2.4%) smokes cigarette. Symptoms of peripheral neuropathy was found in 30(73.2%) of the subjects while abnormal vibration perception threshold was found in 12(29.3%) of the subjects. There was positive correlation between vibration perception threshold and age, duration of DM, BMI, WHR and FBS (P= 0.004, 0.204, 0.423, <0.001, 0.164, r= 0.442, 0.208, 0.134, 0.549,0.237) respectively.

Conclusion: Symptoms of peripheral neuropathy do not always indicate peripheral neuropathy in type 2 diabetes. The risk of peripheral neuropathy in type 2 DM significantly increases with increasing age and waist hip ratio.

Abstract #232

JUMPING INTO DIABETES CONTROL

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Objective: The construct of this study (named JUMP) is to provide diabetic patients with a group setting that focuses on self-empowerment through multidisciplinary education, collaborative learning, peer support, motivational interviewing, and development of diabetes-specific social capital, ultimately to improve glycemic control.

Methods: This project established a multidisciplinary group composed of one to two resident physician facilitators, a clinical diabetic educator, and 5-10 patients with diabetes. Each session had a loose framework with the majority of the discussion being patient-led. The core program was comprised of three weekly sessions. Patients were recruited from the Internal Medicine Resident Clinic of the Greenville Health System, which provides primary care to a largely underserved population with a payer mix of approximately 40% Medicare, 20% Medicaid, and the rest self-pay/hospital sponsorship. JUMP has graduated 24 participants. As a comparison group, 24 control patients were pooled from the list of clinic patients who expressed interest in the program but subsequently were unable to enroll (primarily due to scheduling difficulties). The primary endpoint of this study was glycemic control, measured by patients’ pre- and post-JUMP hemoglobin A1c (HgbA1c).

Results: JUMP participants showed a statistically significant decrease in HgbA1c. The average pre-JUMP HgbA1c was 9.3 ± 2.5, and post was 8.0 ± 1.9. This yielded a mean drop in HgbA1c of 1.3 (p-value <0.001). This is compared to the control group which yielded pre-JUMP HgbA1c of 9.0 ± 2.2 and post 9.2 ± 2.3, a variation with no significant change (p-value 0.418).

Discussion: The United Kingdom Prospective Diabetes Study found that the rate of microvascular complications from diabetes (eg retinopathy, nephropathy, neuropathy) fell by 25% when comparing patients with a mean HgbA1c of 7.9% to those more tightly controlled at 7.0%. Among those who successfully controlled their hemoglobin A1c, the incidence of diabetes-related deaths, myocardial infarctions, and all-cause mortality was significantly lower (25%, 18%, and 7%, respectively) for each one percent
improvement in HgbA1c. This is promising given that the mean decline in HgbA1c for JUMP was 1.3%.

**Conclusion:** JUMP demonstrates that physician/health care team facilitated diabetes group sessions that utilize motivational interviewing to discuss lifestyle modification, proper medication use, and diabetes education results in a significant decrease in hemoglobin A1c. Given that microvascular complications from diabetes are reduced with better HgbA1c control, and these classes result in lower HgbA1c levels, JUMP proves to be an effective way to encourage and develop better diabetes control.

**Abstract #233**

**OUTCOMES WITH CANAGLIFLOZIN IN PATIENTS BY AGE SUBGROUPS: RESULTS FROM THE CANVAS PROGRAM**

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**Objective:** Canagliflozin is a sodium glucose co-transporter 2 inhibitor that reduced the risk of a cardiovascular (CV) composite comprising CV death, nonfatal myocardial infarction (MI), or nonfatal stroke, by 14% in patients at high CV risk in the CANagliflozin Cardiovascular Assessment Study (CANVAS) Program. The effects of canagliflozin among patients ≥65 years of age and <65 years of age were pre-specified for evaluation.

**Methods:** The CANVAS Program randomly assigned 10,142 participants with type 2 diabetes who were ≥30 years with established CV disease or ≥50 with ≥2 CV risk factors to canagliflozin or placebo. The CV and renal outcomes and the overall safety of canagliflozin were further analyzed in subgroups based on age (≥65 years and <65 years). The mean age of the 5,578 <65 years of age (mean age, 57.4 y; HbA1c, 8.3%; BMI, 32.5 kg/m²; eGFR, 82.1 mL/min/1.73 m²; history of CV disease, 62.5%) and 4,564 ≥65 years of age were pre-specified for evaluation.

**Results:** Among CANVAS Program patients, 5,578 were <65 years of age (mean age, 57.4 y; HbA1c, 8.3%; BMI, 32.5 kg/m²; eGFR, 82.1 mL/min/1.73 m²; history of CV disease, 62.5%) and 4,564 were ≥65 years of age (mean age, 70.6 y; HbA1c, 8.1%; BMI 31.3 kg/m²; eGFR, 69.6 mL/min/1.73 m²; history of CV disease, 69.4%). The primary outcome occurred in 2.26 patients <65 years of age and 3.70 patients ≥65 years of age per 100 patient-years. Risk reductions were observed for the primary outcome, hospitalization for heart failure, and progression of albuminuria in both subgroups (Figure). There was statistical heterogeneity in outcome for all-cause mortality, which was lower in patients <65 years of age (P = 0.01) but should be interpreted with caution given the large number of subgroup analyses.

**Conclusion:** The benefits canagliflozin provides on the primary outcome, hospitalization for heart failure, and albuminuria appear consistent across age groups, but the benefit of canagliflozin on all-cause mortality may be greater in younger patients.

**Abstract #234**

**HIGH PREVALENCE OF SYSTEMIC COLLAGEN VASCULAR DISEASE IN WOMEN WITH T1DM**

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**Objective:** Persons with type 1 diabetes (T1DM) are at risk for other autoimmune diseases (AIDs), including systemic collagen vascular disease (SCVD). The prevalence and clinical characteristics of SCVD in T1DM are not well described. We examined a large cohort of adults with T1DM to answer these questions.

**Methods:** A total of 1,167 adults with T1DM provided informed consent. Data was captured from a questionnaire and medical record review. Demographics, AID diagnoses, and ages of onset were recorded. Multivariate logistic regression was used to evaluate the independent effects of gender, race, and T1DM age of onset on the prevalence of SCVD, as well as additional autoimmunity. The focus of this report will be women with T1DM, who were at much higher risk of SCVD and AIDs than men.

**Results:** Women with T1D were significantly more likely to develop SCVD than men (OR:2.9 (95%CI: 1.7, 4.9); p=0.001). The mean age of the 586 females in the study cohort was 47.6 ± 15.2; 520 (89%) were Caucasian, 66(11%) were African-American. 58 (10%) of all women with T1DM developed SCVD, current mean age 53.8 ± 12.6; compared to 46.9 ± 15.3 (p=0.0009) in women without SCVD. Women age >60 were at the highest risk of SCVD (OR:7.2 (95%CI: 2.2, 24.2); p=0.0013) compared to those <29. Race was also a factor with 14.3% of African-American women and 9.4% of Caucasian women developing a SCVD (p=0.2476), NS. The SCVD diagnoses included: rheumatoid arthritis (5%), SLE (2%), psoriasis (3%), Sjogren’s (1%), granulomatosis with polyangitis (<1%), MCTD (<1%), juvenile rheumatoid arthritis (<1%), scleroderma (<1%). Women with T1DM and SCVD had a greater AID burden than those without SCVD, including 40% hypothyroidism (p=0.0370), 16% hyperthyroidism (p=0.0074), 12% pernicious anemia (p=0.1106), 10% celiac disease (p=0.0035), 9% alopecia (p<0.0001), and 5%
uveitis or other neurologic AID (p<0.0002). After adjusting for race and age, female T1DM patients with SCVD were significantly more likely to develop >2 additional AIDs (OR:2.8 (95%CI: 1.5, 5.2); p= 0.0007)).

Discussion: Women with T1DM are at high risk for developing SCVD, 10%, compared to 1-2% of women overall, with rheumatoid arthritis being the most common. The risk factors for SCVD are age and African-American race. Persons with T1DM and SCVD had a strikingly high prevalence of other autoimmune diseases. In nearly all cases, T1DM was diagnosed years before the SCVD, and the majority had other antecedent AIDs.

Conclusion: The high prevalence of SCVD and other AIDs in women with T1DM suggests that global or progressive loss of immune tolerance occurs. This phenomenon deserves more study.

Abstract #235

DIABETIC MYONECROSIS IN A YOUNG FEMALE PATIENT

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Objective: Diabetic myonecrosis is a rare complication of poorly controlled diabetes presenting with non-traumatic swelling and pain of the extremities. We present a case of diabetic myonecrosis in a patient with uncontrolled type1 DM.

Case Presentation: A 30-year-old female with PMH of uncontrolled Type 1 DM of 19 years duration with complications of peripheral neuropathy, proliferative diabetic retinopathy, diabetic nephropathy, and gastroparesis presented to the ED with complaints of gradual onset right thigh and knee pain for about 2 weeks prior to admission. She had no history of fall or trauma. Her other history included hypothyroidism, hypertension, iron deficiency anemia. Her medications included insulin, levothyroxine, duloxetine, metoprolol, metoclopramide and tramadol. On arrival, she was afebrile, pulse-108/min; RR-18/min; BP-168/90 mm Hg, Spo2 -100% on room air. On examination, she was very lean with BMI of 20.9 kg/m2 and noted to be in moderate painful distress with tenderness, swelling and warmth over the right lateral and anterior thigh. Rest of her examination was unremarkable. Lab work up showed normal WBC count, ESR 110 (0-20 mm/hr), Total CK- 357u/L (26-308), CRP- 1.40 (0-0.3 mg/dl), eGFR -40, TSH-112.0(0.3-3.74 u/ml), A1C -9.9%. Venous Doppler was negative for DVT. MRI of the thigh showed nonspecific increased signal intensity of multiple muscles with differential of muscle necrosis or infectious or inflammatory myositis. She was admitted and treated with a dose of IM ketorolac and prn morphine. Autoimmune work up showed positive ANA and Anti RNP. With suspicion of myositis, she was prescribed a short course of steroid and ibuprofen and discharged to home. She subsequently presented to the endocrine clinic few weeks after and noted to have persistent pain and swelling in the right thigh. Her clinical presentation and imaging studies were suggestive of Diabetic Myonecrosis,a rare complication of poorly controlled Diabetes. She was advised rest, prn tramadol and tighter glucose control.

Discussion: Diabetic Myonecrosis is a rare complication of diabetes seen in patients with long standing poorly controlled diabetes. They present with unexplained muscle pain, swelling and tenderness involving the extremities, typically in the thigh or calf. MRI can be useful imaging modality in diagnosis. Biopsy can show muscle necrosis and edema. It is a self-limited condition with treatment options being supportive care, NSAIDS and antiplatelet agents.

Conclusion: Diabetic myonecrosis should be suspected in patients with long standing poorly controlled diabetes presenting with muscle pain and swelling especially thigh and calf and have no other features of infection or muscle injury.

Abstract #236

RESPONSE TO HYPOGLYCEMIA AT A TERTIARY CARE HOSPITAL: A QUALITY IMPROVEMENT PROJECT

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Objective: Hypoglycemia is associated with increased morbidity and mortality among hospitalized patients. Despite many attempts to reduce its incidence, it remains a major problem in many hospitals. The aim of this study was to evaluate the causes of hypoglycemia and the measures taken to prevent further hypoglycemic episodes at a tertiary care hospital.

Methods: Blood glucose data for patients admitted to the hospital between July 2015 and January 2016 were obtained from the hospital’s electronic database for analysis. Hypoglycemia was defined as point of care or laboratory blood glucose value ≤70 mg/dL. Manual chart reviews were then performed to identify hypoglycemic episodes. Data collected included insulin regimen, diet order and nutritional intake at the time of hypoglycemia, nutritional insulin and meal timing, and actions taken after the hypoglycemia including physician notification and adjustments to the insulin regimen.
Results: Review of all blood glucose data showed an average monthly incidence of hypoglycemia at 7.88%. We randomly selected 70 hypoglycemic episodes that occurred among 34 patients on antidiabetic therapy across multiple floors for manual chart review. All 34 patients were receiving insulin therapy. The most common causes of hypoglycemia included insulin and mealtime mismatch, decrease in nutritional intake without insulin dose adjustment, excess basal insulin, and insulin stacking. As per hospital protocol, a physician was supposed to be notified at the time of any hypoglycemic episode. However, a physician was notified in only 13 (9%) of the cases. Changes in the treatment regimen to prevent further hypoglycemia were made in only 16 (23%) of the cases, whether a physician was contacted or not at the time of hypoglycemia. Hypoglycemia led to an endocrinology consultation in 3 out of 34 patients.

Discussion: Consistent with other studies, our data shows that inpatient hypoglycemia is a common problem and causes of hypoglycemia are multi-factorial. Our data also suggests that provider (nurses as well as physicians) response to prevent further hypoglycemic episodes is suboptimal. Although these data are specific to one hospital, we suspect similar problems in other hospitals. We suggest physician and nursing education with more involvement of endocrinologists for the treatment of diabetes and prevention of hypoglycemia in the hospital setting.

Conclusion: Provider response to prevent inpatient hypoglycemia is suboptimal and needs urgent attention.

Abstract #237

THE EFFECT OF THE SMART GLUCOSE MANAGER (SGM) ON GLYCOSYLATED HEMOGLOBIN (A1C)

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Objective: Smartphone use is growing rapidly in developing countries and mobile applications have begun to be utilized in the field of diabetes. However, existing mobile applications have not shown sufficient improvement on diabetes care. The aim of this study is to investigate the effectiveness of a newly designed unique mobile application called the Smart Glucose Manager (SGM) on diabetes outcome compared to the existing monitoring methods.

Current evidence suggests that the prevalence of diabetes in South Asians is high and rising in both South Asian countries, as well as in the diaspora. One in five adults in Sri Lanka has either diabetes or pre-diabetes.

Methods: A prospective randomize control trial was conducted at the Sri Jayawardenapura Hospital in Sri Lanka. Patients with an A1c ≥ 8.0% and access to Android Smart phone were recruited to participate in the study (27 in the SGM group and 25 in the control group). The SGM group was trained to use the SGM, which has unique features including reminders to check blood glucose, take medications, eat on time, and do exercise. It also allows users to enter their daily blood glucose numbers, making a table and graph of the data. The A1c levels were measured at baseline and every three months. The control group patients were asked to continue their current glucose monitoring methods. Paired t-tests and ANOVA were used for statistical analysis of the A1c values.

Results: The mean age of the study participants was 52±11 years and 40 % were female. Mean A1c of the SGM group was significantly reduced from the baseline (mean 9.7% ± 1.3) to the 3-month follow-up (8.2% ±1.0), p =0.001. The mean A1c of the control group was 9.5%±1.6 at the baseline and after the 3-month follow-up it was 8.2%±0.6. (p =0.008). The SGM group showed significant improvement of A1c from 3 months to 6 months (8.3%±0.6 vs 7.3%±0.6), p=0.005, but the control group showed no significant improvement of A1c from 3 months to 6 months (8.2 vs 7.9±0.6), p=0.16. In the 3-month follow up, the A1c of the SGM and control groups were not significantly different, p=0.98 but in 6 months the SGM group A1c showed significantly lower value compared to the control group, p=0.01.

Discussion: Reduction of mean A1c was shown in both groups 3 months after the baseline clinic visit, but after 6 months, only the SGM group continued to show statistically significant reduction of A1c.

Conclusion: The SGM has displayed a significant improvement of A1c beyond 3 months in uncontrol diabetes patients due to increased compliance via the unique features of the SGM. The SGM is a useful tool in the management of diabetes and further studies are warranted to assess the long-term impact of the SGM on diabetes care.
ABSTRACTS – Diabetes Mellitus/Prediabetes

Abstract #238

EFFICACY AND SAFETY OF LIXISENATIDE AS ADD-ON IN PATIENTS WITH T2D AGED ≥70 YEARS UNCONTROLLED ON BASAL INSULIN IN THE GETGOAL-O STUDY

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Objective: Patients aged ≥70 years are often excluded from T2D clinical trials. The GetGoal-O trial (NCT01798706) specifically enrolled elderly, nonfrail patients with T2D uncontrolled on their current therapy. This analysis assesses the efficacy and safety of lixisenatide as add-on therapy to basal insulin (BI) in these patients with or without renal insufficiency.

Methods: A post hoc subgroup analysis was performed in nonfrail patients ≥70 years, randomized to receive once-daily 20 μg lixisenatide or placebo on a background of BI ± OAD for 24 weeks. Patients were stratified by background antidiabetes therapy and presence of renal insufficiency (defined as having an estimated glomerular filtration rate (eGFR) of 30 ≤ eGFR <60 or eGFR ≥60 mL/min/1.73m²) at screening.

Results: In total, 108 patients met the inclusion criteria, of whom 36 had 30 ≤ eGFR <60 mL/min/1.73m². Average BI dose at baseline was 0.47 U/kg, indicating that most patients were approaching a point where they would require postprandial glucose control.

Overall, patients randomized to lixisenatide, compared with placebo, had significantly greater reductions in A1C, 2-hour postprandial glucose, average 7-point self-monitored plasma glucose, and weight. No significant differences between treatment arms were observed for change in fasting plasma glucose, eGFR, or daily BI dose by weight. Treatment-emergent adverse events (TEAEs) occurred more frequently in the lixisenatide group. Incidence of documented symptomatic hypoglycemia (<60 mg/dL) was low in both groups: 5.7% of lixisenatide and 12.7% of placebo-treated patients. There were no instances of severe symptomatic hypoglycemia in either treatment group. Significantly more patients treated with lixisenatide achieved >0.5% reduction in A1C with no documented symptomatic hypoglycemia compared with the placebo group (P=0.002)(Table).

Although reduction in A1C also remained significantly greater in lixisenatide-treated patients regardless of baseline eGFR, the difference was slightly greater in those with renal insufficiency (~0.68% vs ~0.55%). No significant differences for other efficacy outcomes were observed between patients stratified by baseline eGFR; insufficient numbers were available for a meaningful analysis of hypoglycemia or TEAEs.

Conclusion: This post hoc analysis suggests that adding lixisenatide in nonfrail patients with T2D aged ≥70 years uncontrolled with BI is efficacious and has a good safety profile. Furthermore, despite small expected increases in exposure and a very small sample size, this treatment approach suggests similar efficacy of lixisenatide in patients with mild-to-moderate renal insufficiency, with no dose adjustments required.

Abstract #239

INSULIN DEGLUDEC/LIRAGLUTIDE (IDEGLIRA) ACHIEVED NON-INFERIOR A1C REDUCTION, WEIGHT LOSS AND FEWER HYPOGLYCEMIC EPISODES WHILE USING A SIMPLE REGIMEN WITH FEWER INJECTIONS AND DOSE ADJUSTMENTS COMPARED WITH BASAL–BOLUS THERAPY: AN ANALYSIS OF DUAL VII

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Objective: Complex treatment regimens, such as basal–bolus insulin therapy (BB), are associated with lower compliance, greater treatment burden and poor patient satisfaction. Complex regimens are also a major concern for physicians, since they require more resources and clinical decisions – both of which become more problematic as T2D progresses. In DUAL VII (NCT02420262), IDegLira resulted in non-inferior A1C reductions (as per the trial design), weight loss (~0.9 vs. 2.6 kg), and an 89% reduction in rates of hypoglycemia compared with BB in patients with type 2 diabetes (T2D). This post hoc analysis evaluated the treatment complexity of IDegLira vs. BB in terms of number of injections and dose adjustments.

Methods: In a 26-week, open-label trial, patients with T2D uncontrolled on metformin and 20–50 U insulin glargine 100 U/mL (IGlar U100) were randomized 1:1 to IDegLira (N=252) or BB (IGlar U100 + insulin aspart ≤4 times/day; N=254). IDegLira was initiated at 16 U (16 U insulin degludec + 0.58 mg liraglutide); initial IGlar U100 dose was the pre-trial dose (mean 33 U). Both were titrated twice-weekly, based on the mean of 3 pre-breakfast self-monitored plasma glucose (SMPG), to a target of 72–90 mg/dL. Insulin aspart was initiated at 4 U/main meal and titrated twice-weekly to a pre-prandial
and bedtime SMPG target of 72–108 mg/dL. This analysis reports the observed mean number of insulin injections and dose adjustments during 26 weeks.

**Results:** Despite the lower starting basal insulin component dose with IDegLira vs. BB, the number of basal insulin dose adjustments were similar during treatment (Figure). The mean number of bolus insulin adjustments increased steadily during the trial to 200 per patient (median [min; max]): 218 [1; 569]). 66.5% of patients in the BB group were receiving ≥3 bolus injections/day at Week 26 in addition to their basal insulin and SMPG measurements in connection with each injection.

**Discussion:** Burdensome regimens impact on patients’ quality of life, treatment adherence and ability to achieve good glycemic control. Up to 41% of patients cite complexity-related concerns as the reason for delayed addition of bolus insulin (Brod et al. Curr Med Res Opin 2016;32:981–9). In DUAL VII, there were fewer injections and dose adjustments with IDegLira vs. BB, with each injection requiring SMPG readings and each adjustment requiring clinical decisions.

**Conclusion:** Compared with BB, the clinical benefits of IDegLira (comparable A1C reduction, lower hypoglycemia rates and weight loss) are achieved using a more convenient regimen with fewer daily injections, SMPG readings and dose adjustments in DUAL VII.

**Abstract #240**

**WEIGHT LOSS TRAJECTORY FOLLOWING RANDOMIZATION TO BARIATRIC SURGERY ON LONG-TERM DIABETES OUTCOMES**

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**Objective:** The 5 year outcomes of the STAMPEDE show that bariatric surgery is effective in producing both sustained weight loss and long term improvement in T2DM. However, it is unclear whether acute weight loss or the chronic trajectory of weight loss is more important for long-term T2DM improvement.

**Methods:** This is an ancillary analysis to the STAMPEDE trial cohort. 96 patients with T2DM randomized to bariatric surgery. Of these, 66% were women, mean age (± SD) was 48.1±8.2, mean BMI was 36.5±3.6, and mean HbA1c was 9.4±1.6. The 5-year follow up data following Roux-en-Y gastric bypass (RYGB, n= 49) and sleeve gastrectomy (SG, n= 47) were studied. Percent weight loss in the first year was defined as the percent decrease from baseline weight to lowest weight in the first year. Percent weight regain was defined as the percent change from lowest weight in first year to the weight at 5 years follow up. Percent weight change and baseline T2DM duration were correlated with HbA1c at 5 years using Spearman rank correlations.

**Results:** Findings are reflected in Table 1. In RYGB, less weight loss in the first year was positively correlated with higher HbA1c (r +0.50, p 0.0003) at 5 yrs. In SG , greater weight regain from nadir was positively correlated with higher HbA1c (r +0.43, p 0.003). Duration of T2DM prior to surgery was positively correlated with higher HbA1c in the RYGB cohort. In SG , those who lost more weight in the first year (≥22%) had longer duration of DM (67% had DM ≥8 years) as opposed to those who lost less (<22%, 21% had DM ≥8 years).

**Discussion:** There have been no studies previously assessing the question of whether acute or chronic weight changes play a greater role in T2DM improvement post bariatric surgery. This study suggests that acute weight loss is more important for T2DM outcomes in RYGB while chronic maintenance of weight loss is more important in SG. However, it is possible that the effect of acute weight loss in the SG cohort was obscured as individuals with more weight loss in SG had a longer duration of T2DM and likely more resistant T2DM at baseline. This finding has implications for clinician intervention post bariatric surgery.

**Conclusion:** The 5 year data for STAMPEDE shows that improvement in T2DM is most strongly correlated with first year weight loss in the RYGB cohort and chronic trajectory of weight loss in the SG cohort.


**Abstract #241**

**GLYCATED HAEMOGLOBIN AS A SCREENING TOOL IN THE DIAGNOSIS OF DIABETES MELLITUS AMONG HYPERTENSIVE ADULTS**

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**Objective:** There is the need for a convenient screening tool for Diabetes mellitus among populations at risk. Hypertension is a significant risk factor for developing type 2 diabetes. The aim of this study was to determine the prevalence of Diabetes mellitus among newly diagnosed hypertensive patients in a tertiary hospital in Southern Nigeria comparing the Glycated
Abstracts – Diabetes Mellitus/Prediabetes

Abstract #242

WORSENING GLYCEMIC CONTROL LEADS TO DIAGNOSIS OF PANCREATIC ADENOCARCINOMA IN A PATIENT WITH TYPE 2 DIABETES MELLITUS.

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Objective: Pancreatic Adenocarcinoma (PA) is associated with a high mortality. It can be cured only if diagnosed very early in its course. 50-80% of pancreatic adenocarcinoma (PA) patients have Type 2 Diabetes Mellitus (DM2), however pathological mechanisms have not been fully determined. PA may present as new onset of diabetes or worsening glycemic control in patients with pre-existing Type 2 DM. We present a patient with history of Non-Hodgkin’s Lymphoma (NHL) in remission, in which weight loss and worsening DM2 control led to the diagnosis of PA.

Case Presentation: We present a 63 year old female with DM2 for 11 years without micro or macrovascular complications. Her DM2 has been fairly well controlled with HbA1c ranging 6.0-7.2% on metformin/alogliptin and recently started Empagliflozin.

Patient presented with worsening glycemic control over last 3 months (elevated HbA1c of 8.1%). She reported no changes in her life style, dietary preferences and activity. There were no clinical symptoms or signs to suggest any evidence of infection. However in last few months, she had mildly decreased appetite and 15 lb weight loss. She attributed the weight loss to recent initiation of Empagliflozin. Otherwise she had unremarkable vitals and physical examination.

Patient had history NHL which was in remission after being treated with chemo-radiation about 10 years ago. Her family history was negative for pancreatic cancer. She has never smoked, or used tobacco products and does not consume alcohol.

Due to worsening glycemic control, she was started on basal bolus insulin regimen with Lantus and Humalog in addition to her oral diabetes agents. Given her unexplained worsening glycemic control despite weight loss, we decided to evaluate for pancreatic malignancy. CT abdomen with contrast showed a pancreatic head mass, confirmed by endoscopic ultrasound (EUS) to be 1.5x1.5 cm in size with possible abutting of superior mesenteric vein but no evidence of local or distal metastatic disease or suspicious lymphadenopathy. EUS guided biopsy was consistent with PA. Patient is being started on neoadjuvant chemoradiation followed by planned surgical resection of...
tumor. It is expected that patient will have a favorable prognosis due to early diagnosis of PA.

**Conclusion:** Unexplained changes in glycemic control in DM-2 patients, should warrant consideration of pancreatic malignancy. In our patient, unexplained worsening glycemic control in association with otherwise subtle symptoms led to PA diagnosis at a relatively earlier stage with potential for a favorable treatment outcome. Early diagnosis and treatment could be lifesaving in these patients.

**Abstract #243**

**INSULIN-INDUCED LIPOATROPHY: A RARE COMPLICATION OF HUMAN INSULIN**

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**Case Presentation:** A 58-year-old female with an 11-year history of type 2 diabetes mellitus noted onset of an indentation of the medial, proximal left arm over six-to-eight months. The patient had been managed with a basal/bolus regimen of insulins aspart and detemir for approximately seven years, and she alternatively administered insulin into the skin of both upper arms for the entire duration of insulin therapy. She denied pain, discoloration, or weakness of the left upper extremity. On examination, lipoatrophy was observed over the proximal and medial portion of the long head of the left triceps muscle. No rash, erythema, scarring, or tenderness were noted. Muscle strength, sensation and reflexes were intact. Electromyography (EMG) and a nerve conduction study ordered by the patient’s primary care provider failed to identify myopathy or nerve conduction deficits, respectively, and ultrasonography demonstrated an intact triceps muscle. The patient was advised to avoid using the lipoatrophic site for insulin injections, and she began to notice improvement approximately 2-3 months later.

**Discussion:** Insulin injection site lipoatrophy is characterized by localized loss of subcutaneous adipose tissue. Prior to the availability of recombinant human insulins, lipoatrophy was reported in ~ 25-55% of patients treated with animal insulins. Insulin induced lipoatrophy is now rare, though it has been reported with recombinant human regular and neutral protamine Hagedorn (NPH) insulins as well as rapid-acting and basal insulin analogs. Lipoatrophy may occur in either intermittent injection or continuous subcutaneous insulin infusion regimens. Lipoatrophy appears to be induced by inflammation at sites of insulin administration, and histopathology from biopsies of lipoatrophic sites reveals infiltration by inflammatory cells, antigen-antibody complexes, and deposition of immunoglobulin M with activated components of the complement system. Prolonged cessation of insulin injections at affected sites, local injections of dexamethasone, and topical application of the mast cell stabilizer cromolyn sodium have been reported to lead to improvement or resolution of lipoatrophy.

**Conclusion:** Insulin-induced subcutaneous lipoatrophy is a rare complication of therapy with recombinant human insulins, though it is important to identify as insulin absorption from affected sites can be unpredictable and contribute to poor glycemic control. Localized loss of subcutaneous fat is most clearly demonstrated by computed tomography (CT) or magnetic resonance imaging (MRI), though the diagnosis can be made clinically from a history of insulin injections at the affected site and careful examination.

**Abstract #245**

**EFFICACY AND SAFETY OF SEMAGLUTIDE IN ELDERLY SUBJECTS WITH TYPE 2 DIABETES: A POST HOC ANALYSIS OF THE SUSTAIN 7 TRIAL**

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**Objective:** The SUSTAIN 7 trial investigated the efficacy and safety of semaglutide, a glucagon like peptide 1 analog, vs dulaglutide in subjects with type 2 diabetes (T2D). This post hoc analysis compared the efficacy and safety profile of elderly (>65 years old) vs non elderly (<65 years old) subjects receiving semaglutide vs dulaglutide in the SUSTAIN 7 trial.

**Methods:** Elderly and non elderly subjects with T2D were randomized to once-weekly subcutaneous semaglutide or dulaglutide for 40 weeks. Semaglutide 0.5 mg was compared with dulaglutide 0.75 mg; semaglutide 1.0 mg was compared with dulaglutide 1.5 mg. Post baseline HbA1c and body weight (BW) data were analyzed using mixed model for repeated measurements.

**Results:** This analysis comprised 1,199 subjects (260 elderly and 939 non elderly; mean ages 69.3 and 51.9 years, respectively). Reductions in HbA1c and BW were similar in elderly and non elderly subjects across all treatment arms, and were greater with semaglutide than dulaglutide across subgroups (all p<0.05, except for HbA1c when comparing elderly subjects receiving semaglutide 1.0 mg vs dulaglutide 1.5 mg where p=0.12). The proportions of subjects achieving HbA1c <7.0% and ≤6.5% were higher...
in elderly than non elderly subjects across all treatment arms, and were higher with semaglutide than dulaglutide across subgroups (Table).

More elderly than non elderly subjects reported adverse events (AEs) with semaglutide 1.0 mg and dulaglutide 1.5 mg. More elderly than non elderly subjects reported serious AEs in all treatment arms except semaglutide 1.0 mg. Most AEs were mild to moderate in severity. A higher proportion of elderly than non elderly subjects discontinued semaglutide 1.0 mg due to AEs. The proportion of subjects discontinuing treatment due to AEs in other treatment arms was similar (Table).

Discussion: Change in HbA1c and BW from baseline was similar in elderly and non elderly subjects across treatment arms, while greater reductions were observed with semaglutide vs dulaglutide. The greater improvements from baseline in glycemic control were not associated with an increased risk of hypoglycemia.

Conclusion: In the SUSTAIN 7 trial, reductions in HbA1c and BW were comparable in both elderly and non elderly subjects. These improvements in glycemic control in elderly subjects were not associated with a higher incidence of hypoglycemia. The overall safety profile for semaglutide was in line with the SUSTAIN 1–5 trials and these results may inform treatment considerations in elderly patients with T2D.

Abstract #246

DOES PERIOPERATIVE HYPERGLYCEMIA INCREASE THE RISK OF POST-OPERATIVE VENOUS THROMBOEMBOLISM?

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Objective: The aim of this study was to assess whether perioperative hyperglycemia has any association with an increased risk of VTE. The ultimate goal was to utilize the data to design a better perioperative glucose monitoring and management protocol.

Methods: We conducted a retrospective observational study. 23 patients who had DVT/PE as a postoperative complication and met our inclusion/exclusion criteria were included as subjects in the study. 64 controls were selected randomly from the list of the patients who underwent similar procedures during the same specified period as subjects; October 2015 to December 2016. Analysis of variance was performed to compare all normally distributed continuous variables between subjects and controls; Mann Whitney U for non-normally distributed data. Chi-square analyses were used to determine associations between categorical variables. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 20.0 (Armonk, NY: IBM Corp).

Results: 39% (9/23) of subjects and 16% (10/64) of controls had a known history of diabetes. Median premeal blood glucose levels during the first three postop days were higher for diabetics in the subject group compared to diabetics in the control group (p<0.05 postop day 1 and 2 lunch and postop day 1 before bed) and in several instances it was found that subjects had a premeal median blood glucose level > 180mg/dl. Fasting blood glucose on postop days one, two, and three, were not significantly different between nondiabetic subjects and nondiabetic controls.

Discussion: Our results support our hypothesis that poor perioperative glycemic control is associated with the occurrence of VTE in the postoperative period. 87% of subjects were out of bed by POD#1, - suggesting that apart from early mobilization there are other factors that need to be optimized during the peri operative period.

Our study is limited by a small sample size, lack of patients’ pre-operative blood glucose data and inadequate inpatient blood glucose data. Additional studies are needed with a larger sample size to validate the association of perioperative hyperglycemia and increased VTE risk in the post-operative period. If similar results are demonstrated in larger studies, adhering to strict perioperative glucose control may improve patients overall outcome.

Conclusion: Current inpatient blood glucose monitoring guidelines are mostly based on studies on patients admitted to ICU level of care. We believe there is need for more prospective studies to help improve the perioperative glycemic care in patients admitted to non ICU settings.

Abstract #247

A RARE, UNDERREPORTED COMPLICATION OF ANTITUBERCULOUS THERAPY: DIABETIC KETOACIDOSIS

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Objective: To describe a rare case of diabetic ketoacidosis (DKA) related to antituberculous (antiTB) therapy in a patient with prediabetes.

Case Presentation: A 65 year old man with history of diet-controlled prediabetes, pulmonary tuberculosis treated 43 years prior, and recently diagnosed tuberculous scleritis, presented to the emergency department (ED) with nausea and vomiting for 3 days. He had a 20lb weight loss over 2 months and polyuria and polydipsia for several weeks prior to presentation. 5 months prior to presentation, due
to reactivation of ocular TB, he began 2 months of RIPE (Rifampin, Isoniazid, Pyrazinamide, Ethambutol) therapy. Therapy was then changed to rifampin, pyridoxine and isoniazid (INH), which he continued until the time of ED presentation. His glycosylated hemoglobin (A1C) the month before starting RIPE therapy was 6.3%. On examination in the ED, he had dry mucous membranes. Laboratory evaluation revealed an anion gap of 19mEq/L, glucose level of 335mg/dL, moderate urine ketones, beta-hydroxybutyrate >4.5 mMol/L, A1C 14.1%, fructosamine 694microMol/L, and c-peptide 0.84ng/mL. His pancreatic and liver enzymes, abdominal and chest imaging were unremarkable. No other precipitants for DKA were identified. Following treatment with fluid resuscitation, potassium replacement and insulin infusion, he was transitioned to a subcutaneous insulin regimen and required 120-130 units of insulin per day to maintain euglycemia. He was medically optimized prior to discharge to home, with close follow up with the infectious disease and endocrine teams.

Discussion: DKA is a rare and underreported consequence of antiTB therapy. To the best of our knowledge, DKA in the setting of RIPE therapy has been described in only one other published case report. However, 8 cases of DKA in patients taking ethambutol and 18 cases in patients taking INH, have been reported to the US Food and Drug Administration. Pancreatic insufficiency as a possible mechanism for worsening glycemic control has been described with rifampin. INH may also increase glucagon secretion and block specific steps in Krebs cycle.

Conclusion: Patients with prediabetes, diabetes mellitus or other metabolic risk factors should be monitored closely for worsening glycemic control when started on antiTB therapy, particularly given the possible life threatening complication of DKA. Physicians should have a low threshold to suspect drug-induced hyperglycemia in patients on RIPE therapy. Appropriate education regarding signs and symptoms of hyperglycemia should be provided to patients before the initiation of antiTB therapy.

Abstract #248

DIABETES MELLITUS: OVERDIAGNOSIS AND OVERTREATMENT

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Objective: Current trend in diabetes care is towards early diagnosis and aggressive management of A1c. We set out to define the criteria by which T2DM is identified in our Community-Academic practice and the number of individuals detected on routine labs reporting no symptoms plausibly related to diabetes.

Methods: The Michigan State University Centricity Business and Health team databases was interrogated for the period 2003 - 2016 to identify patients with new onset T2DM using a simple search algorithm looking for: Patients seen at least twice, once when they had no diabetes related code (250.xx dx) and a subsequent visit when they did.

A total of 2529 patients met the above criteria and 100 patients were randomly selected to be reviewed. Among them, 48/100 patients were evaluable. We reviewed how the diagnosis of DM was made. We hypothesized that an abnormal A1c found during work up of plausibly diabetes-related symptoms (polyuria, polydipsia, weight loss, fatigue) would be the most common reason for identification.

Results: Among the 48 patients with new onset diabetes, 41.7% were tested based on complaints of plausibly diabetes-related symptoms while 58.3% were uncovered on routine blood testing. 43.8% were diagnosed by serum blood glucose alone while 41.7% were diagnosed by A1C alone and 14.5% were diagnosed by both (both tests done at the same time). Abnormal tests were rarely confirmed prior to initiation of treatment.

Discussion: The diagnosis of T2DM was made, almost equally by abnormal A1c and fasting plasma glucose. The majority were diagnosed on routine blood samples drawn on asymptomatic individuals. Current ADA guidelines, encompassing testing everyone over the age of 45 or with any risk factors encourage finding (false positive) in many healthy individuals. Abnormal tests were rarely confirmed prior to initiation of treatment. This is in contrast to the landmark UKPDS as is the practice of treating without confirming the diagnosis. This has at least 2 major flaws; first it exposes many individuals to potentially hypoglycemic agents without a confirmed diagnosis and second introduces potential lead-time bias into outcome studies. In addition. The ADA guidelines of initial dietary management is rarely attempted (personal observation, we are currently reviewing our dataset for treatment strategies)

Conclusion: Current trends in diabetes management focus on early diagnosis and intervention with rather aggressive goals for A1c, However, there is little evidence to support aggressive glucose management in type 2 diabetes mellitus (T2DM) for the prevention of mortality. There is evidence supporting improved microvascular disease outcomes with relatively modest rather than aggressive A1c reduction.
Abstract #249

INSULIN-INDUCED INSULIN RECEPTOR DOWNREGULATION: A CASE SERIES

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Objective: Diabetes mellitus is a disease that affects different organ systems and therefore requires a multifaceted approach. For diabetes treatment, exogenous insulin, an anabolic hormone, is used to address a deficit from decreased synthesis or increased resistance. However, when taken in excess, hyperinsulinemia can create a vicious cycle of dependence. It can cause hypoglycemia, which in turn increase hunger and lead to excess calorie intake, weight gain, worsening obesity and further insulin resistance. This case series examines how patients on excessive doses of insulin successfully controlled their diabetes by deliberately decreasing their dosage of insulin, with direct, clear-cut teaching about their diet.

Methods: In this series, data from 17 patients was analyzed, with specific attention to the initial dose of insulin and hemoglobin A1c. Doses of long-acting insulin ranged from Lantus 40 units to 150 units daily. For insulin-dependent patients, we cut daily insulin requirement in half or in some cases to less than a third of their initial dose. Prior to this, the attending physician had a very straight forward conversation about the patient’s diet and the best way to improve it. He also had the patients call him every 3-4 days for the first couple of weeks with a report on their blood glucose readings. He would then adjust their medication regimen in real-time and follow up later.

Case Presentation: Initially, patients were on multiple medications with very high doses of insulin. At their initial encounter, we adjusted their medications, and they followed this regimen for at least three months. The majority of patients saw a decrease, both in their hemoglobin A1c and the amount of medicine they were taking. Other peripheral measures, such as weight loss, also improved for most patients.

Discussion: The fact that the patients’ A1c declined for the most part, despite a significant decrease in insulin, suggests that in some way, the amount of insulin influenced the demand. Previous biological research has shown that the insulin pathway is a negative feedback loop where higher levels of insulin decrease the number of receptors, their affinity for insulin and their effectiveness in signal transmission. In this way, hyperinsulinemia makes insulin less effective, causing some physicians to increase the dosage. Thus, our initial approach was to decrease the dose, which improved insulin sensitivity and effectiveness.

Conclusion: In closing, diabetes management requires a multifaceted approach. This series shows the impact of diet counseling and close follow-up and that when it comes to the medications, especially insulin, perhaps less is more.

Abstract #250

INSULIN USE IN THE HIMALAYAS

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Results: The diabetes pandemic knows no geographical boundaries. Along with modernization, diabetes has reached the remote Himalayan areas located at an altitude of 8000-16,000 feet above sea level. The unique geographic conditions and far and scarce medical service impose great challenges for the health system and for the management of diabetes in this part of the world. The challenges posed by diabetes on top of the world have been addressed in an innovative manner: Three patients from tribal areas living at an “altitude” of 9500, 12000 & 14500 feet at a distance of 250 & 550 Km from state capital were prescribed insulin for uncontrolled blood sugar. The unique geographic condition of these areas, and peculiar social habits and dietary patterns of the inhabitants, imposes unique challenges for the use of insulin in this part of the world. Besides having the danger of hypoglycemia, however, the biggest challenge remains how to store insulin in the winter when outside temperature dips to minus 30oC mostly during midnight and inside temperature of the living room, goes up to 40o to 70o C due to constant burning of “Bukhari” made up of iron. Difficulty in access and storage of insulin creates a need for crafting a locally relevant, improvised solution for the same. In winters, people of these areas wear warm clothes made up of sheep and yolk wool to protect from severe cold. One such unique cloth people wear in the winter is an abdominal binder, which measures 2-3 feet in width and 5-15 feet in length. Seeing a woman wearing the traditional attire in a hospital, an innovative idea of insulin storage that was “locally” relevant and easily acceptable came to my mind: “It was planned to store insulin in multiple layers of abdominal binder, which prevents it from freezing in winter” and was discussed with patients on their follow-up visit. They were advised to “wrap the insulin vials and/ or pens in “multiple layers” in the abdominal binder (where the temperature recorded was between 5-10oC). The success of this practice was evident from the normal HbA1c values, and the smiles
on their faces, when they visit state capital for routine medical consultation.

**Conclusion:** Normally; we think of living with diabetes at normal altitude, not for those living in the extreme conditions of the world; one like those living “in the Himalayas”. Improving the technology to synthesis a stable insulin; a insulin that is stable at sub zero temperature, one like seen in the Himalayas, will be a step forward in a better diabetic care to individual living in such harsh environment.

**Abstract #251**

**FACTORS AFFECTING STEROID INDUCED HYPERGLYCEMIA IN COMMUNITY HOSPITALS**

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**Objective:** Corticosteroids are well known to induce hyperglycemia, especially when given in higher dosages for conditions such as Asthma or COPD exacerbation. For our community hospital setting of an inner city and suburban area of Philadelphia, we evaluated modifiable and non-modifiable factors associated with steroid induced hyperglycemia.

**Methods:** This is a retrospective study of a total of 622 patients admitted during 2015 and 2016. Inclusion criteria were patients who received Intravenous or oral steroids for either Asthma or COPD exacerbation. We compiled the data for demographic variables, associated co-morbidities and Hemoglobin A1c, Medications for Diabetes Mellitus and in-hospital data including daily finger stick glucose, Insulin correction factor coverage received, daily steroid dose, diabetic diet order and nutrition consult ordered during hospitalization. Multiple regression analysis was performed with response variable of average blood glucose level for the entire length of stay.

**Results:** Mean age for the patients included in the study was 61 years with SD +/- 15. Of the 622 patients, 64% were Females, 66% were African American patients and they had mean BMI of 32 Kg/m2 with SD +/- 10 Kg/m2. Sixty- five percent of the patients were non diabetic on admission to the hospital. Hemoglobin A1c data was available for 212 patients with the mean of 7.17 SD +/- 1.96. Mean fasting blood glucose for total length of stay was 160 and for lunch, dinner and bedtime blood glucose averaged more than 180.

**Discussion:** For the response variable of total blood glucose for the entire length of stay, dependent variables of CKD, DM, BMI, diabetic diet and day 1 steroid dose were statistically significant with a P value of less than 0.05. Steroid induced hyperglycemia is a well-known entity. We conclude that the physiological phenomenon of steroid induced hyperglycemia has modifiable factors. Hyperglycemia, on general medical or surgical units, is associated with longer length of stay and a higher admission rate to an intensive care unit. It is an important marker of poor clinical outcome and mortality in patients with and without a history of diabetes. Diabetic diet orders with calorie restriction even for non-diabetic patients is important. We found that the day one steroid dose affected the total length of stay blood glucose in our patient group.

**Conclusion:** Our study emphasizes need for recognition of hyperglycemia from steroids even in non-diabetic patients and for institution of protocols to mitigate such hyperglycemia thereby reducing mortality and length of hospital stay. We recommend starting such patients on Insulin correction factor, diabetic diet and reducing the dose of steroids.

**Abstract #252**

**LATENT AUTOIMMUNE DIABETES IN THE OBESE PATIENT: A CASE SERIES**

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**Objective:** Latent autoimmune diabetes of adults (LADA) is a heterogeneous disease with a variable phenotype that overlaps with that of Type 2 Diabetes (T2DM). This phenotypic overlap presents a diagnostic and therapeutic challenge in obese patients. We present a case series of two obese patients with LADA highlighting clinical presentations which should raise suspicion for LADA, and successful management with insulin and novel antidiabetic agents.

**Case Presentation:** Patient 1 is a 62 y/o female, BMI 32 with hypertension and hyperlipidemia, diagnosed with T2DM at age 45. She was initially treated with Humulin 70/30. She then received a trial of metformin 1000mg twice daily, detemir 25 units daily, and liraglutide 1.2mg daily. She displayed labile blood sugars with extreme insulin sensitivity concerning for LADA. Work up showed GAD-65 12.1 (<1.0 U/ml), IA-2 1.1 (<0.8U/ml), insulin antibody 2.8 (<0.4 uL/ml), and c-peptide level <0.10 (0.80-3.10ng/ml) X 2, consistent with LADA. Prandial lispro 8 units was added. A1c improved from 10.4 to 8.9. Patient 2 is a 34 y/o male, BMI 41, diagnosed with T2DM at age 29. He lost 100lbs with diet and exercise. He presented with BMI 28 and A1C 8.7, on metformin 2000mg daily, glimepiride 4mg twice daily, canagliflozin 100mg daily, and sitagliptin 100mg. LADA was suspected due to
poor control requiring more anti-diabetic agents despite significant weight loss. Work up showed GAD-65 21.3 (0-5.0 U/ml), IA-2 4.8 (<1 U/ml), insulin antibody <5.0 (<5.0 uU/ml), and c-peptide 0.6 (1.1-4.4 ng/ml). Glimepiride was stopped and detemir 8 units was started. A1c improved to 7.8. To offset use of prandial insulin he was treated with sitagliptin and canagliflozin with careful monitoring given the risk of DKA. Autoimmune diabetes progressed over the next year with decreasing c-peptide to 0.2 (1.1-4.4 ng/ml). A1C increased to 9.1. Prandial lispro was added and A1C improved to 7.9. As his diabetes progressed, CGM was used with plans for a closed loop insulin pump.

**Conclusion:** The prevalence of LADA in obese patients is unknown. Given the obesity epidemic, we expect to see an increasing number of cases of LADA in obese patients. These cases may be misdiagnosed as T2DM and managed with treatments that do not preserve beta cell function. LADA, particularly in the early stages, can look phenotypically similar to T2DM making the diagnosis difficult in obese patients. We suggest work up with antibodies and c-peptide levels in patients with uncontrolled diabetes despite multiple non-insulin anti-diabetic agents and brittle diabetes. Earlier diagnosis of LADA can help select therapy to improve glycemic control while delaying beta cell decline by using insulin and novel antidiabetic agents.

Abstract #253

**DIABETES HEALTHCARE PROFESSIONALS USE A MULTITUDE OF CONTINUOUS GLUCOSE MONITORING DATA FEATURES TO ASSESS GLYCEMIC CONTROL**

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**Objective:** Continuous glucose monitoring (CGM) offers improved data density and a multitude of derived data features compared to HbA1c and contextual blood glucose checks. However, although CGM provides an enrichment of glucose information to diabetes healthcare professionals, an understanding of how endocrinologists and diabetes educators actually make use of CGM data to assess glycemic control is currently lacking.

**Methods:** We asked 38 diabetes healthcare professionals (29 endocrinologists; 9 diabetes educators) to assess CGM data from ten people with type 1 diabetes (7 contiguous days of CGM data each), and to rank order each day’s qualitative glycemic control from “best” to “worst”. In addition, participants were also asked to indicate the CGM data features that were considered in making those rankings. Concordance of ranks among participants was quantified using Kendall’s coefficient of concordance (W), a non-parametric statistic used to assess agreement among raters.

**Results:** As a whole, diabetes healthcare professionals demonstrated agreement in how they ranked daily glycemic control from CGM data (W = .51, P = .0019). As a group, diabetes educators were in greater agreement (W = .54) than endocrinologists (W = .46; Wilcoxon-Mann-Whitney U = 19, P = .0018). Hypoglycemia and variance were the features that were most commonly endorsed as indicators of glycemic control (89.7% and 82.8% of all participants, respectively). Hyperglycemia (44.8%), time in- (37.9%) and out-of-range (34.5%), and mean daily blood glucose (24.1%) were also commonly endorsed as indicators of glycemic control. No differences were observed between endocrinologists and diabetes educators in the endorsement of any particular feature. As a group, 28.9% of participants endorsed using 1-2 different data features in ranking daily glycemic control, 47.4% endorsed using 3-4 data features, and 23.7% endorsed using 5-8.

**Discussion:** As a group, diabetes healthcare professionals showed agreement in how they use CGM data to assess glycemic control despite the qualitative nature of the task. Hypoglycemic excursions and variance throughout the day were nearly unanimously endorsed by participants as important indicators of glycemic control. Participants endorsed using multiple CGM data features in making such assessments.

**Conclusion:** The richness of CGM data should be leveraged by considering multiple data features when assessing glycemic control.

Abstract #254

**DIURNAL CHANGES IN INSULIN PUMP SETTINGS THROUGHOUT PREGNANCY IN PATIENTS WITH TYPE 1 DIABETES**

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**Objective:** In pregnant women with type 1 diabetes (T1D), tight glycemic control has been shown to improve maternal and fetal outcomes. Insulin doses increase during pregnancy; however the pattern of increase is not well studied. The objective of this study was to analyze pump settings in pregnancies complicated by T1D to characterize the change in insulin requirements throughout the day as
pregnancy progresses.

Methods: Twenty-five pregnancies occurring in 2012-2017 in 22 patients seen by endocrinologists with expertise in T1D in pregnancy at 2 institutions were retrospectively reviewed. Patients who had a HbA1C >7.5% before or in early pregnancy were excluded given changes in initial settings would reflect optimization as opposed to pregnancy physiology. Pump settings at initial visit and 2 weeks per trimester (6-8, 10-12, 21-23, 26-28, 32-34, and 36-38) were analyzed. Median basal doses by time of day (10pm-5am, 5am-9am, 9am-4pm, and 4pm-10pm), median carbohydrate ratio (CR) (breakfast, lunch, dinner), and median insulin sensitivity factor (ISF) (overnight, breakfast time, lunch time, dinner time) were calculated. Monthly HbA1C, maternal weight, and pregnancy outcomes were also recorded.

Results: Average HbA1C during pregnancy was 5.9%. Compared to visit 1, basal doses overnight and in the morning decreased during the 1st trimester and rose in the 2nd and 3rd trimesters. Midday and evening doses peaked during the late 2nd trimester to early 3rd trimester before plateauing during the last month of pregnancy. CR became more aggressive after week 12 with the earliest change in settings seen at breakfast. By the end of pregnancy, CR had decreased by an average of 45%. ISF became more aggressive starting in the late 2nd trimester resulting in a 20% change from baseline by the end of pregnancy. Average birth weight was 3463g with 2 macrosomic babies.

Discussion: Our data further reinforces that basal doses are lower during early pregnancy, but increase during the 2nd and 3rd trimesters. The timeline of these changes revealed that breakfast CR became quickly aggressive which may be explained by changing levels in counterregulatory hormones. By the end of the pregnancy, all CR were more aggressive consistent with an overall increase in insulin resistance. Variation among patients is expected given variability in baseline weight and glycemic control, hormonal variation, and provider practice.

Conclusion: The increase in insulin requirements during pregnancy is most pronounced in the late 2nd and 3rd trimesters, however variability can be found throughout the day. Further studies are needed to confirm these trends in larger cohorts in order to help clinicians proactively adjust insulin settings.

Abstract #255

EARLY INTENSIFIED INSULIN THERAPY IN NEWLY DIAGNOSED TYPE 2 DIABETES LEADS TO SUSTAINED IMPROVEMENT IN GLYCEMIC CONTROL AND IMPROVED BETA CELL FUNCTION

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Objective: Type 2 diabetes (T2D) is a progressive disease characterized by relentless deterioration of pancreatic β-cell function. Traditionally, insulin is used in later stages of T2DM. This study looks at use of insulin at time of diagnosis of T2D and its effect on glycemic control and beta cell function.

Methods: This is a prospective observational study conducted in symptomatic newly diagnosed type 2 diabetes adults (>18 years) who presented with glycated hemoglobin (A1C) levels > 9%. For the initial 8 weeks, patients were treated with pre-mix insulin after which they were changed over to oral agents, and followed up for next three years.

Results: Of 122 study participants, who completed the study, 50% were female and 90% were from rural areas. Average age of participants was 51.4 ± 9.6 years. Baseline mean fasting plasma glucose (FPG), post prandial plasma glucose (PPPG) and A1C were 267 ± 76 mg/dl, 408 ± 101 mg/dl and 11.5 ± 1.4% respectively. At the end of insulin therapy (8 weeks), the mean FPG, PPG and A1C reduced to 107 ± 10 mg/dl, 145 ± 24 mg/dl and 7.3 ± 0.8% respectively all of which were highly significant. The mean post-prandial C-peptide significantly increased from 1.8± 0.6 to 2.8± 0.9 ng/dl. An average of 1.7 kg weight gain and 0.97 episodes of mild to moderate hypoglycemia were observed. At the end of study (156 weeks), the mean FPG, PPG and A1C were 99 ± 14 mg/dl, 152 ± 12 mg/dl and 6.7 ± 0.4%.

Conclusion: helps to maintain long term normoglycemia and improves β-cell function. Early insulin therapy in treatment naïve patients with type 2 diabetes results in rapid improvement of glycemic control
Abstract #256

REAL LIFE EXPERIENCE WITH THE COMBINATION OF GLARGINE INSULIN AND LIXISENATIDE IN OBESE TYPE 2 DIABETIC PATIENTS IN MEXICO CITY.

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Grupo Medico Rubi

Objective: The objectives were to demonstrate the glycemic control, weight and body composition changes with the use of this treatment combination. Secondary objectives were frequency of hypoglycemia and side effects.

Methods: We conducted an open, longitudinal study of glargine insulin and lixisenatide on glycemic control and weight loss in obese type 2 diabetic patients treated for 12 months. We included 8 female and 6 male patients (between 38-60 years) who have failed to other insulin+oral treatments and did not show any relevant chronic complications or intercurrent illness. Oral AD agents were stopped and original insulin dose continued. All patients followed a 1500 Kcal diet (55/30/15 nutrients ratio), 50 minutes exercise a day, and were started with lixisenatide 20 mcg once a day for the study period. Insulin dose was adjusted according to attain best control. Biochemical analysis were made in a commercial lab using Beckman automated enzymatic methods. HbA1c was measured using HPLC. Body composition analysis was made with impedence test using a mbcA115 analyzer. Comparisons were made with parametric tests between visits for HbA1c, glucose, lipids, BMI, weight and body fat percentage.

Results: At start, mean weight was 111.6±16.2 males 93.8±7.8 females, BMI was 35±4.7 males and 34.8±3.21 females; HbA1c were 8.78±0.3, 8.8±0.5; glucose 204±10, 208±20 mg% males and females respectively. At 12 months a significative (p<0.00001 first vs last visit) mean weight loss of 7.9 kg/7.4 Kg; fat% 8 and 9; HbA1c reduction 1.97/2.26, and glucose levels of 106 mg%, 166 mg% (72 %, 71% attained control goals of HbA1c =<7%). Nausea was present in around a third of patients, and we recorded 6 episodes of severe hypoglycemia that needed treatment.

Discussion: The use of the combination of basal insulin and postprandial GLP-1 mimetic resulted in improved glycemic control in type 2 DM while reducing total and fat weight with minimal side effects being nausea the most common but usually tolerable. Hypoglycemia was relatively rare with only 6 episodes of severe hypoglycemia during the study year.

Conclusion: A combination of 2 injectable antidiabetic treatments could be synergistic and weight loss with adequate control obtained.

Abstract #257

THE EFFECT OF WARFARIN ON INSULIN RESISTANCE.

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Objective: Vitamin K supplementation improves insulin response and sensitization and reduces progression of insulin resistance in patients with low vitamin K levels. No studies to date have examined the effect of the vitamin K antagonist warfarin on insulin resistance. The primary objective of this exploratory study was to evaluate the effect of warfarin on insulin resistance as measured by the homeostasis model assessment (HOMA-IR) at baseline and after six months of warfarin treatment. Secondary outcomes were fasting serum glucose, fasting serum insulin, and weight.

Methods: Men age 18-99 years (including type 2 diabetics) initiating warfarin therapy at the Dayton VA Medical Center were recruited during the first week of starting treatment. Men with and without diabetes not taking warfarin were enrolled as well. Subjects were recruited during clinic visits or hospital stay. Table 1 shows the exclusion criteria. Patients were followed for six months. HOMA-IR, fasting serum glucose, fasting serum insulin, and weight were measured at baseline and after six months of treatment. Mann-Whitney Test and Fisher’s Exact Test were performed using IBM SPSS 22.0 software.

Results: Twenty-one patients were recruited, 11 patients in the warfarin group (W) and 10 in the no warfarin group (NW). The groups did not differ in age (W = 61.9 years vs. NW = 65.1 years; p=0.81), and all patients were male while all but one was Caucasian. Five of 11 patients in W were diabetic, and two of 10 patients in NW were diabetic (p=0.36).

At six months, HOMA-IR decreased from 5.8 to 5.0 in W but increased from 2.5 to 9.4 in NW (p=0.31). Glucose increased from 108 to 134 in W and from 98 to 114 in NW (p=0.15). Insulin decreased from 22.6 to 16.3 in W, but increased in NW from 9.8 to 25.0 (p=0.51).

Discussion: Our exploratory study had small sample sizes. Consequently, the differences between W and NW patients in HOMA-IR, glucose, and insulin at six months, while not statistically significant, may be clinically notable. The difference in mean change for HOMA-IR was 7.7, for glucose 10.9, and for insulin 21.5. Further, we included diabetics in our study, but subgroup analysis of diabetics was not meaningful due to small sample sizes.
(n = 5 for W and
n = 2 for NW).

**Conclusion:** In this exploratory study warfarin did not have effect on insulin resistance. Further larger scale studies are warranted.

**Abstract #258**

**SPECTRUM OF PERIPHERAL ARTERIAL DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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**Objective:** To study the prevalence of Peripheral Arterial Disease (PAD) in patients with Type 2 diabetes mellitus using Ankle Brachial Index (ABI).

**Methods:** It was a prospective study, conducted in medicine ward, D.M.C.H Ludhiana, Punjab. Patients with age ≥ 40 years, Type 2 DM (duration > 5 years) were evaluated for PAD on the basis of ABI. Patients were assessed for symptoms, risk factors for PAD and presence of other cardiovascular diseases. Blood was collected for fasting and random blood sugar levels, fasting lipid profile, renal function tests & HbA1c. Fundus examination, blood pressure, BMI and ABI were done. Chisquare test was used to determine correlates of PAD.

Results: 100 diabetic patients were enrolled. 24% patients had PAD (ABI of <0.9) with only 1% having severe PAD (<0.4). 10% patients were asymptomatic, while 14% were symptomatic with symptoms of claudication, rest pain, non healing ulcer (p < 0.000). Mean age with PAD was 60.67 years with range of 40-89 years and M:F was 2:1. Mean duration of diabetes was 11.47+/−6.540 with range of 6-35 years (p<0.004). Mean HbA1C was 9.3 with 5.6-13.7 range. 55 patients had hypertension, 78 dyslipidemic, 15 obese, 19 had CKD and 6 were smokers. Mean BMI was 26.08 in patients with PAD. Correlates of PAD included CKD (p<0.017) and smoking (p<0.039). Presence of an ABI<0.9 predicts cardiovascular risk to the same extent as diabetes as 9(37.5%) of CAD patients had PAD (p<0.000) while only 3 (12.5%) of CVA had PAD. Out of 24 patients of PAD, 17(70.8%) revealed NPDR and 3(12.5%) had PDR (p<0.002).

**Discussion:** According to our study the prevalence of PAD as measured by ABI is 24%. Smoking, increasing duration of diabetes & CKD were found to be predictors of PAD. Our study suggests significant correlation of PAD with CAD & Diabetic retinopathy. Stastical significant difference was not found in relation to HbA1C and BMI but increasing prevalence with increasing trend is seen. We did not find any correlation with age, sex, hypertension and dyslipidemia.

**Conclusion:** The prevalence of PAD in type 2 DM as measured by ABI was 24%. Smoking, increasing duration of diabetes & CKD were found to be predictors of PAD. Our study suggests significant correlation of PAD with CAD & Diabetic retinopathy. We did not find any correlation with other risk factors for PAD. Focus should be done on screening PAD in patients with PDR in clinical practice. Further studies are needed to establish relationship of PAD with PDR.

**Abstract #259**

**MIFEPRISTONE DECREASES THE USE OF CONCENTRATED U-500 INSULIN IN PATIENTS WITH ENDOGENOUS HYPERCORTISOLISM WHO HAVE TYPE 2 DIABETES MELLITUS**

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**Case Presentation:** Excess endogenous cortisol activity contributes to insulin resistance and complicates the treatment of type 2 diabetes mellitus (T2DM). Recent studies show that mifepristone (MIFE, Korlym®, Corcept Therapeutics), a competitive glucocorticoid receptor antagonist, improves insulin sensitivity and glycemic control, often leading to reduction or elimination of other agents to control hyperglycemia (including insulin) in T2DM patients secondary to hypercortisolism. We previously reported the results of screening for hypercortisolism in a cohort of T2DM patients with severe insulin resistance requiring the use of concentrated insulin (U-500, Humulin®R U-500, Eli Lilly) (AACE 2017). Sixty percent of the patients screened (21/34) had endogenous hypercortisolism. Subsequent imaging revealed patients with pituitary adenomas, adrenal adenomas/hypertrophy, or an unknown source. We now report the results of medical therapy with MIFE in a cohort of patients using U-500 Insulin (6 with adrenal hyperplasia, 4 with adrenal adenomas and 4 with an unknown source) who refused surgery or were not candidates for surgery. Fourteen patients (7 men, 7 women) with hypercortisolism demonstrated by at least 1 positive test [1 mg dexamethasone overnight suppression cortisol ≥ 1.8 µg/dL (DST) or late night salivary cortisol ≥ 90ng/dL (LNST)] had an average cortisol of 2.26 µg/dL after a DST. These
patients had an average duration of 15 years with T2DM (range: 6–29 yrs.) and an average HbA1c of 8.6 % (range: 6.3–10.8 %) while using an average daily dose of 251 IU U-500 Insulin (range: 50–450 IU/d). Patients were started on MIFE (300 mg/d QD) and titrated after 2 weeks based on tolerability and response. Three months of treatment with MIFE (avg. dose 477.5 mg/d) decreased average HbA1c to 7.6 % (HbA1c range: 5–10.3 %). This 1 % decrease in HbA1c was accompanied by a 44 % reduction in the average daily dose of U-500 Insulin from 251 to 144 IU/d (range: 25–390 IU/d). MIFE therapy was discontinued in 2 patients after 3 months due to cortisol withdrawal symptoms and MIFE dose was limited to 300 - 600 mg/d in 5 patients with chronic renal disease. Nevertheless, after 6 months of MIFE therapy (587.5 mg/d avg. dose), average HbA1c remained at 7.6 % on 42 % less U-500 Insulin (149 IU/d avg. dose).

Conclusion: In diabetic patients with severe insulin resistance who require the use of concentrated U-500 Insulin, identification of underlying hypercortisolism and treatment with mifepristone improves insulin sensitivity. Consequently, substantially less U-500 Insulin may be needed to significantly improve glycemic control.

Abstract #260

FACTORS ASSOCIATED WITH EARLY READMISSION IN ADULT PATIENTS WITH DIABETIC KETOACIDOSIS AND HYPERGLYCEMIC HYPEROSMOLAR STATE

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Objective: Diabetic Ketoacidosis (DKA) and Hyperglycemic Hyperosmolar State (HHS) are potentially fatal but preventable complications of diabetes mellitus. Early hospital readmission, i.e. within 30 days, is an important measure of high-quality care. Prior studies found male gender, comorbidity burden, length of stay, lower education level and unemployment as predictors of readmission among diabetic patients. However, data on risk factors for early readmission in DKA/HHS is sparse. A case-control study identified age < 35, history of depression, self-pay or publicly funded insurance and drug/substance abuse history as risk factors for early readmission in DKA/HHS. The aim of our study was to identify various factors associated with 30-day readmission among patients with DKA/HHS.

Methods: We used data from the Healthcare Cost and Utilization Project- Nationwide Readmission Database (NRD), 2014. We identified individuals with index hospitalizations for DKA and HHS. We performed univariate and multivariate regression analyses to calculate odds ratio (ORs) of various demographic and clinical factors with 30-day readmission in DKA/HHS. Results: We identified 77,628 (estimated total of 172,638 in the US) index DKA/HHS discharges for the year 2014; 15,562 (estimated 34357, 19.90%) of whom were readmitted within 30 days of discharge. Female sex (OR 1.23, 95 % CI 0.97–0.980, p<0.0001), charlson comorbidity index > 3 (OR 1.91, 95 % CI 1.78–2.04, p < 0.0001), mood disorders (OR 1.45, 95 % CI 1.37–1.53, p < 0.0001), alcohol and substance use (OR 1.34, 95 % CI 1.27–1.42, p < 0.0001), number of diagnoses and procedures on the patient record > 5 (OR 1.49, 95 % CI 1.40–1.60, p < 0.0001 and 1.42, 95 % CI 1.19–1.70, p < 0.0001 respectively), were associated with increased risk of readmission. Sepsis (OR 1.25, 95% CI 1.10-1.40, p < 0.0001) during index hospitalization was associated with only a slightly increased readmission risk. Increasing age (OR 0.98, 95 % CI 0.979-0.983, p < 0.0001) was associated with reduced odds of readmission. Also, increasing age and higher income quartile had lower odds or readmission. Identifying and effectively targeting these high-risk factors may reduce many preventable readmissions and aid in the appropriate allocation of healthcare resources.

Abstract #261

SMARTPHONES AND SMARTER PATIENTS--MOBILE APPS AND ADVANCING DIABETIC CARE

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Objective: Though technology in disease management is rapidly advancing, evidence shows that these tools are underutilized. In diabetes, this includes Bluetooth enabled glucometers, remote sharing of continuous glucose monitors, and mobile applications (apps). One study reports only 8% of type 2 diabetics (T2D) and 24% of type 1 diabetics use these apps. We highlight a case of a non-compliant T2D whose hyperglycemia drastically improved
with a medication reminder app called MyTherapy.

**Case Presentation:** A 42 year-old morbidly obese Caucasian man presented with uncontrolled T2DM with high insulin requirements. Upon diagnosis in 2000, he was well controlled on orals. After 2006, he was initiated on insulin with increasing requirements and progressive weight gain. In July 2013, he was on glargine 100 units twice daily and metformin 2gm daily. Working as a truck driver made it difficult to carb count and exercise, resulting in an A1c of 11%. He underwent gastric bypass surgery a year later. On his regimen of U-500, A1c improved to 8.6% two months later. Treatment was modified to metformin 1000 twice daily, Tradjenta 5mg daily, and Jardiance 25mg daily. Stress and financial constraints plagued the patient, and A1c peaked at 13.3% in January 2017. He started the MyTherapy app, a free pill and medication reminder and health journal for weight tracking with improvement of A1c to 8.9%, an improvement of 4% over four months. Other apps include Healthline's best diabetes apps of the year. Fooducate focuses on weight loss and monitors carbs, hunger, sleep, and exercise. Glooko simplifies management by integrating data from continuous glucose monitoring, blood glucose meters, insulin pumps, and fitness trackers. Health2Sync has the unique option of adding family or friends to the app for support. The utility of mobile apps is not limited to diabetes. In atrial fibrillation, the simple mobile AF (mAF) App significantly improved patients’ knowledge, quality of life, compliance, and anticoagulation. The app also reduced anxiety and depression compared to usual care.

**Conclusion:** Medication app reminders can play a crucial role in improving a patient’s health. This case highlights the potential of these apps, particularly in maintaining compliance in those who have had limited success after bariatric surgery, as well as in diabetics with complex medication regimens and demanding work schedules. Physicians should be familiarized with these technologies so they can better educate their patients on the tools available.

**Abstract #262**

**EFFECTS OF CANAGLIFLOZIN (CANA) ON HBA1C AND CHANGES IN AHAS IN THE CANAGLIFLOZIN CARDIOVASCULAR ASSESSMENT STUDY (CANVAS) PROGRAM**

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**Objective:** CANA improved glycemic control by reducing HbA1c in a broad range of patients with type 2 diabetes (T2D) across its clinical trial program. This analysis examines the effects of CANA on HbA1c and changes in use of antihyperglycemic agents (AHAs) in patients with high cardiovascular (CV) risk in the CANVAS Program.

**Methods:** The CANVAS Program randomly assigned 10,142 participants with T2D and established CV disease or ≥2 CV risk factors to treatment with CANA or placebo (PBO). Least-squares (LS) mean changes from baseline HbA1c and initiation of new AHAs were analyzed in the on-treatment population (patients receiving CANA/PBO or within 30 days after discontinuation; n = 10,134).

**Results:** From a baseline mean HbA1c of 8.2%, the maximum difference between CANA and PBO (PBO-subtracted difference [95% CI]:–0.64% [–0.68, –0.61]; mean 8.1% vs 7.5%) was observed at Week 26. After Week 26, the curves began to converge, reaching a minimum difference between CANA and PBO of –0.23% (–0.33, –0.14; 8.2% vs 8.0%) at Week 286. At the end of the study (Week 338), the mean difference HbA1c with CANA versus PBO was –0.24% (–0.37, –0.10; 8.1% vs 7.9%), with a mean reduction of –0.58% (–0.61, –0.56) with CANA versus PBO over the entire follow-up period. Discontinuation from study drug was about the same in both treatment groups during the first year of the study; after Week 52, more patients discontinued PBO versus CANA.

At baseline, the treatment groups were well-balanced with respect to AHA use. Almost all patients (98.6%) were being treated with ≥1 AHA at baseline (18.7% on 1 AHA, 43.6% on 2 AHAs, and 36.3% on ≥3 AHAs). The most common AHAs at baseline were biguanides (77.2%), insulin (50.3%), and sulfonylureas (43.0%). Over the course of the study, approximately 22% of patients initiated new AHAs during treatment with study drug, with DPP-4 inhibitors and insulin being the most common newly initiated AHAs (Table). A higher proportion of PBO-treated patients initiated AHA therapy across all classes, including insulin. Through the first and second years of
the study, patients in the PBO group initiated new AHAs approximately twice as often as CANA-treated patients (first year: 6.3% and 14.7% with CANA and PBO; first 2 years: 11.3% and 22.9% with CANA and PBO).

**Conclusion:** In the CANVAS Program, patients treated with CANA had greater reductions in HbA1c compared with patients treated with PBO. After 52 weeks of treatment, the difference in HbA1c between the CANA and PBO groups began to decrease likely due to the joint effects of discontinuation of randomized therapy and a higher rate of initiating new AHA therapies in the PBO group.

**Abstract #263**

**TWICE DAILY INSULIN GLARGINE FOR PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES**

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**Objective:** Insulin glargine is commonly used for patients with diabetes and is usually prescribed once daily. Limited data and clinical experience suggest that insulin glargine could be used twice daily in certain patients to optimize glucose control. The aim of this study was to examine changes in glucose control in patients with uncontrolled type 2 diabetes after switching from once daily to twice daily insulin glargine therapy.

**Methods:** A cohort of 50 patients with type 2 diabetes with uncontrolled glucose despite titration of once daily insulin glargine administered at bedtime was evaluated. The reason for switching from once to twice daily insulin glargine therapy was the inability to control glucose values before dinner despite titrating meal insulin doses at lunch and/or the occurrence of hypoglycemia during early morning or before breakfast periods which limited the titration of insulin glargine. To examine predictors of twice daily insulin glargine therapy a secondary analysis was performed using multivariate logistic regression by using a matched control group of 210 patients with type 2 diabetes on once daily insulin glargine.

**Results:** A total number of 50 patients on twice daily insulin glargine were included. Males formed 58% of the cohort; mean age was 55.34 ± 8.2 years; mean duration of diabetes was 17.6 ± 8.2 years; mean body mass index was 32.8 ± 5.5. Mean HbA1c decreased significantly from 10.3 ± 1.5% while on once daily insulin glargine to 8.4 ± 1.3% (p < 0.001) on twice daily therapy. Mean insulin glargine dose increased from 53 ± 20.9 units daily on once daily therapy to 77.8 ± 29.4 units daily on twice daily therapy. In the secondary analysis, HbA1c level (adjusted odds ratio, 1.65; 95% CI, 1.3 to 2.0, p < 0.001) and insulin glargine dose (adjusted odds ratio, 1.35; 95% CI, 1.2 to 1.5, p < 0.001) were found to be independent predictors of twice daily therapy.

**Discussion:** Data on the use of twice daily insulin glargine in patients with diabetes are limited. Most of the published data included patients with type 1 diabetes and have shown improvement in glucose control in the majority of the studies. There is only 1 published study on the use of this therapy in patients with type 2 diabetes. The indication for this therapy is limitation of titration of once daily insulin glargine given at bedtime due to nocturnal or pre-breakfast hypoglycemia and/or elevated glucose levels before dinner despite titrating meal insulin doses at lunch.

**Conclusion:** Twice daily insulin glargine is effective in improving glucose control in selected patients with type 2 diabetes. Prospective randomized trials are needed to confirm these findings.

**Abstract #264**

**DOES STRICT GLYCEMIC CONTROL LEAD TO BETTER OUTCOMES IN NON-ICU TYPE II DIABETIC PATIENTS WITH SEPSIS**

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**Objective:** Studies have proven better outcomes in surgical patients with better glycemic control, but not among medical patients. The purpose of this research is to investigate if strict glycemic control leads to shorter hospital stay, lower mortality and re-admission in diabetic patients with sepsis.

**Methods:** This retrospective study included 395 type 2 diabetics with sepsis between 2015-2017. Recorded data included Charlson’s comorbidity score, qSOFA score, A1C, percentage of glucose controlled, length of stay, 30-day mortality, 3-month re-admission and type of insulin used. Pre-admission A1C < 7.5 was defined as controlled diabetic. Hospital glucose that was >180 for >50% of the time was defined as well controlled.

**Results:** 51.6% of total were controlled diabetics and 21.5% of those became uncontrolled during the hospital stay. 48.4% of total were uncontrolled diabetics and 56.5% of those remained uncontrolled during the hospital stay. The well-controlled group length of stay was 6.41 days versus 5.95 days (p = 0.145) in the uncontrolled group. 30-day mortality was 3.7% in the well-controlled group and 13% in the uncontrolled group (p = 0.266). Re-admission rate at 3 months was 17.4% in the well-controlled group and 20.9% in the uncontrolled group (p = 0.503). Sliding
scale had glucose controlled success rate of 59.9% compared to 33.5% (p<0.001) with basal + bolus. Re-admission at 3 months was strongly associated with high Charlson’s comorbidity score of 4.14 (p=0.008).

Discussion: A study of 32,851 non-selective patients found tight blood glucose control in non-critically ill patients decreased length of stay by 0.31 (P<0.01), decreased mortality by 0.47 (p<0.00001), and decreased re-admission by 2.47 (p<0.0000). The poorly controlled group was composed of uncontrolled diabetics with multiple comorbidities which explained the longer length of stay and mortality. The data was considered skewed by adding all the non-diabetics in the study. Our study was based on a similar study design, but only type 2 diabetics were included and the results didn’t support the strong finding in the previous research. This study validated the importance of Charlson’s comorbidity score in prediction of re-admission. Our study suggested sliding scale is superior to basal + bolus in glucose control. However, 73% of patients placed on sliding scale were well controlled diabetics and took an oral agent at home. In this group of patients, the glucose will fall in well-controlled range even without sliding scale. Therefore, there is no benefit of using sliding scale over oral agents.

Conclusion: Our study could not support better outcomes with tight glycemic control from previous study after limiting the study objects to only type 2 diabetics.

Abstract #265

LOWER INSULIN REQUIREMENTS AND IMPROVED METABOLIC CONTROL IN MEXICAN PATIENTS WITH TYPE 1 DIABETES WHO EXERCISE

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Objective: There is limited information regarding the degree of physical activity performed by patients with Type 1 Diabetes (T1D) in Mexico. An online platform (RENACED DT1) was developed for the longitudinal recording of real life data of patients with T1D.

Methods: Descriptive analysis of 894 patients with type 1 diabetes in 20 Mexican States up to October 8th, 2017.

Results: Fifty percent of patients were diagnosed in the last 10 years. The mean age at diagnosis was 12.5 years old (yo). However, it was significantly lower (p=0.03) in men (11.8 yo) than in women (13 yo). Of the 894 patients, 860 were still active at the cutoff date. Of them, 60% were female. The mean age at the time of analysis was 24.6 yo, being women (25.4 yo) significantly (p<0.05) older than men (23.4 yo). The mean BMI and A1c were 22.3 Kg/m2 and 8.5%, respectively. Fiftythree percent of patients exercise, men exercising more than women (58.4 vs 50%, p=0.045). Fifteyeight percent of patients with an A1c <7% exercise, vs 42% of patients with an A1c above 9% (p=0.003, Fig.). The proportion of patients who exercised was higher in those who used insulin-pump vs. MDI
(75.6% vs. 49.7%, p<0.05). HbA1c (8.2 vs. 8.9, p<0.05) and daily insulin dose (0.7 vs. 0.8, p<0.05) were significantly lower in people who exercised. People who exercised were 2.8 times (95% CI 1.8 - 4.4) more likely to have a meal plan and 2.8 (95% CI 2.0 - 4.0) times more likely to perform carbohydrate counting than those who did not exercise. People who exercised used 5.4 (IC95% 1.8 - 22.1, p<0.05) times more continuous glucose monitoring (CGM) and perform 2.7 times more capillary glucose monitoring (95% CI 1.3 - 5.6, p<0.05) than those who do not exercise.

**Discussion:** As has been reported elsewhere, exercise is associated with increased insulin sensitivity, decreased insulin requirements and improved glycemic control. It is interesting to note that insulin pump users exercise more than those that are on MDI. In addition, those patients who exercise are more likely to perform other attributes associated with a healthy lifestyle (meal plan, carbohydrate counting, increased glucose monitoring, CGM).

**Conclusion:** Exercise improves metabolic control with lower insulin requirements in Mexican T1D patients. The finding of a greater amount of exercise in patients who use insulin pump and CGM, will need to be studied further to look at the long term impact in cardiovascular disease.

**Abstract #266**

**AN UNCOMMON CASE OF DIABETIC MASTOPATHY**

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**Objective:** Diabetic mastopathy (DMP) is an uncommon fibrous disease of the breast, most commonly found in premenopausal women with type 1 diabetes exposed to long-standing insulin therapy. Often mimicking breast cancer clinically and on imaging, this condition poses a diagnostic challenge requiring pathological confirmation.

**Case Presentation:** A 68-year-old woman with type 1 DM and a family history of breast cancer in paternal aunt had an abnormal screening mammogram showing a lobular nodular density in the subareolar region deep to the nipple measuring atleast 2.5 cm in the left breast. Ultrasound (US) showed a hypoechoic, heterogeneous mass 2 cm from the nipple, measuring 41 x 13 x 46 mm with relatively circumscribed margins, demonstrating some internal blood flow on Doppler. Lymph nodes were normal. Patient underwent US-guided biopsy. Pathology showed hyalinized stromal fibrosis and chronic mastitis. Within a short period of time, patient presented with a painless palpable area in the right breast. Mammography and US of right breast showed a very dense tissue in the palpable area of concern, corresponding to heterogeneous, slightly hypoechoic mass with relatively circumscribed margins measuring 38 x 18 x 65 mm with internal vascularity. It had a very similar appearance to the area that was biopsied on the left breast. Given the bilaterality and history of diabetes, a preliminary diagnosis of bilateral diabetic mastopathy (DMP) was made. A decision was made to follow up annually with regular mammography. Later, patient developed retraction in the skin and nipple areolar complex in both breasts. Mammogram and US of both breasts revealed large densities that were relatively stable, however the skin changes prompted repeat biopsies. Thickened tissue on both breasts was excised and sent for pathology revealing features consistent with DMP.

**Discussion:** Patients with DMP clinically present with painless, irregular, hard, unilateral or bilateral breast masses. It is rare as it represents 0.6% to 13% of benign lesions observed in woman with type 1 diabetes. The pathogenesis is not fully understood but many theories involving the effects of sustained hyperglycemia and glycosylated end products on the connective tissues of the breast have been proposed. Malignant transformation has not been described.

**Conclusion:** This case underlines the importance of considering diabetic mastopathy in the differential diagnoses when evaluating breast lesions in women with diabetes. Recognizing the presentation of this rare condition can help avoid unnecessary surgical intervention.

**Abstract #267**

**SELENPORTEIN S ATTENUATES HIGH GLUCOSE-INDUCED VASCULAR ENDOTHELIAL APOPTOSIS THROUGH THE PKCβII/JNK/BCL-2 PATHWAY**

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**Objective:** Vascular endothelial apoptosis is closely associated with the pathogenesis and progression of diabetic macrovascular diseases. Selenoprotein S (SelS) participates in the protection of vascular endothelial and vascular smooth muscle cells from oxidative and ER stress-induced injury. However, whether SelS can protect the vascular endothelium from high glucose (HG)-induced apoptosis, as well as the underlying mechanism, remains unclear.

**Methods:** Aortic endothelial apoptosis and SelS expression in diabetic rats and the effects of different glucose concentrations on HUVECs apoptosis and SelS expression were observed. In addition, the pcDNA3.1-SelS recombinant plasmid and SelS-specific small interfering RNAs were constructed to up- or downregulate
SelS expression in HUVECs followed by HG intervention, then cell apoptosis and PKCβII, JNK, and Bcl-2 phosphorylation levels were examined.

**Results:** HG induced vascular endothelial apoptosis and upregulated endothelial SelS expression in vivo and in vitro. Overexpression of SelS in HUVECs suppressed HG-induced increase in apoptosis and cleaved caspase3 level, accompanied by reduced PKCβII, JNK, and Bcl-2 phosphorylation levels. In contrast, inhibiting SelS expression in HUVECs further aggravated HG-induced apoptosis and cleaved caspase3 level, accompanied by further increased PKCβII, JNK, and Bcl-2 phosphorylation. Pretreatment with PKC activators blocked the protective effects of SelS, increased apoptosis and cleaved caspase3 level in HUVECs.

**Conclusion:** Increased SelS expression in the aortic endothelium of diabetic rats in vivo and in HG treated HUVECs in vitro preliminarily suggest that SelS might participate in HG-induced endothelial injury. Further studies indicate that SelS protects vascular endothelium from HG-induced apoptosis, and this was achieved through the inhibition of PKCβII/JNK/Bcl-2 pathway to eventually inhibit the activation of caspase3. SelS might become a promising target for the prevention and treatment of diabetic macrovascular complications.

**Abstract #268**

**A RARE CASE OF EUGLYCEMIC DIABETIC KETOACIDOSIS COMPPLICATED BY HYPERTRIGLYCERIDEMIA**

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**Objective:** SGLT2 inhibitors have been associated with diabetic ketoacidosis (euDKA). We describe a case report of a patient with euDKA, in the setting of SGLT2 inhibitor use, complicated by hypertriglyceridemia (HTG).

**Case Presentation:** 28 year of female with a history of gestational diabetes mellitus and subsequent type 2 diabetes mellitus(T2DM), one prior episode of HTG induced pancreatitis, and obesity presented with 1 week history of polyuria, polydipsia, poor appetite, and vomiting. 2 weeks prior to presentation, she was treated with a 5 day course of amoxicillin for a respiratory tract infection. She was also on atorvastatin, gemfibrozil, metformin, glipizide and dapagliflozin for T2DM and HTG. Physical examination on presentation was significant only for dry oral mucosa. Pertinent laboratory findings were: glucose 111mg/dl, bicarbonate 18mmol/l, anion gap 20, triglycerides 508 mg/dL, total cholesterol 122 mg/dL, HbA1c 10%, and venous pH of 7.27. Serum ketones levels could not be assessed as blood samples kept hemolyzing due to significant lipemia. Patient was initially admitted for starvation ketosis as she reported poor oral intake for 3 days. On day 2 of hospitalization, her anion gap was still elevated at 20 and triglyceride level peaked at 2050 mg/dL. She was treated with insulin drip for euDKA and HTG with reduction in anion gap to 13 and triglycerides to 1400 mg/dl within 24 hours. Her euDKA was thought to be precipitated by her respiratory tract infection in the setting of SGLT2 inhibitor use.

**Conclusion:** This is the first case report about euDKA in the setting of SGLT2 inhibitor use, complicated by HTG, in an adult. SGLT2 inhibitors have been shown to cause euDKA mainly in insulin deficiency states characteristic of type 1 DM, although it has been reported with type 2 DM as well.2 Our patient may have had insulin deficiency after her episode of HTG associated pancreatitis. In pediatric case reports of HTG causing euDKA, it is thought it does so by causing pseudonormoglycemia.3 As HTG can prevent the detection of ketonemia, clinicians must use alternative tools such as urine ketones and venous pH when suspicion for DKA is high.

**References:**

**Abstract #269**

**DILEMMA IN MANAGEMENT OF NON-KETOTIC HYPEROSMOLAR HYPERGLYCEMIA TRIGGERED BY HEMODIALYSIS IN A PATIENT WITH DIABETES MELLITUS TYPE 2 WITH END STAGE RENAL DISORDER**

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**Objective:** Non ketotic hyperosmolar hyperglycemia (HHS) is one of the dreaded hyperglycemic emergencies. Incidence of HHS is lower than that of diabetic ketoacidosis (DKA) .The reported mortality rate of HHS is between 10 and 20%, which is about 10 times higher as compared to that of DKA. Major precipitating factors include
infection, trauma, inadequate hydration, cerebrovascular accident (CVA), myocardial infarction, drugs. We report a case of HHS precipitated by hemodialysis (HD) in an African American (AA) diabetic male with end stage renal disorder (ESRD).

**Case Presentation:** 56 years old AA male with known medical history of insulin dependent diabetes mellitus (DM) ESRD on HD, CVA, active tobacco use, chronic obstructive lung disease, peripheral vascular disease, Hypertension, presented with hypertensive emergency, hypercarbic respiratory failure and pulmonary edema. Patient was on HD a thrice week and had additional session of HD 2 days prior to presentation in view of respiratory insufficiency. On admission, blood pressure was 220/110 mmHg, had tachycardia and tachypnoea. Chest X-Ray showed diffuse pulmonary edema, BNP > 4968ng/L, Troponin was indeterminate. Blood glucose 890 mg/dl, serum osmolality 323mosm/kg, negative for acetone, lactic acid was 1 mmol/L, arterial pH is 7.33. Serum bicarbonate was 27mEq/L. Urinalysis not done as patient was anuric. Insulin Infusion was started at 8 units/hour. At this point intravenous fluid (IVF), which is the mainstay of treatment in HHS, could not be given as patient had pulmonary edema. We faced with the challenge of two active conditions with opposite managements, fluid restriction for pulmonary edema and fluid resuscitation for HHS. IVF was not initiated until urgent HD was started and about one liter ultra filtrate was removed, thereafter IVF was administrated with HD. Blood glucose monitoring was done hourly. After resuscitation with 3 L fluid, serum osmolality started getting lower. Insulin infusion was titrated down according to blood glucose levels. Within 48 hours, serum osmolality was started and about one liter ultra filtrate was removed, thereafter IVF was administrated with HD. Blood glucose monitoring was done hourly. After resuscitation with 3 L fluid, serum osmolality started getting lower. Insulin infusion was titrated down according to blood glucose levels. Within 48 hours, serum osmolality was within normal range. Patient was discharged after 3 days, with a close follow up schedule.

**Conclusion:** In this case, an additional session of ultra filtration in HD provoked dehydration and resulted in HHS. Risk factors in this case were diastolic dysfunction, left ventricular hypertrophy, active smoking and renal failure. There have been reported cases of HHS after renal transplant, after general anesthesia, acute renal failure syndrome, however this is a unique presentation and no such case has been reported so far. For such patients with low threshold for developing HHS, continuous glucose monitoring or insulin infusion during HD could be beneficial.

**Abstract #270**

**KNOWLEDGE, ATTITUDE AND PRACTICE AMONG CAMBODIAN TYPE 2 DIABETIC PATIENTS**

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**Objective:** The aim of this study is to evaluate the level of knowledge, attitude and practice of patients with type 2 diabetes in Cambodia.

**Methods:** This is a multicenter cross-sectional study involving calculated sample size of 139 patients, carried out a university hospital and a privat clinic. After validating by two senior endocrinologists, questionnaires were pilot with 15 diabetic outpatients to evaluate their coherence suitability to local context. Face-to-face interviews were held to fill questionnaires with the agreement of the patient. The data was analyzed by using STATA 13.1.

**Results:** 139 patients with T2DM (92 females and 47 males) participated in the study. Mean age of respondents is 57.9 (±12.1). About 35% of them are housekeepers, 55.4% live in Phnom Penh and only about 31% completed at least high school. Mean BMI, diabetes duration (in year) and HbA1c were respectively 24.2(±3.4), 7 (±6.98) and 8.17 (±1.93). Up to 64% of respondents have high blood pressure, 52.5% are dyslipidemia and up to 76% do exercise. The mean score of patients’ knowledge, attitude and practice were 16.94 (±3.72) or 68%, 12.22 (±5.28) or 80.55%, 4.65 (±1.42) or 58.18% respectively. Patients’ knowledge were significantly different among smoker and non-smoker (14.4 vs 17.1, p-value:0.02), those who do exercise and those who don’t 17.3 vs 15.8, p-value:0.05). Those who received higher educations seem to have higher knowledge’s score (p-value: 0.04). For practice, the scores are significantly different among those who well controlled HbA1c and those who did not (4.99 vs 3.57, p-value < 0.001). There were significant negative correlation between patients’ knowledge with age and HbA1c and practice with HbA1c. The knowledge is decrease while age is increased (r = -0.18, p-value:0.03) and HbA1c is increase (r = 0.18, p-value:0.03). While practice’ score increase, HbA1c is decrease (r = -0.33, p-value<0.001). Attitude and practice increase while knowledge is increase (r= 0.58, p-value<0.001 and r= 0.3, p-value<0.001 respectively). Positively correlation is also observed between practice and attitude (r= 0.21, p-value:0.01).

**Conclusion:** This study found that the score on knowledge, attitude and practice among T2DM patients are moderate. Promoting patients’ knowledge, attitude and practice play key role in the management of type 2 diabetes.
Abstract #271

THE EFFECTS OF A "MEDS TO BED" PHARMACY DISCHARGE PROGRAM ON HOSPITAL READMISSIONS

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Objective: There is a significant interest in identifying interventions that reduce hospital readmission. We instituted a “meds to bed” program for select patients with a new diagnosis of diabetes felt to be at increased risk for readmission in a safety-net hospital as part of an existing comprehensive diabetes consult service. Patients received all medications and a glucose meter prior to discharge.

Methods: A historical control group was used to compare hospital readmissions and HbA1c change before and after the intervention.

Results: There were 46 patients in the control group and 56 patients in the intervention group. Baseline demographics were similar between the two groups but the intervention group had a higher proportion of uninsured patients (16.1% vs 4%) and also a higher Charlson Comorbidity Index (3.69 vs 2.98). Diabetes was in poor control in both groups (HbA1c 10.7 in the control group vs 11.1 in the intervention group). There was no difference in readmission rates between groups at 30 and 90 days. Only a very small number of readmissions had diabetes as the primary reason for readmission (<5%). There were insufficient HbA1c values post discharge to compare changes between groups. The intervention group had a higher rate of endocrine outpatient attendance (56.8% vs 48.3%) and a lower rate of no-show (27.1% vs 41.9%) following discharge.

Discussion: In this pilot study we did not see a decrease in readmissions after instituting a meds to bed program. This may be due to the fact that many patients were readmitted for reasons unrelated to diabetes, and also because the intervention was specifically administered to patients felt to be at high risk for readmission.

Conclusion: Further studies are needed to determine the utility of a meds to bed program to improve patient outcomes and reduce readmissions.

Abstract #272

PREVALENCE AND RISK FACTORS FOR IMPAIRED GLUCOSE REGULATION AMONG FIRST DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES MELLITUS IN MAIDUGURI NORTH-EASTERN NIGERIA

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Objective: To estimate the prevalence of IGT and IFG and its associated risk factors in FDRs of patients with T2DM in North-eastern Nigeria

Methods: This was a hospital based comparative cross-sectional descriptive study of FDRs of T2DM patients conducted between March 2009 and March 2010. A total of 320 FDRs of T2DM outpatients aged 25yrs and above (145 males, 175 females) and 160 persons (76 males, 84 females) who were age and sex matched with the study subjects were also selected as control with no family history of diabetes or hypertension. All subjects completed an interviewer administered questionnaire and underwent anthropometric and laboratory assessments after an overnight fast and 2HPG value after OGTT with 75g anhydrous glucose. FBG of 6.1-6.9mmol/L and 2HPG value of 7.8-11mmol/L were used to define IGT and IFG respectively. Statistical analysis was carried out using SPSS version 16, and p value <0.05 was considered significant

Results: The mean SD age of study subjects and controls were 38.4(12.3) and 38.9(10.3) years respectively. The prevalence of both IGT and IFG in FDRs 28.1% vs.18.1%, p=0.019 and 10.3% vs. 5.6%, p=0.0001 respectively. The prevalence of IGT was found to be higher among females than males in both study 34.9% vs 20%, p=0.004 and controls 21.4% vs 14.5%, p=0.04. Prevalence of IFG was also found to be higher in females than in males in both FDRs 13.7% vs 6.2%, p=0.038 and controls 6% vs 5.3%, p=0.66

Multivariate analysis revealed abnormal waist circumference, OR=10.97, 95% CI:5.4-22.3, p=0.001 and waist-hip ratio, OR= 7.8%, 95% CI:1.1-58, p=0.0005, being FDR, OR= 3.70, 95% CI: 1.08-29.1, p=0.0016 and SBP, OR=2.99, 95% CI:1.07-12.7, p=0.019, were
significantly associated with IGT in the study population, only abnormal WC, OR=9.50, 95%CI:2.84-31.9, p=0.001, being FDR OR=4.70, 95%CI:7.5-16.9, p=0.015 and elevated SBP OR=2.94, 95%CI: 0.92-20.7, p=0.035 were found to be significantly associated with IFG

Discussion: Prevalence of IGT and IFG were higher in FDR of patients with T2DM than in controls of similar age and sex. Independent risk factors most closely associated with IGT were abnormal WC and WHR, FDR, elevated SBP and DBP while those closely associated with IFG were abnormal WC, FDR and elevated SBP. These emphasize the importance of controlling all known risk factors especially overweight and obesity in FDRs. These findings may prove useful in identifying a specific group at particular risk of developing metabolic disturbances known to predispose to cardiovascular disease and T2DM

Conclusion: First degree relatives of patients with T2DM are at higher risk of developing pre-diabetes and eventually DM. Regular screening and early diagnosis may prove useful in prevention

Abstract #273

FOCAL NEUROLOGICAL DEFICITS AND RARE RADIOLOGICAL CHANGES: UNUSUAL PRESENTATION OF NON-KETOTIC HYPERGLYCEMIA

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Objective: Focal neurological changes that mimic stroke, though reported in literature, are rarely observed. We report a case of such focal neurological deficits and unusual radiological findings in a non-ketotic hyperglycemic patient with newly diagnosed diabetes mellitus

Case Presentation: After presenting with oliguria, dyspnea and fatigue, a 57-year-old obese male with COPD required pressor and ventilatory support for acute respiratory failure. Initial serum evaluation was consistent with hyperosmolar non-ketotic hyperglycemia and acute kidney injury (glucose 1308 mg/dl, osmolality 306 after 7 L of normal saline, creatinine 5 mg/dl, Anion gap 23, bicarbonate 16, betahydroxybutarate 0.73 mmol/L). Insulin drip and aggressive hydration were initiated. Acute GI bleed in the ER necessitated blood transfusion with resultant hemoglobin of 9.5 g/dl. While hyperglycemia resolved in 48 hours, initial A1c returned at 6.5%. Fructosamine was 173; corrected for albumin of 2, fructosamine was 325 correlating to A1C of 8%. Following extubation, patient reported left vision loss and right sided hemiplegia. Head CT showed bilateral basal ganglia subacute-chronic hypoattenuation. MRI was not an option due to patient’s obesity (BMI 35.7). These radiological findings were persistent on follow up CT in 2 weeks. Blood glucose was well controlled and patient’s neurological symptoms improved gradually but did not resolve.

Discussion: Patients with acute hyperglycemia often present with mental obtundation and coma. Our patient had a complex presentation. His newly diagnosed diabetes was not reflected in the A1c measurement as it was falsely low due to anemia and recent transfusion. Fructosamine though informative, was not completely accurate due to hypoalbuminemia. Focal neurological deficits during acute hyperglycemia have been reported in case studies. The pathophysiology and threshold of hyperglycemia over which focal neurologic changes develop are unknown. Bilateral basal ganglia changes are typical radiological findings. Although clinical and radiological changes are reversible, the latter tends to resolve earlier with normalization of glucose level. This is indeed the case in our patient as his CT head finding lags behind neurological improvement. Patient must be educated about the importance of follow up as the risk of neurological changes is high with recurrence of hyperglycemia.

Conclusion: Hyperglycemia should be high in the differential during evaluation of acute neurological symptoms mimicking stroke especially because these symptoms are reversible with better glycemic control. A1c, though widely used, should not be relied upon as it can be spuriously elevated due to multiple confounders.

Abstract #274

KETOALKALOSIS: A RARE AND MASKED PRESENTATION OF DIABETIC KETOACIDOSIS

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Objective: To present a unique case of Diabetic Ketoacidosis with alkalotic pH secondary to intractable vomiting

Case Presentation: A 25-year-old Male with history of Type 1 Diabetes Mellitus and Non-adherence with Insulin presenting with severe nausea, intractable vomiting, and fatigue for last 24 hours. On admission, patient’s was breathing 24 breaths/minute with deep and prolonged. Physical examination showed dry oral mucosa, tongue and decreased skin turgor. Laboratory analysis revealed serum Sodium 133 meq/dl, Chloride 93 meq/dl, Bicarbonate 20 meq/dl, Albumin 3.5 g/dl, and Serum ketones Large positive. Blood Gas showed pH 7.43, pCO2 28 mm Hg and Bicarbonate 19 meq/dl. Anion gap (corrected with
intermittent fasting strategies have showed good results in weight reduction, however must be used in caution due to possible development of metabolic problems. We aim to present a rare case of euglycemic diabetic ketoacidosis on Dapagliflozin, ketogenic diet, and intermittent fasting.

**Case Presentation:** Presenting a 35-year-old male admitted as a case of euglycemic diabetic ketoacidosis (euDKA) secondary to SGLT2 inhibitor intake, ketogenic diet and intermittent fasting. He presented with light-headedness, nausea, and vomiting. Baseline work-up revealed normal serum glucose of 8.0mm/L, elevated urine ketones, elevated urine glucose, and high anion gap. The patient was treated with hydration, regular insulin drip, and continuous glucose infusion. Glycemic control was then shifted to basal-bolus insulin regimen after anion gap was corrected. He was discharged on metformin (1000mg/day) and losartan (50mg/day) with advice to follow a 1,800-kcal diet: 50% carbohydrate, 20% protein, and 30% fat.

**Conclusion:** EuDKA is a rare condition but with increasing incidence in the advent of SGLT2 inhibitors. Ketogenic diet and intermittent fasting can trigger the occurrence of euDKA in patients taking SGLT2 inhibitors. This condition may be easily missed in ill T2D patients on SGLT2 inhibitors having euglycemia. The authors recommend to have a high index of suspicion of euDKA in patients on SGLT2 inhibitors presenting with clinical signs of possible diabetic ketoacidosis.

**Abstract #276**

**HYPERGLYCEMIA INDUCED BY INSULIN GLARGINE BIOSIMILAR SUBSTITUTION IN A PATIENT WITH CONTROLLED TYPE 2 DIABETES MELLITUS**

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**Objective:** LY2963016 (Basaglar) is a biosimilar of insulin glargine (Lantus) manufactured by biotechnological methods, which was approved by FDA in USA in 2015. Many patients who were using Lantus have been automatically switched to Basaglar since several insurance companies replaced Lantus with Basaglar as preferred formulary drug. We report a case of hyperglycemia induced by automatic substitution of Basaglar for Lantus with restoration of normal blood glucose on switching back to Lantus, in a patient with type 2 diabetes mellitus (T2DM).

**Case Presentation:** Forty eight years old Hispanic male with T2DM, diabetic neuropathy was followed in Endocrine clinic past 2 years for diabetes management. He was taking metformin 500 mg twice daily, Lantus
54 units once at bedtime and Apidra 16-20 units prior to each meal. His glycated hemoglobin (HbA1C) was 9.5\% and his glucose accuchecks were between 164 and 260 mg/dl shortly before patient was switched to equivalent dose of Basaglar when auto substitution was initiated by pharmacy. Patient was seen 2 months after the switch and his glucose readings noted to be in much higher range of 211 and 544 mg/dl. Despite that his glucose remained within range of 278 and 558 mg/dl. Patient had no active illness or dehydration, metabolic panel was within normal range except severe hyperglycemia, he had no recent changes in lifestyle and was complaint with his insulin regimen. Repeated HbA1C was 10.5\% which was 1.0\% higher as compared to previous value. After unsuccessful attempts of controlling blood glucose over 12 weeks, we switched Basaglar back to equivalent dose of Lantus 68 units (after obtaining prior authorization for the insurance) and we lowered dose of Apidra to 18 units. Thereafter daily log was reviewed over next 6 weeks, patient’s blood glucose was restored back to normal range with fasting ranges 123-129 mg/dl, premeal 127-169 mg/dl. We also noted minimal fluctuation of glucose values. We communicated to pharmacy staff to ensure avoidance of any insulin interchange in future without notifying provider.

**Conclusion:** Despite of evidence suggesting similar efficacy of Basaglar and Lantus, there is lack of data on safety profile and interchangeability of these agents at the individual level. Prescribers should be aware that this can result in worsening diabetic control and trigger hyperglycemic emergencies, even if substitution is for a brief period of time. Further evaluation regarding the long term adverse effects of using biosimilar insulin and strict regulatory control over drug substitution needs to be in action.

**Abstract #277**

**AIR POLLUTION: IS IT THE FORGOTTEN FACTOR IN RISING PREVELANCE OF TYPE 2 DIABETES?**

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**Objective:** Industrialization and overpopulation and has led to air pollution in urban areas of many parts of the world and many people breath sub quality air than recommended in World Health Organisation(WHO) Air Quality Guidelines. New data indicate the possibility of air pollution (measured in terms of particulate matter) not only exerting a greater impact on established health endpoints, but is also associated with a broader number of disease outcomes. Particulate matter 10 (PM10) describes inhalable particles, with diameters that are generally 10 micrometers and smaller. Prevalence of type 2 diabetes is rising in all regions in the world and the aim of this study was to see the relationship between air quality and prevalence of type 2 diabetes in each of WHO regions.

**Methods:** Data on Air pollution (PM10 valves) in different WHO regions were obtained from WHO ambient (outdoor) air pollution database 2014. The prevalence rates of type 2 diabetes for each WHO region were obtained from WHO global status report on noncommunicable diseases 2014.

**Results:** Type 2 diabetes prevalence rate and air pollution, represented by annual mean concentration of particulate matter 10 (PM10) valve for each WHO region is listed in Figure 1. Eastern Mediterranean region had the height prevalence of diabetes of 13.7\% followed by South-East Asia region and western pacific regions with a diabetes prevalence of 8.6\% and 8.4\% respectively. Lowest diabetes prevalence was noted in African region (7.1\%). In terms of air pollution measured by PM10, highest value was noted in Eastern Mediterranean Region (208 ug/m3) and second highest air pollution rate (PM10 128 ug/m3) was noted in South-East Asia Region. Europe region had best air quality among all the WHO regions (PM10 49 ug/m3) and the type 2 diabetes prevalence in Europe was 7.3\%. Type 2 diabetes and air pollution level showed a very strongly positive correlation (r = 0.91, p<0.05).

**Discussion:** WHO recommends a annual mean PM10 vales of 20 ug/m3 and all regions had much higher air pollution level than this. Eastern Mediterranean region and South-East Asia region had the highest and second highest prevalence of type 2 diabetes and also had highest and second highest air pollution rates respectively. Europe with a lower prevalence of type 2 diabetes had the best air quality among the regions.

**Conclusion:** Although small in number these data indicate a possible association with air quality in these WHO regions and the prevalence of type 2 diabetes which need to be looked in more detail considering individual countries.
Abstract #278

KNOWLEDGE, ATTITUDE AND PRACTICE OF PEOPLE WITH TYPE 2 DIABETES WITH END STAGE RENAL DISEASE AT PREAH KETMEALEA AND CALMETTE’S HEMODIALYSIS CENTERS

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Objective: The aim of this study is to evaluate the level of knowledge, attitude and practice of people with type 2 diabetes with end stage renal disease at Calmette and Preah Ketmealea Hospital’s hemodialysis centers and its relationship with diabetes-related data.

Methods: This is a cross-sectional study involving a calculated sample size of 59 patients, carried out in the hemodialysis ward of Preah Ketmealea hospital and CHEA SIM hemodialysis center of Calmette hospital, Cambodia. Face-to-face interviews were held to fill questionnaire with the agreement of the patients.

Results: 59 diabetic patients on hemodialysis (29 females) with the mean age of 63.9 (±7.4) were enrolled in the study. The mean score for patients’ KAP were 9.85 (±3.51), 0.90 (±3.9), 2.90 (±1.14), respectively. There was a significant correlation between patients’ knowledge, attitude and practice scores, higher knowledge level was significantly correlated with better attitude (r = 0.872, p-value <0.001) and practice (r = 0.332, p-value = 0.01) score. Patients on medication and higher education level were associated with significantly higher knowledge, attitude and practice score.

Conclusion: This study found a low level of knowledge, negative attitude and bad practice among Cambodian type 2 diabetic patients with end stage renal disease. More understandable educational materials should be created to fit the socio-cultural background of Cambodian people and commitment at the national level is needed to redirect resources toward this effort.

Abstract #279

SERUM FERRITIN AND ULTRASENSITIVE REACTIVE C PROTEIN IN PREDIABETICS WITH NON-ALCOHOLIC FATTY LIVER AND ITS ASSOCIATION WITH PARAMETERS OF DISEASE PROGRESSION.

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Objective: To determine the levels of serum ferritin and ultrasensitive reactive C protein in prediabetics and no prediabetics with non-alcoholic fatty liver (NAFLD) and its association with parameters of disease progression.

Methods: 105 asymptomatic people Peruvian from 30 to 70 years old, 60% were woman. We found 55 prediabetes (PD) and 50 Non-prediabetes (NoPD), according to the criteria of the ADA. The diagnosis of NAFLD was based in abdominal ultrasound on exclusion of other causes and a significant history of alcohol consumption. It was determined fasting Glucose (G), AST, ALT, GGT, HbA1c, serum Ferritin, Transferrin, ultrasensitive Reactive C-Protein (hsCRP); G and insulin at 60 and 120 minutes after TTOG. The progression parameters of NAFDL were AST/ALT ratio >1, The homeostasis model insulin resistance HOMA-IR > 3, hsCRP> 3.5 mg / L, serum Ferritin levels , women> 200 and in men> 300 ng / ml). People con NAFDL were 44 PD and 40 NoPD and without NAFDL 21 (11 PD and 10 NoPD). The analysis of the variables and association was made with the statistical package SSPS v21.

Results: In those with NAFLD, The mean age was lower (PD 47.2 , NoPD 51.9 years old p=0,02), BMI (PD 32.2 , NoPD 30.6 kg/m2 p=0,16). The PD had significantly higher levels HOMA-IR, ALT, GGT y hsCRP. The AST/ALT ratio >1 (PD 11.4% , NoPD 22.5% p= 0,54) and high levels of serum ferritin (PD 25%, NoPD 15% p=0,25). The HOMA-IR >3 (PD 79.5%, NoPD 47.5% p= 0,002), hsCRP>3.5 (PD 43.2%, NoPD 2.5% p<0,001). There was a positive correlation between Ferritin levels with ALT and GGT transaminase levels p <0.05, as well as between hsCRP levels with HOMA-IR levels, p <0.001.

Discussion: It has been suggested in the literature that NAFLD is a cause of hyperferritemia and that it would be associated with severe liver disease. The high levels of serum ferritin were present in 20% of the population with NAFLD studied, however, there was no statistical difference when comparing ferritin levels in prediabetics with non-prediabetics, as well as the AST / ALT ratio> 1, which could indicate a lower degree of hepatic necroinflammatory activity and fibrosis. The progression of the liver disease from simple benign steatosis to
steatohepatitis (NASH) would be related to greater insulin resistance and high levels hsCRP, in obese prediabetics and NAFDL in this study. 

**Conclusion:** Prediabetics with nonalcoholic fatty liver disease would have an increased risk of liver disease progression, so early intervention and follow-up are necessary to decrease insulin resistance and inflammatory markers. 

**Abstract #280**

**A CASE OF STEROID IMPROVED HYPERGLYCEMIA**

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**Objective:** To describe a patient encounter in which a patient’s blood sugars improved significantly after being exposed to steroids.

**Case Presentation:** An 87 year-old male is admitted for management of hyperglycemia after being transferred from an outside hospital. His PMH is significant for T2DM, HTN, AFib. His diabetes was managed as an outpatient with metformin and sulfonylurea alone. Three weeks prior, he was hospitalized for a CVA. His HbA1C was 10.9. During the initial hospitalization for the CVA, he was managed on a sliding scale of short acting insulin and was discharged on long-acting Lantus® 15 units and short-acting Novolog® 7 units with meals. While in rehab, his blood sugars were difficult to control, worsening throughout his time there. Three weeks after his initial admission, he presents again, this time with DKA. He was managed on a sliding scale of short acting insulin and was discharged on long-acting Lantus® 15 units and short-acting Novolog® 7 units with meals. While in rehab, his blood sugars were difficult to control, worsening throughout his time there. Three weeks after his initial admission, he presents again, this time with DKA. He was managed on a sliding scale of short acting insulin and was discharged on long-acting Lantus® 15 units and short-acting Novolog® 7 units with meals. While in rehab, his blood sugars were difficult to control, worsening throughout his time there.

**Discussion:** This case reports an example of hyperglycemia which was actually improved by steroids. This case is in direct contrast with the expected effects of steroids on blood sugars. It is difficult to tell what insulin, exogenous or endogenous, that led to the development of antibodies.

**Conclusion:** This case of steroid improved hyperglycemia was rare and counter-intuitive to typical management. However, in scenarios in which patients require extremely high amounts of insulin, insulin antibody development should be considered and immunosuppressants should be considered in treatment.

**Abstract #281**

**EMPAGLIFLOZIN INDUCED EUGLYCEMIC DIABETIC KETOACIDOSIS: A CLASS EFFECT OF SGLT2 INHIBITOR**

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**Objective:** Serum-glucose cotransporter-2 (SGLT-2) inhibitors have been associated with euglycemic diabetic ketoacidosis (eDKA). Most reports to date have involved canagliflozin (Invokana). Here, we report a case of eDKA in a patient with type 2 diabetes treated with empagliflozin (Jardiance).

**Case Presentation:** We describe a 68 year old patient with type 2 diabetes mellitus who presented with a Psoas abscess. On admission, he was found to have Serum bicarbonate of 12 mmol/L, Anion gap 27 with serum glucose 229 mg/dl. His beta hydroxybutyrate was 8.12 mmol/L. Lactic acid was 1.3mmol/L. Urinalysis showed 3+ ketone. He was on Jardiance. Glipizide up until 4 months ago when his PCP added Jardiance to his regimen. During hospitalization, he was maintained on adequate hydration and insulin sliding scale regimen. Glipizide, Janumet and Jardiance were added Jardiance to his regimen. During hospitalization, he was maintained on adequate hydration and insulin sliding scale regimen. Glipizide, Janumet and Jardiance were held. Over the next few days, his bicarbonate increased progressively to normal and his blood glucose levels were in the range of 160 to 200 mg/dL. It took 6 days for his anion gap to close. His complete metabolic recovery occurred 8 days after her last dose of Jardiance.

**Discussion:** Canagliflozin, dapagliflozin and empagliflozin are the SGLT-2 inhibitors. Although SGLT-2 inhibitors have shown to be effective in addressing many of the diabetes related complications including cardiovascular mortality, eDKA appears to be a worrisome adverse event associated with SGLT-2 inhibitors. FDA announced a post-marketing warning on the drug class for the increased risk euglycemic DKA. Most of the patients reported to develop eDKA so far were treated
with canagliflozin, likely because it was first to market and has the greatest exposure in the population. Other SGLT-2 inhibitors including empagliflozin are similar in action. However, not that many empagliflozin related eDKA cases have been reported. As eDKA is a class effect and that patients with type 2 diabetes may develop eDKA during treatment with any SGLT2 inhibitor, it would be prudent to be aware of this complication and to monitor the patients with serial labs including anion gap and ketones when they develop ketoacidosis.

**Conclusion:** eDKA appears to be a worrisome adverse event associated with SGLT-2 inhibitors. While the frequency and mechanism of this complication require more study, the patients should be counseled when prescribing any of the SGLT2 inhibitors and instructed to check urine or blood ketones if he or she feels unwell, even if plasma glucose is normal.

**Abstract #282**

**EFFECT OF MULTIFACTORIAL INTENSIVE INTERVENTION ON RENAL DAMAGE IN SHORT-DURATION TYPE 2 DIABETES**

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**Objective:** To explore the effect of multifactorial intensive intervention on urinary albumin to creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) in patients with type 2 diabetes mellitus (T2DM) without renal impairment.

**Methods:** In this 7-year randomized controlled study, a total of 150 type 2 diabetes patients had a mean age of 49.8±7.3 years, 51% were male, with disease duration < 1 year and without evidence of atherosclerosis were randomized into an intensive intervention group (IG), in which patients received multiple risk factors intervention by the special project team and tried to reach the predetermined intervention goals, and a conventional group (CG), in which patients received standard diabetes care by the clinic doctor. The prespecified microvascular end point was development of renal damage (change from baseline in UACR and eGFR).

**Results:** 70 patients in IG and 68 patients in CG completed the study. The UACR in the IG was significantly lower than that of the CG in each year (P < 0.01). Any albuminuria was present in 9 (12%) participants in the IG and 21 (28%) in the CG (P > 0.05) respectively. Multiple stepwise regression analysis showed that the effects of sex, FPG, HbA1c and SBP on UACR were statistically significant β= -5.112, P = 0.015; β= 0.908, P = 0.045; β= 2.087, P = 0.038; β= 2.787, P = 0.002 respectively, and the effect of aging on eGFR was statistically significant β= 0.447, P = 0.000.

**Conclusion:** multifactorial intensive intervention can effectively reduce the risk of albuminuria in short-duration type 2 diabetes. FPG, HbA1c and SBP are the risk factors for the increase of UACR, and aging is a risk factor for the decline of eGFR.

**Abstract #283**

**MANAGEMENT OF DIABETIC PERIPHERAL NEUROPATHY (DPN) USING LOW FREQUENCY PULSED ELECTROMAGNETIC FIELD (LF-PEMF) POST UNSATISFACTORY PHARMACOLOGICAL TREATMENT.**

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**Objective:** To evaluate the effectiveness of LF-PEMF in the management of DPN symptoms.

**Methods:** An observational study of 70 patients, male and female (1:1) aged 55 to 80 years. Enrolment criteria - known diabetics of > 4 years, HbA1c 7 to 12 and DPN of 0-5 years, post unsatisfactory pharmacological treatment. DPN in the patients was established using diabetic neuropathy symptom score (DNS) and Michigan neuropathy screening instrument (MNSI). Study period - 60 days. Primary endpoints were comparison of DNS and MNSI scores at the end of 15 days and 60 days follow-up compared to baseline DPN scores. Results were assessed at baseline and fortnightly follow-ups using DNS and MNSI score.

**Intervention:** Two sets of emitters of 20 and 6 MTL were used. Frequency: 10Hz. Instrument used Almag-02 manufactured by Elamed. Treatment session of 15 minutes each for 15 days, repeated after an interval of 30 days.

**Results:** Only 68 / 70 patients completed the first session of treatment period of 15 days and 61 / 70 completed the second session of treatment and follow-up. An intent-to-treat analysis based on all patients demonstrated a 38% reduction in DPN symptoms from baseline to end of first session of treatment period of 15 days with moderate to severe DPN on the basis of DNS and MNSI scores. The reduction in DPN symptoms increased to 52% from baseline at the end of study of 60 days. Overall 77% of the patients had some relief in DPN symptoms like aching pain, prickly sensation, numbness and ankle reflex.
at the end of treatment and follow up. The patients with good glycemic control had significant improvement in pain score. Neuropathic pain from peripheral neuropathy arises from ectopic firing of unmyelinated C-fibers with accumulation of sodium and calcium channels. PEMF safely induce extremely low frequency quasirectangular currents that can depolarize, re-polarize and hyperpolarize neurons. LF-PEMF therapy significantly facilitated regression of DPN symptoms assessed on the basis of DNS and MNSI scores.

**Conclusion:** The present study provides convincing data regarding the effectiveness of LF-PEMF therapy in the management of DPN symptoms. LF-PEMF is a safe and effective therapy for neuropathic pain in patients with diabetes and is able to modify some parameters of peripheral nerve function. Non-invasive angiogenic stimulation by LF-PEMF may be useful to prevent ulcer formation, necrosis and amputation in diabetic patients. The usage of pharmacological therapy is limited due to the high frequency of adverse events and dependence. Considering the benefits and safety, LF-PEMF can be used as an effective therapy in the management of DPN cases. No safety issues or adverse events were observed during the study.

**Abstract #284**

**CLINICAL EFFECTIVENESS OF SGLT-2 INHIBITORS IN PATIENTS WITH DIABETES MELLITUS TYPE 2 AND ESSENTIAL HYPERTENSIVE DISEASE**

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**Objective:** Diabetes mellitus type 2 [DM 2] and essential hypertensive disease [EHD] are interrelated diseases requiring the search for effective treatment. This research work aimed to investigate the clinical effectiveness of Dapagliflozin, a Sodium-Glucose Linked Transporter-2 [SGLT-2] inhibitor in patients with DM 2 and EHD.

**Methods:** The study involved 82 patients (39 females and 43 males) with DM 2 and EHD degree 1-2, stage II; average age (58.6 ± 5.2) years. All patients were divided into two groups: 42 patients treated for 3 months with Metformin 1500 mg/day, Diabetone® MR 60 mg/day and Ramipril 5-10 mg/day constituted Group I [GI]; 40 patients treated for 3 months with Metformin 1500 mg/day, Diabetone® MR 60 mg/day, Ramipril 5-10 mg/day and Dapagliflozin 10 mg/day constituted Group II [GII]. Groups were randomized based on age, sex and BMI. The control group was made up of 40 healthy volunteers. General clinical examinations, HbA1C, microalbuminuria [MAU], GFR, total cholesterol [TC], triglycerides [TG], LDL, HDL tests were performed in all patients. HbA1C level was determined by automatic analyzer D-10 (US). Biochemical Analyzer BA-88 (China) was used to determine microalbuminuria. Laboratory tests were performed according to the recommendations of manufacturers of diagnostic test kits in the laboratory using modern technologies. All tests were carried out in accordance with the Helsinki Declaration concerning human research.

**Results:** After treatment, HbA1C in Group II was reduced to 7.67±0.59% versus 9.48±0.72% before treatment and in Group I patients to 8.93±0.64% versus 9.65±0.81% before treatment. GFR increased in 22.7% of Group II patients and reduced in 9.1% of Group I patients. BP in all Group II patients did not exceed 150/90 mmHg, which was exceeded in Group I patients.

**Discussion:** Apart from changes in HbA1C, GFR and BP in GI and GII, remarkable changes were also seen in GII patients with regards to lipid profile and overall BMI. Total cholesterol content in GII was (6.67 ± 0.43) mmol/L (p <0.05) and reduced to (5.72 ± 0.35) mmol/L (p <0.05) after treatment. This was lower than that of GI patients by up to 18.68% (p <0.05). Reduction in BMI was more in GII patients than in GI patients.

**Conclusion:** SGLT-2 inhibitors e.g. Dapagliflozin increases the clinical effectiveness of complex treatment in patients with DM 2 and EHD.

**Abstract #285**

**CLINICAL CHARACTERISTICS AND OUTCOMES OF INDIVIDUALS WITH CHRONIC PANCREATITS REFERRED FOR TOTAL PANCREATECTOMY AND ISLET AUTOTRANSPANTATION – RELEVANCE TO CLINICAL ENDOCRINOLOGISTS**

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**Objective:** Chronic pancreatitis (CP) has a prevalence of ~ 50/100000 population and is well known to lead to secondary diabetes (Type 3c DM). In a recent study in the UK, Type 3c DM was the second most common type of newly diagnosed DM. For individuals with CP and unrelenting pain, total pancreatectomy offers the best relief. However, this invariably leads to DM. Auto-transplantation of islets (TPIAT) has shown increasing promise in mitigating the development of DM. Recent advances in remote islet processing have increased the possibility of performing TPIAT in a larger number of centers. It is anticipated that endocrinologists will be
increasingly called upon to manage these individuals. 

**Methods:** A retrospective chart review was performed of all individuals who had been referred to the University of Louisville Endocrinology Division for endocrine evaluation prior to TPIAT. Clinical and laboratory data before and after TPIAT was collected. All subjects were managed perioperatively and postoperatively by a team including Endocrinologist, Transplant Surgeon, Pain Management, and Gastroenterologist.

**Results:** Sixty subjects (33 female and 27 male) were evaluated over a 2 and 1/2 year period. The mean age was 47.68 +/-10 years with mean duration of pancreatitis of 9.39 +/- 7.16 years. The mean BMI was 24.49 +/- 5.23. 11.6% were obese. The mean comorbidities were 3.34. Vitamin D level was low in 68% of subjects. Impaired glucose tolerance (2 subjects) or DM (23 subjects) was present in 41.67% of subjects. Only 12% of individuals with Type 3c DM were obese. Individuals who had abnormal glucose levels had higher A1c (7.37 +/-1.97 vs 5.5 +/- 0.41 %, p <0.05) and fasting glucose (173.7 +/- 78.62 vs 93 +/-21.1 mg/dL, p < 0.05). However, there was no significant difference in the fasting c-peptide between those with and without DM. Twenty two subjects underwent TPIAT, including 6 subjects who had DM and one who had prior partial pancreatectomy. 42.9% of subjects with no prior DM achieved insulin independence and had a mean A1c of 6.1 +/- 2.2%. Individuals with DM who underwent TPIAT were able to maintain A1c levels similar to pre- TPIAT (7.35 +/- 1.69 vs 7.45 +/- 2.2%).

**Discussion:** There was a high prevalence of Type 3C DM, vitamin D deficiency, and comorbidities. Even those with Type 3C DM could benefit from TPIAT without worsening DM. More research is needed to better understand mechanism of Type 3C DM to preserve islet function in CP, before and after TPIAT. These could help develop new strategies to improve outcomes.

**Conclusion:** Chronic pancreatitis presents unique challenges to the endocrinologist before and after TPIAT. A coordinated multidisciplinary effort is likely to yield the best outcomes.
samples. Both in diabetic and non-diabetic subjects, E coli was the most frequent bacteria [p .72].

**Conclusion:** ESBL infection was frequent among diabetic than non-diabetic subjects. Glycemic status was worse in subjects with ESBL infection and those with non-ESBL infections. E coli was the most frequent bacteria isolate.

**Abstract #287**

**SHORT-TERM EVALUATION DEMONSTRATES IMPROVED GLYCEMIC CONTROL WITH NEW INSULIN DELIVERY DEVICE**

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**Objective:** Diabetes is associated with high morbidity and mortality. Poor glycemic control (HbA1c > 9.0 %) places patients at high risk for long-term complications and negatively impacts health care costs. Non-adherence to therapeutic regimens has been attributed to poor glycemic control. Exploring new treatment options which translate into improved glycemic control can benefit patients, health care delivery systems and society-at-large by improving care.

**Methods:** This 3 month evaluation was conducted in patients diagnosed with type 2 diabetes across multiple clinics within Southern California Kaiser Permanente Group to evaluate if simplifying insulin delivery with a new insulin delivery device (V-Go) resulted in improved HbA1c control in patients not controlled on prior regimens. This evaluation was pragmatic in nature to test the effectiveness of V-Go in a broad routine clinical practice setting. Each participating clinician initiated and intensified therapy based on standard clinical practice. Three months of V-Go devices per patient were provided by manufacturer. Patients were initiated on the device between February 2015 and March 2017. Efficacy variables evaluated were change in HbA1c, percentage of patients achieving an HbA1c ≤ 9.0% and change in insulin total daily dose (TDD). Descriptive statistics were applied, and two-sided t-tests and Chi-square test were used, defining a P-value of <0.05 as being statistically significant.

**Results:** Out of 85 patients initiated on V-Go, 60 (71%) completed the evaluation with a baseline mean HbA1c of 9.8 ± 1.7% and TDD of 72 ± 39.7 units/day (range 30 to 200 units/day). Prior to initiating V-Go, HbA1c values were ≤ 9.0% in 40% of patients with 60% of patients by deduction at high risk. Insulin delivery with V-Go resulted in significant mean reductions in HbA1c (-1.3%; p<0.0001) and TDD (-24 units/day; p<0.0001). Change in HbA1c was significant regardless of baseline TDD. Achievement of HbA1c ≤ 9.0% was achieved in 78% of patients after 3 months of V-Go use.

**Discussion:** Evidence supports improvements in glycemic control minimize the risk of complications and ease the burden of total healthcare costs. This short-term evaluation of V-Go shows promising results with a 63% reduction in patients at high risk (HbA1c > 9.0%). We contribute this improvement to better therapy adherence and improved insulin delivery. Long-term impacts to glycemic control and healthcare cost implications need further evaluation.

**Conclusion:** V-Go resulted in significant reductions in HbA1c, insulin TDD and resulted in more patients achieving glycemic targets than prior treatment regimens.

**Abstract #288**

**EFFICACY OF CANAGLIFLOZIN 300 MG IN OVERWEIGHT AND OBESE TYPE 2 DIABETES MELLITUS PATIENTS IN A REAL WORLD SETTING**

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**Objective:** We aim to evaluate the clinical efficacy of canagliflozin 300 mg in overweight and obese type 2 diabetes mellitus (T2DM) patients in real world setting. We also aim to determine the effect of Canagliflozin 300 on determinants of adiposity like body mass index (BMI) and waist circumference (WC).

**Methods:** We conducted a retrospective analysis across the medical records database of an established centre delivering both primary care and a secondary care providing a comprehensive care approach. We analysed patients of T2DM with BMI > 25 kg/m² who were initiated canagliflozin 300 / day at any time before 24 weeks (± 2 weeks). Changes in A1C, fasting plasma glucose (FPG), post-prandial glucose (PPG), weight, BMI, WC and occurrence of adverse effects events were evaluated.

**Results:** There were 86 overweight and obese individuals with T2DM who were initiated with canagliflozin 300 with an average age of 53.6 years and 41.9% were female. Mean A1C, FPG, PPG, weight, BMI and WC at baseline were 9.1%, 184.3 mg/dl, 256.1 mg/dl, 81.3 kg, 29.2 kg/m² and 85.3 cm, respectively. At 12 weeks, mean A1C decreased by 1.08%, PPG reduced by 58.2 mg/dl, weight decreased by 2.1 kg, BMI reduced by 0.73 kg/m² and WC reduced by 0.4 cm. At 24 weeks, outcomes were improved further: 1.6% reduction in A1C, 62.7 mg/dl reduction in FPG, 97.4 mg/dl reduction in PPG, 4.4 kg reduction in weight, 1.57 kg/m² reduction in BMI and 1.2 cm reduction in WC. Seventeen patients reported incidence of genital mycotic infections and one patient reported urinary tract infection.

**Discussion:** In clinical trials, canagliflozin 300 has shown...
efficacy in reducing A1c, FPG, PPG and body weight. The present study demonstrated efficacy of canagliflozin 300 in overweight and obese T2DM patients under real world setting with similar reductions in A1c and body weight but slightly higher reductions in FPG and PPG than those shown in clinical trials. The study also showed reductions in determinants of adiposity like BMI and waist circumference.

Conclusion: The real-world data suggests that canagliflozin 300 improved parameters of glycemic control, adiposity and body weight in overweight and obese T2DM patients in line with clinical trial outcomes.

Abstract #289

INSULIN LIKE PROTEIN FROM CAMEL MILK AND SIMILARITY WITH HUMAN INSULIN

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Objective: From experimental studies, clinical studies and epidemiological studies it is proved beyond doubt that camel milk has a potential role in prevention and treatment of diabetes. The main purpose of the study to isolate camel milk protein and compare its similarity with human insulin so that camel milk can be used as adjunct therapy for diabetes.

Methods: 30ml of raw camel milk was used for isolation of protein and peptides. The complete process included trypsin digestion, peptide fractionation and LC-MS technique. Digested and fractionalized peptide sample was processed further for liquid chromatography and mass spectra/tandem mass spectra were recorded in positive-ion and high sensitivity mode. MS/MS spectra were automatically calibrated during dynamic LC-MS. Raw data files were converted to Mascot Generic Format (MGF) and these MGF files were searched against UniPort, NCBI and common MS contaminant database.

Results: In our study 13 proteins and 22 peptide sequences were found similar to insulin/insulin like growth factor and isoform. In our study some very large peptide sequence were identified which were seen similar to NUAK family SNF1-like kinase and this peptide sequence gives evidence of role of camel milk effect in cancer treatment.

Conclusion: Observing so many similar peptides in camel milk sample with human insulin, isoform of insulin, receptors and others give strong evidence that camel milk has proteins/peptides of such proteins similar to human insulin and give support to finding that camel milk contains insulin-like molecules that mimic insulin interaction with its receptors.

Abstract #290

MODIFIED NCEP ATP III OR IDF CRITERIA: WHICH IS BETTER IN DIAGNOSING METABOLIC SYNDROME IN TYPE 2 DIABETES PATIENTS?

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Objective: The main aim of this study was to compare the IDF criteria with modified NCEP ATPIII criteria for diagnosing Metabolic syndrome (MetS) in a group of Type2 Diabetes(T2DM) patients presenting to the diabetic clinic of a premier tertiary care hospital in Sri Lanka to find out which criteria is better suited in this cohort of patients.

Methods: Cross sectional study was carried out by recruiting consecutive newly diagnosed adult T2DM patients (diagnosed within 12 months).Anthropometric, blood pressure measurements and laboratory investigations were carried out following the standard protocols. Prevalence of MetS was calculated using the IDF criteria and revised NCEP ATP III criteria.

Results: 72.1 % were females, 27.9 % males. Mean duration of Diabetes was 3 months (SD+ 2.9) 48 % of the subjects had a BMI over 25 kg/m2 and 22% had a BMI between 23-24.9 kg/m2. Crude prevalence of MetS was 63.7 % with IDF criteria and 73.9 % with modified NCEP ATP III criteria. Prevalence of MetS among males and females were 42.2 % and 72 % (P<0.001) for IDF criteria and 58.7 % and 79.8 % (p<0.001) for modified NCEP ATP III criteria respectively. There were 40 (18 males and 22 females) or 10.2 % who were diagnosed as having MetS by NCEP ATP III criteria but missed by the IDF criteria. There were no participants diagnosed by IDF criteria but missed by the NCEP ATP III criteria. Among those who were diagnosed to have MetS, 86.2% were identified equally by both criteria. The agreement between these two definitions as measured by the Kappa statistic was 0.76 (+0.05). Prevalence of MetS was found to be age dependant (Table 1).

Discussion: Overall prevalence of MetS was high in this group regardless of the criteria used. Similar levels of prevalence was recorded in the newly diagnosed patients in Bangladesh ( Nahar S,2011).MetS increased with age but was low in the oldest age group. Presence
of significantly higher level of MetS in women is notable and has been reported in other similar studies from South Asia (Pokharel DM, 2016). This can be attributed to many factors unique to women in this region like gestational weight gain, different socioeconomic standing, less contribution to workforce due to more male-dominant culture. Although the two criteria used in this study showed a good agreement in diagnosing MetS in Type 2 Diabetic patients, NCEP ATP III criteria diagnosed higher number of MetS. This was mainly due to the fact that in IDF criteria, abnormal waist circumference is a prerequisite to diagnosed MetS but in modified NCEP ATP III criteria it’s one of the three criteria needed.

**Conclusion:** The modified NCEP ATP III criteria may be better suited in diagnosing MetS in this group of Type 2 Diabetes patients.

**Abstract #291**

**RECURRENT MIGRATORY DIABETIC MYONECROSIS**

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**Objective:** To describe a case of recurrent diabetic myonecrosis with an unusual involvement of both the lower and upper extremity.

**Case Presentation:** A 46-year-old man with poorly controlled diabetes complicated by neuropathy, retinopathy and end stage renal disease on hemodialysis presented with right thigh pain. Labs showed a creatinine kinase of 1180 unit/L (nl: 30-233 unit/Liter). Right thigh MRI showed diffuse myositis along with subcutaneous edema. Due to concern for necrotizing fasciitis, a fasciotomy of the right anterior thigh was performed. The biopsy of the muscle showed necrotic, acutely inflamed skeletal muscle with negative cultures consistent with diabetic myonecrosis. Rheumatologic work up including myositis panel was negative. A month later the patient was readmitted for left toe ulcer and left calf pain. MRI of the left lower extremity showed increased T2 signal within the intrinsic foot musculature consistent with chronic neuropathic and microangiopathic changes. Four weeks later the patient was readmitted for left upper extremity edema. Physical exam demonstrated edema of the left forearm with tenderness to active and passive range of motion. MRI of the left upper extremity showed extensive subcutaneous edema with muscle edema within the proximal brachioradialis. Endocrinology was consulted during this episode for further evaluation of diabetic myonecrosis. Hemoglobin A1c was 7.6% in the setting of anemia. Left upper extremity venous duplex done did not show evidence of deep venous thrombosis. He underwent muscle biopsy of the left upper extremity which showed muscle with generalized atrophy and a small number of necrotic fibers. Rheumatology re-evaluated the patient but work up was consistent with recurrent diabetic myonecrosis. We proceeded with conservative therapy including tight glycemic control using the American Diabetes Association (ADA) inpatient glycemic goal as our target, rest and analgesia. He was discharged to a rehab with Endocrinology follow up and has not had recurrent episodes to date.

**Discussion:** This case was interesting because the patient was re-admitted with multiple episodes of migratory myalgias. During each episode a different extremity was involved and we made sure to rule out infection before making the diagnosis of diabetic myonecrosis.

**Conclusion:** It is important to suspect diabetic myonecrosis while evaluating for other common causes of muscular pain; especially if the patient has more poorly controlled diabetes with multiple microvascular complications. In patients with diabetic myonecrosis the current therapy is conservative management with tight glycemic control, rest and analgesics.

**Abstract #292**

**ATYPICAL CASE OF TYPE 1 DIABETES MELLITUS TREATED WITH BASAL INSULIN AND Dipeptidyl Peptidase-4 Inhibitor**

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**Objective:** To describe a patient with type 1 diabetes mellitus (DM1) who achieved good glycemic control with low dose basal insulin and a dipeptidyl peptidase-4 (DPP-4) inhibitor, sitagliptin.

**Case Presentation:** A 35 year-old man presented to the endocrine clinic for diabetic management in September 2013. He was diagnosed with DM1 eight months earlier during an admission for diabetic ketoacidosis. He weighed 80kg with BMI 23 and creatinine 0.9 mg/dL. Anti-glutamic acid decarboxylase and zinc transporter 8 antibodies were positive. Anti-islet cell antigen antibodies were negative. He was on Lantus 16 units at bedtime and Humalog with 1:15 insulin to carbohydrate ratio. Initial outpatient labs showed HbA1c 5.6% and C-peptide 2.2 (1.1-1.4 ng/mL) with corresponding serum glucose of 66 mg/dL. About 18 months after diagnosis, he had recurrent hypoglycemic episodes on the same insulin regimen with HbA1c 4.9%. Lantus dose was decreased gradually to 6 units. In
April 2015, HbA1c was 5.3% and C-peptide 1.6 ng/mL. Humalog was discontinued, and a trial of sitagliptin 100mg daily with Lantus was started. Upon change in therapy, the frequency and severity of hypoglycemia improved. Four years after diagnosis, HbA1c was 7.3%, C-peptide 1.0 ng/mL, with good glycemic control recorded on home glucometer. In November 2017, labs revealed HbA1c 7.7% and C-peptide 0.9 ng/mL. Continuous subcutaneous glucose monitoring indicated post-prandial glucose spikes. Therefore, low dose mealtime Humalog was reintroduced.

**Discussion:** DPP-4 inhibitors have become widely incorporated into the treatment of type 2 diabetes mellitus, but limited studies have been conducted to evaluate their efficacy in patients with DM1. Our patient had DM1 with residual beta cell function or possibly latent autoimmune diabetes of adult (LADA) associated with positive antibodies. His response to sitagliptin may be due to endogenous insulin secretion in the honeymoon phase or due to slower progression of disease in LADA. DPP-4 inhibitors have been shown to provide longer preservation of beta cell function and possibly attenuate autoimmunity due to its T-cell immunomodulatory effect.

**Conclusion:** This case illustrates that DPP-4 inhibitor achieved good glycemic control in a patient with DM1 in combination with basal insulin. Glucose and C-peptide levels were monitored closely to evaluate his endogenous insulin production. This patient may have been in the honeymoon phase of DM1. However, he maintained good control with Lantus and sitagliptin for 32 months, which is longer than the usual duration of honeymoon period. Further studies are needed to assess the benefit of long-term use DPP-4 inhibitors in DM1 or LADA and its role in beta cell preservation.

**Abstract #293**

**FREQUENCY AND PREDICTORS OF ERECTILE DYSFUNCTION IN BANGLADESHI DIABETIC MALE**

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**Objective:** The objective of the study was to determine the frequency of erectile dysfunction (ED) and explore its risk factors in type 2 diabetic (T2DM) men in Bangladesh.

**Methods:** During August 2013 to July 2014, 506 diabetic men aged 30-69 years were interviewed at the OPD of BIRDEM, Dhaka. Recent biochemical data (within last 6 months) were collected from patient’s diabetes guide book and hospital records. Erectile function (EF) was assessed by using the validated Bengali version of the International Index of Erectile Function-15 (IIEF-15) questionnaire.

**Results:** The overall frequency of erectile dysfunction was 60.2%. The frequency of smokers was high in ED group than without ED (56.86% vs. 40.09%, p=0.000) and the smokers in ED group smoked more pack-year cigarettes than no-ED group (16.49±1.44 vs. 6.09±0.23, p=0.000). More patients in ED group were physically inactive or sedentary (25.49% vs. 19.40%, p=0.137). The frequency of HTN was more in ED group (64.70% vs. 24.75%, p=0.000). ED group also had higher frequency of dyslipidemia (48.07% vs. 34.65%, p=0.003). BMI (25.20±2.15 vs. 23.71±3.43, p=0.000) and waist circumference (86.2±5.5 vs. 85.6±9.8, p=0.454) were higher in no-ED group. None of the subjects without ED had any micro- or macrovascular complications of diabetes. Patients with ED had significantly higher levels of fasting plasma glucose (10.03±4.59 vs. 6.77±1.24), HbA1c (11.04±2.42 vs. 7.32±0.88), serum creatinine (1.43±0.86 vs. 0.85±0.10), TG (178.59±6.07 vs. 176.40±8.51) and LDL Cholesterol (114.92±2.43 vs. 96.04±1.56) than those without ED. Estimated GFR was significantly lower in ED group (71.48±28.72 vs. 106.45±9.69). The mean IIEF-15 score was also significantly lower in ED group than no-ED group (14±6 vs. 28±1). The frequency of ED increased with age, ED frequency was 100% among 60–69 years group in comparison to the frequency of 35.5% in 28-39 years group (P=0.0001). The percentage of patients with severe ED increased to 77.40% in age group 60-69 years from 5.5% in age group 28-39 years. The frequency of ED increased with the duration of DM, ranging from 20.2% for DM 0-5 years to 100% for DM >20 years. The frequency of severe ED also increased with increasing duration of diabetes (2.4% severe ED in 0-5 years duration group in comparison to 100% severe ED in >20 years diabetes duration group). In men with uncontrolled diabetes the frequency of ED frequency was 71.6% in comparison to only 3.5% in controlled diabetes group. None with HbA1c<7% had severe ED in contrast to 28.4% in those with HbA1c≥7%.

**Conclusion:** Frequency of ED is very high among T2 DM Bangladeshi male and the frequency & severity of ED may be reduced by improving glycemic status.
Abstract #294

EUGLYCEMIC DIABETIC KETOACIDOSIS IN TYPE 2 DIABETES POST WHIPPLE PROCEDURE AND INTRAOPERATIVE EXTERNAL BEAM RADIATION THERAPY CASE REPORT

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Objective: Diabetic ketoacidosis (DKA) is one of the acute complication of diabetes, as when there is no or insufficient insulin to block the hepatic ketogenesis which lead to accumulation of ketone body, and subsequent acidosis, usually blood glucose will be high as diagnostic for this condition. In 1973, Munro et al, described euglycemic DKA, which have ketosis and acidosis with no much elevation in blood sugar (80-300 mg/dl). Mechanisms proposed, include insulin deficiency, substrate insufficiency like muscle disease, starvation, alcohol use, depression and use of sodium glucose cotransport inhibitor. The way includes elevated urinary losses of glucose, triggered by release of counterregulatory hormones, and or decreased rates of hepatic glucose production during fasting are possible mechanisms for euglycemia in the setting of DKA.

Case Presentation: 71 years old lady have type 2 diabetes for more than 13 years on oral hypoglycemic agent till 6 months ago when she developed ascending cholangitis secondary to biliary stricture related to pancreatic mass, at this time her diabetes were not controlled with HbA1c 12% and required insulin 19 glargine and 12-14 units of aspart TID premeal, in March 2017 the patient underwent whipple procedure and intraoperative external beam radiation as treating pancreatic cancer, patient tolerate the surgery with no major complication, and kept nil per Orem (NPO) with intravenous fluid (IVF) dextrose at rate of 50 ml per hours in addition to nasogastric tube which emptying gastric as well as bilious content. Two days later patient developed persistence acidosis with fever, leukocytosis, and central line related sepsis, so imipenem started with vancomycin, and fluconazole, later still she had persistence acidosis and ketonuria with blood glucose range from 6-11 mmol/l (table 1), and total parenteral nutrition started; clinically the patient was in pain managed with analgesia, her diabetes was controlled with sliding scale within 24 hours requirement range 7-14 units. She received NaHCO3 bolus of 150-mmol infusions. Later endocrine team where contacted and euglycemic DKA was establish management started as DKA with fixed rate of insulin infusion 4 units per hours with IVF 100 ml per hour and glargine 20 units, she received 7 hours total of infusion with no major hypoglycemia but stopped for 2 hours in between for hypokalemia and subsequent ketone in urine were resolve (table 2). Later patient was adjusted the insulin dose to total requirement 20-30 units per day.

Conclusion: Euglycemic DKA is emerging condition which need more attention, the limitation found that lack of similar condition experience lead for delay of best management option.

Abstract #295

GLP-1 RECEPTOR AGONISTS AND DEATH FROM ANY CAUSE IN ELDERLY PATIENTS WITH TYPE 2 DIABETES MELLITUS: A POST-HOC ANALYSIS

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Objective: Managing elderly patients with type 2 diabetes (T2DM) is typically challenging considering comorbidities and the risk of hypoglycaemia. It is unclear whether GLP-1 Receptor Agonists (GLP1-RA) confer additional mortality benefit in this specific subset of patients with T2DM.

Methods: We re-analysed data from a population-based open cohort study using The Health Improvement Network database. Elderly patients with T2DM exposed to GLP1-RA were compared to age, gender, body mass index, duration of T2DM and smoking status-matched patients with T2DM unexposed to GLP1-RA (N=2834). The minimum age for a patient to be characterised as elderly was the 70. Estimates were derived from Poisson regression.

Results: Elderly patients with diabetes receiving GLP1-RA were significantly less likely to die from any cause compared to matched control patients with diabetes (Adjusted Incidence Rate Ratio: 0.63, 95% Confidence Interval: 0.49-0.80, p-value < 0.001).

Discussion: GLP1-RA treatment in a real-world setting may confer additional mortality benefit in elderly patients with T2DM, thus confirming a consistent cardioprotective effect across age-groups. However, this finding should be interpreted in the context of the study limitations, importantly the retrospective nature of the evidence. If confirmed, this significant reduction in the risk of all-cause mortality, along with the already established low risk of hypoglycaemia and the favourable renal metabolism, may provide compelling arguments that treatment of GLP1-RA may be considered early in the management of elderly patients with T2DM.
Conclusion: GLP1-RA treatment may lower the risk of death from any cause in elderly patients with T2DM.

Abstract #296

STEM CELL TRANSPLANTATION IN TYPE 1 DIABETES- ONE YEAR RANDOMISED CASE CONTROL STUDY

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Objective: We conducted a randomized case control study for the utility of stem cell transplantation in type 1 diabetes and followed the patients for 1 year. We aim to understand the clinical effect of stem cell intervention and conventional insulin therapy in the treatment of type 1 diabetes

Methods: Stem Cell Therapy involving mesenchymal cells by Reelabs was performed on 22 T1DM patients (case group) and 17 patients were in the control arm who were provided with the standard care of therapy without any intervention with stem cells. Total 5 doses of stem cells, at the pre-defined fortnightly intervals over a period of 3 months were administered. The evaluation of the glycemic parameters for the % change in the HbA1c, Fasting Blood Glucose (FBS), Post Prandial Blood Glucose (PPBS), C-peptide and the decrease in the insulin dose as compared to the baseline for both the groups were compared after 1 year and recorded at 0, 3, 6, 12 months

Results: The mean age in the case and the control group was 16 years and 15 years, respectively. The mean baseline HbA1c were 11 % in each group, the mean FBS was 260, 314 mg/dl, mean PPBS was 387, 414 mg/dl, C-peptide was 0.61, 0.45 ng/ml and the daily insulin dose at the initiation of the study was 58, 71 units, respectively. There was significant difference in the percent change of FBS (-6.75 %), PPBS (-5.54%) and the daily insulin dose requirement (-18.15) in the case as compared to the control arm. However, there was a numerically superior percentage increase in the C peptide levels across the groups, but the difference did not achieve statistical significance (Figure).

In the case arm, after 12 months, there was 44.14% reduction in insulin dose (mean insulin dose at 12 months (32.4 ± 6.6 units), reduction in insulin dose was found to be statistically significant (p<0.0001). There was 25.2% reduction in HbA1c (p<0.0001), 54.75% reduction in PPBG (p<0.0001) and 47.2% reduction in FBS (p<0.0001)

Discussion: The superior reduction in the daily dose of insulin needed in T1DM patients is an important finding which demonstrates and corroborates with benefits of the stem cell therapy across other glycemic parameters

Conclusion: Mesenchymal stem cell therapy is a realistic goal in T1DM patients

Abstract #297

IMPACT OF CYST FIBROSIS AND CYSTIC FIBROSIS-RELATED DIABETES (CFRD) ON LUNG TRANSPLANT OUTCOMES

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Objective: The presence of glucose in the airways in patients with cystic fibrosis predisposes to bacterial growth. CF-Related Diabetes (CFRD) is a major risk factor for lung function decline and weight loss, however, the impact of CFRD in lung transplant outcomes is not very well known. The aim of this study was to evaluate the effect of CFRD on lung transplant outcomes at a tertiary care center.

Methods: Retrospective chart review of patients undergoing lung transplant (LTx) from the Adult Cystic Fibrosis Center at the University of Florida, Gainesville between 2011 and 2015. There were 14 CF patients who received a LTx, they were paired to 14 age-controlled, non-CF transplant patients. Variables included: diabetes treatment before and after lung transplant, glucose level during first seven days, type of insulin therapy, length of hospitalization and mortality at 12 months.

Results: Nine CF patients (9/14) had CFRD diagnosed before LTx, only 3 of them (3/9) were taking insulin. Among controls, 5 had diabetes diagnosed before LTx, 2 on ssi, 2 on oral agents and 1 had no treatment. Hyperglycemia over 200 mg/dl and hypoglycemia (<70mg/dl) were present in 14 and 8 patients respectively during the first 7 days after lung transplant. Among controls, only 6 and 4 developed hyperglycemia and hypoglycemia respectively the week after LTx.

At discharge, nearly all CF patients (13/14) were on insulin, though 4 out of 13 had sliding scale insulin (SSI) alone. Only 2 controls required insulin at discharge (SSI). A year after transplant, 10 out of 13 CF patients were still on insulin, 3 out of those 10 patients were on SSI alone. In contrast, only one non CF patient required insulin 12 months after LTx. Remarkably, within the first year after LTx, 4 non cf patients passed away, none in the CF group. Two of them were diabetic before the transplant. Length of stay was similar between CF and Non CF patients regardless of diabetes status.

Conclusion: Overall CF patients have better LTx
outcomes compared to age-matched controls. CFRD does not seem to affect LTx outcomes such as survival or length of stay during LTx.

Abstract #298

EFFICACY AND SAFETY OF SEMAGLUTIDE IN SUBJECTS WITH TYPE 2 DIABETES ACROSS RACE AND ETHNICITY SUBGROUPS: A POST HOC ANALYSIS OF THE SUSTAIN TRIALS

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Objective: The SUSTAIN clinical trials investigated semaglutide, a glucagon like peptide 1 analog, in subjects with type 2 diabetes (T2D). This post hoc analysis compared the efficacy and safety of semaglutide in race and ethnicity subgroups pooled from SUSTAIN 1 to 5 and 7.

Methods: Subjects with T2D were randomized to once weekly subcutaneous semaglutide 0.5 or 1.0 mg (only 1.0 mg in SUSTAIN 3) vs placebo (SUSTAIN 1 and 5; 30 weeks), sitagliptin (SUSTAIN 2; 56 weeks), exenatide extended release (SUSTAIN 3; 56 weeks), insulin glargine (SUSTAIN 4; 30 weeks) or dulaglutide (SUSTAIN 7; 40 weeks). Efficacy (change from baseline in HbA1c and body weight) and safety (adverse event [AE]) data were pooled and analyzed by race (Asian, Black/African American, Caucasian, Other) and ethnicity (Hispanic or non Hispanic).

Results: The analysis included 3,066 subjects who received semaglutide 0.5 or 1.0 mg, pooled from SUSTAIN 1 to 5 and 7. Estimated changes from baseline to 30 or 40 weeks in HbA1c and body weight by race and ethnicity are shown in the table. HbA1c reductions ranged from 1.3 to 1.5% with semaglutide 0.5 mg. With semaglutide 1.0 mg, HbA1c was reduced by 1.6 to 2.1%; Asian subjects had greater reductions than Black/African Americans or Caucasians. Body weight reductions in Caucasian subjects were 4.2 and 6.0 kg with semaglutide 0.5 and 1.0 mg. In other groups, reductions were 3.1 to 3.3 kg and 4.6 to 5.3 kg with semaglutide 0.5 and 1.0 mg. The proportions of subjects experiencing AEs, serious AEs, gastrointestinal (GI) AEs and AEs leading to treatment discontinuation are shown in the table.

Discussion: HbA1c reductions were consistent for semaglutide 0.5 mg, and greater in Asian than other race groups with semaglutide 1.0 mg, despite similar baseline HbA1c. Body weight reductions were greater in non Hispanics than Hispanics, and lower in Asians, whose baseline weight was lower than in Caucasians and Black/ African Americans. There was no apparent relationship between those with the greatest HbA1c and weight reductions. By race, Asian subjects generally had the most AEs, GI AEs and AEs leading to discontinuation. By ethnicity, there were generally more of each class of AE in non Hispanics than Hispanics.

Conclusion: Semaglutide provided clinically relevant reductions in HbA1c (≥1.3%) and body weight (≥2.6 kg) in subjects with T2D across SUSTAIN 1 to 5 and 7, with slight variations in efficacy and safety across race and ethnicity groups.

Abstract #299

THE STRESS OF INSULIN NON-COMPLIANCE: LESSONS LEARNED FROM A PATIENT WITH PRIMARY ADRENAL INSUFFICIENCY AND RECURRING DIABETIC KETOACIDOSIS

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Objective: Diabetic ketoacidosis (DKA) may be a life-threatening complication of diabetes, however its presentation and outcomes differ as a function of underlying precipitating factors and co-morbidities. We present the case of a patient with type 1 diabetes and primary adrenal insufficiency with recurring DKA due to insulin non-compliance and analyze the impact of differing approaches to steroid management on outcomes of interest across his multiple hospital admissions.

Case Presentation: During a 14-month period, this 21-year old man presented with six episodes of DKA due to insulin non-compliance. He was diagnosed with type 1 diabetes during childhood. His diabetes was poorly controlled during this time (HbA1c 13.6 -14.5 %). During all six hospital visits due to DKA, no other precipitating factor, other than insulin non-compliance, was identified. Vitals signs on admission were stable; body mass index was 15 kg/m2. DKA was confirmed by the presence of anion gap (25-31) metabolic acidosis and plasma/urine ketones; CO2 ranged from 11 to 18 mmol/L and glucose from 326 to 790 mg/dL. Patient was treated with intravenous fluids, electrolyte replacement and insulin infusion until resolution of the acidosis and transition to subcutaneous insulin. However, there was great variability in the approach to steroid replacement at presentation, with continuation of hydrocortisone home regimen during two of his hospital visits, to stress doses of up to 50 mg
intravenously every 8 hours. There was no relationship between the choice of steroid replacement therapy and the severity of the acidosis or the blood pressure range at presentation. There were no hypoglycemic events during acute treatment. When the patient was managed with maintenance hydrocortisone, the median [interquartile range (IQR)] time to resolution of DKA (14.5 [13.8 to 15.3] hours) was shorter than when high dose steroids were administered (25.3 [17.2 to 37.9] hours, respectively). Likewise, when the patient was treated with maintenance steroids, median [interquartile range] length of stay in the intensive care unit (5 [2.5 to 7.5] hours) and in the hospital (36 [28 to 44] hours) were decreased when compared to treatment with stress-dose steroids (37.2 [32.8 to 44.2] and 61 [52.3 to 68.5] hours, respectively).

**Conclusion:** Metabolic decompensation resulting from insulin non-compliance in patients with DKA and a history of adrenal insufficiency may not warrant stress dose steroids if additional precipitating factors are absent. Our data suggest that high dose steroids, in an otherwise non-complicated patient with DKA, prolong resolution of the acidosis, the need for high intensity care and lengthen hospital stay.
HYPOGLYCEMIA

Abstract #300

HYPOGLYCEMIA WITH NORMOINSULINEMIA: THE DIAGNOSTIC CONUNDRUM OF PROINSULINOMA

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Case Presentation: Proinsulinomas comprise a very rare subset of pancreatic neuroendocrine tumors (PNET). Proinsulin is a synthetic precursor to insulin that is secreted by pancreatic beta cells and then converted to C-peptide and insulin in equal amounts. The biological activity of proinsulin is one-tenth that of insulin, but its function is similar to insulin. Therefore proinsulinomas typically present with hypoglycemia accompanied by normal or low serum insulin levels. There is a two-to-one female predominance in published case reports. Most proinsulinomas occur in the body and tail of the pancreas and are smaller than 2 cm. Some proinsulinomas are not visible on CT or MRI, and endoscopic ultrasound is then utilized for anatomic definition.

We present a case of a previously healthy 26-year-old male who presented with episodes of diaphoresis, tachycardia, and hypoglycemia for two years. His family reported that some of the episodes included aggressive and violent behavior accompanied by seizure-like activity, after which the patient had no recollection of the events. Laboratory testing revealed elevated proinsulin level of 101.3 pmol/L (0-10.0 pmol/L), normal insulin level of 15.3 uIU/mL (2.6-24.9 uIU/mL), mildly elevated cortisol of 20.8 ug/dL (6.2-19.4 ug/dL), and normal C-peptide level of 3.1 ng/mL (1.1-4.4 ng/mL) at which time his serum glucose concentration was 56 mg/dL. Abdominal CT did not reveal a pancreatic lesion. He was started on 100 mg diazoxide twice daily with significant improvement in his symptoms. Abdominal MRI scan showed a 1.5 X 1.3 cm lesion in the pancreatic body without lymphadenopathy or metastases. He underwent laparoscopic distal pancreatectomy and splenectomy. Three days later, he was discharged to home and has not required exogenous insulin postoperatively. Pathology of the resected mass revealed well-differentiated PNET confined to the pancreas, with positive staining for insulin. At two month follow up, the patient was doing well.

Conclusion: This case demonstrates that initial laboratory testing must include proinsulin testing in addition to insulin, plasma glucose, C-peptide, beta hydroxybutyrate, cortisol, and screening for oral hypoglycemic medications in patients with recurrent hypoglycemia. Since newer tests for insulin use specific monoclonal antibodies that exclude proinsulin, separate proinsulin testing is now required. Both abdominal CT and MRI scanning may be necessary to localize a small lesion.

Abstract #301

USE OF GLP-1 AGONIST EXENATIDE TO TREAT REACTIVE HYPOGLYCEMIA AFTER GASTRIC BYPASS SURGERY

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Objective: To demonstrate the successful use of exenatide to treat a patient with severe reactive hypoglycemia post Roux-en-Y gastric bypass (RYGB) surgery

Case Presentation: The patient is a 45 year old Caucasian female who presented to clinic with complaints of frequent hypoglycemic events complicated by seizures and fractures. She previously had a RYGB surgery and developed severe hypoglycemia complicated by multiple seizure episodes and falls. She had a 72-hour fast which was consistent with reactive hypoglycemia. CT imaging was negative for pancreatic mass suggestive of insulinoma. Evaluation of continuous glucose monitor (CGM) showed she was hypoglycemic 20% of the time and hyperglycemic 5% with a HbA1c between 4.9-5.1%. She was treated with acarbose, octreotide and diazoxide along with frequent small low-carbohydrate meals without significant improvement.

During this time, she also lost 8 lbs, with total weight loss of 27 lbs by 12 months.

Discussion: Post-prandial hypoglycemia (PPHG) is a potential side effect of RYGB surgery. While the exact mechanism is unknown, proposed mechanisms include early/late dumping, islet cell hyperplasia, and exaggerated secretion of insulin and incretins such as GIP and GLP-1. Management involves dietary adjustments with frequent, small, low-carbohydrate meals, and pharmacotherapy with acarbose, diazoxide and octreotide. GLP-1 agonists used in Type 2 diabetics help stabilize blood glucose levels with reduced hypoglycemia events, and delays gastric emptying. GLP-1 agonists decrease glucagon secretion which likely contributes to decreased glucose spikes and subsequent insulin secretion, allowing for more stable blood glucose levels. The off-label use of GLP-1 agonists for reactive hypoglycemia has been documented in few case studies. Our case demonstrates that GLP-1 agonists can be effective in managing reactive hypoglycemia in patients who do not respond to traditional interventions. Significant weight loss, as was seen with our patient, is an important sequela of treatment that warrants careful monitoring.

Conclusion: Reactive hypoglycemia after RYGB surgery can be difficult to manage. GLP-1 agonists like exenatide are an effective treatment intervention when conventional therapies
are insufficient. Further clinical trials are needed to examine potential side effects and outcomes in post-bariatric surgery patients who develop complications of hypoglycemia.

**Abstract #302**

**MALIGNANT INSULINOMA WITH REFRAC TORY HYPOGLYCEMIA CONTROLLED BY PASIREOTIDE**

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**Objective:** Insulinomas are neuroendocrine tumors (NETs) that cause hyperinsulinemic hypoglycemia. Mostly benign, insulinomas can be malignant in 5-10% of cases. Control of hypoglycemia may be particularly difficult in patients with malignant insulinomas. NETs express somatostatin receptors, with the SST-2 subtype typically being most abundant. The somatostatin analogues octreotide and lanreotide are SST-2 preferential and can effectively inhibit hormone secretion by NETs often resulting in improvement of symptoms but varying depending on the SST subtypes expressed. Pasireotide is a SST multi-receptor ligand with affinity for SST-1, SST-2, SST-3, and SST-5 and this broader binding profile may result in improved suppression of hormone production in certain NETs.

**Case Presentation:** A 28 year-old woman presented with a 9 month history of severe hypoglycemia. Testing revealed findings consistent with insulinoma: Blood Glucose: 40 mg/dL, Insulin: 322 mU/L (< 3), C-peptide: 12.2 ng/mL (< 0.6), and Proinsulin: 532 pmol/L (< 5). CT and MRI showed hypervascular hepatic lesions compatible with extensive metastatic disease. Endoscopic ultrasound revealed a 12 x 8mm mass in the pancreas and FNA biopsy showed NET. Surgery with enucleation of the pancreatic mass and liver wedge resections with radiofrequency ablation was performed. Pathology confirmed metastatic pancreatic NET, grade 2, with Ki-67 proliferation index 25%. Octreotide scan revealed numerous hepatic lesions compatible with metastatic NET. The patient then underwent Y-90 SIR-sphere radioembolization of the liver and was started on everolimus.

During the hospitalization, hypoglycemia continued in spite of diazoxide, octreotide, high dose glucocorticoids, and continuous IV dextrose infusion. Pasireotide was then substituted for octreotide and the blood glucose levels improved dramatically. After initiating pasireotide, the IV dextrose infusion, diazoxide, and glucocorticoids were discontinued and she suffered no further hypoglycemic episodes. She was discharged on pasireotide and everolimus.

**Conclusion:** Our patient with malignant insulinoma and refractory hypoglycemia demonstrated a significant clinical response to pasireotide. Compared to octreotide, pasireotide has greater effects on activation of SST-1, SST-3, and SST-5, but lesser effect on SST-2 activation. Given its broad affinity for SST, pasireotide may be beneficial in patients with NETs who are partially or non-responsive to octreotide, and should strongly be considered as a treatment option.

**Abstract #303**

**ARTIFACTUAL HYPOGLYCEMIA IN RAYNAUD’S PHENOMENON**

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**Objective:** Persistent hypoglycemia is a clinical emergency that warrants medical attention and evaluation to avoid dreadful consequences. However, there are multiple causes for low finger-stick blood glucose, which may subsequently lead clinicians down the wrong diagnostic path. The following report describes a case of erroneously low finger-stick glucose values in a patient with Raynaud’s Phenomenon.

**Case Presentation:** An 88-year-old female with past medical history of coronary artery disease, Raynaud’s phenomenon, and severe pulmonary hypertension was admitted to the hospital for evaluation of recurrent pre-syncopal episodes. On admission, her finger-stick blood glucose was less than 50mg/dL and she was treated with intravenous dextrose. The patient underwent programmed finger-stick glucose monitoring, in view of hypoglycemia being the cause of her pre-syncopal episodes. In spite of having an adequate diet, the values of her finger-stick glucose ranged from 50-60mg/dL, requiring multiple intravenous dextrose treatments. The patient did not have any neuroglycopenic symptoms and was essentially asymptomatic at the times of the low glucose readings. The hypoglycemic evaluation included plasma C-peptide, proinsulin, plasma Insulin level, HbA1c, all of which were within normal limits. Additionally, a cosynepropin stimulation test revealed normal adrenal gland function. Her serum glucose levels were normal and did not correlate with any of the “low” finger-stick blood glucose values. During her hospitalization, examinations noted a purplish hue to her fingers. Finger-stick glucose testing, done after measures to warm her hands, revealed normal values. Hence, it was concluded that this patient’s low finger-stick blood glucose values were due to the vasoconstrictive effect from her Raynaud’s syndrome. Further, polypharmacy-induced orthostatic hypotension was concluded as the etiology of her recurrent pre-syncopal episodes.
**Conclusion:** Following a review of the literature, only seven other case reports of falsely low finger-stick blood glucose have been reported in patients with Raynaud’s disease, Scleroderma and Acrocyanosis, Eisenmenger syndrome and Acrocyanosis. As such, this report underscores the importance of educating healthcare providers on the nuances of Raynaud’s phenomenon such as warming hands prior to or considering ear lobe pricks as an alternative for measuring capillary blood glucose, to improve the accuracy of readings and to avoid extensive workup.

**Abstract #304**

**A RARE CASE OF NONINSULINOMA PANCREATOGENOUS HYPOGLYCEMIC SYNDROME FOLLOWING TRANSHIATAL ESOPHAGECTOMY**

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**Case Presentation:** We present the case of a 64 year old male with a past medical history of esophageal cancer who presented with episodes of severe hypoglycemia. Stage three distal esophageal cancer was diagnosed 12 years prior, for which he underwent neoadjuvant chemoradiation followed by transhiatal esophagectomy. Within one year hypoglycemic episodes appeared. Dumping syndrome was ruled out. He underwent EGD, showing markedly slowed motility in the stomach with pyloric spasm despite pyloromyotomy. Dietary modification was unsuccessful in improving hypoglycemia so he was stared on octreotide 70 mcg three times daily. The octreotide reduced his symptoms from multiple times daily to less than once per week. He continued having hypoglycemic episodes, lowest serum glucose documented at about 20mg/dl, with daytime and nocturnal episodes. He discontinued octreotide for a week, during which time he continued to have hypoglycemia of the same frequency. C Peptide was elevated as was proinsulin, and pancreatic CT did not show mass to suggest insulinoma. Visceral angiogram was performed to select pancreas portion (Left vs Right) with dominant insulin secretion to guide operative therapy. Intra-arterial calcium stimulation test suggested maximum production of insulin at the pancreatic tail after injection of the splenic artery. He underwent distal pancreateosplenectomy, with pathology confirming nesidioblastosis. Six weeks postoperative he was doing well without hypoglycemia on no therapy with serum fasting glucose 99-160 mg/dl.

**Discussion:** Noninsulinoma pancreatogenous hypoglycemic syndrome (NIPHS) is a rare cause of hypoglycemia in adults. NIPHS has been reported with increasing frequency in adults after bariatric and gastric ulcer operations, with even fewer cases not associated with surgery. The cause of NIPHS is unknown, with proposed mechanisms including increased incretin levels with gastric bypass, disruption of insulin homeostasis from rapid weight loss, and other unknown factors, such as disruption of the small intestine.

**Conclusion:** Our case demonstrates an occurrence of NIPHS after esophagectomy. To our knowledge, this is the first case in the literature to show NIPHS with clear histologic evidence of nesidioblastosis after esophagectomy. Many of the proposed theories of the cause of NIPHS are centered on gastric bypass surgery but do not explain how NIPHS could develop after esophagectomy. While the cause of NIPHS is still unknown, our unique case of this condition following esophagectomy suggests that multiple factors contribute to the post-operative development of NIPHS.

**Abstract #305**

**HYPOGLYCEMIA RISK IN HYPERKALEMIA MANAGEMENT WITH INSULIN: A QUALITY IMPROVEMENT STUDY IN SPARROW HOSPITAL**

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**Objective:** Identify the risk of hypoglycemia in hyperkalemia management with insulin

**Methods:** Retrospective data collection of patients receiving IV insulin for the treatment of hyperkalemia during the period of July, 2016 - November 2016, total of 30 patients. We included patient’s age, body weight, if they had a diagnosis of diabetes or using a diabetes medications, hospital unit and prescribing physician service. We also included the lab values of potassium prior and after IV insulin, blood sugar prior and after IV insulin, and timing of the management. We also looked at if Alternative treatments were used like IV diuretics, IV calcium or bicarbonate, Sodium polystrene sulfonate, Inhaled albuterol, Dextrose alone, and dialysis.

**Case Presentation:** The purpose of this study is to determine if the current Sparrow protocol for treating hyperkalemia with IV insulin is causing hypoglycemia. Retrospective chart review showed one patient that developed hypoglycemia, which raised the concern of the importance of developing an order set to adequately monitor blood sugar levels at 1,2,4,6 hours after receiving IV insulin for earlier detection of hypoglycemia.
ABSTRACTS – Hypoglycemia

Through chart review and team work consisting of clinical pharmacy, Nursing, IT, Nephrology and Endocrinology we have formulated the following care set:
A point-of-care blood glucose test 1 hour after administration of insulin and dextrose
A blood glucose lab draw 2 hours after administration of insulin and dextrose
A basic metabolic panel lab draw 6 hours after administration of insulin and dextrose (to recheck K and BG levels)
A PRN IV dextrose infusion set to automatically terminate after 8 hours
Second D50 bolus as a PRN order, in case of hypoglycemia (< 70mg/dL), that will remain active on the patient’s active medication chart for that first six hour period after the Hyperkalemia Order Set is initiated.

Discussion: The hypoglycemic effects of IV insulin last longer than a bolus of dextrose. More than one dextrose dose is often needed when treating hyperkalemia. Insulin’s peak effect occurs at about 60 minutes and this is when hypoglycemia has most often been reported in the literature.

Conclusion: Order sets are key to preventing this common medication error.

Abstract #306

TRANSARTERIAL HEPATIC EMBOLIZATION CAUSING HYPERGLYCEMIA IN A CASE OF MALIGNANT INSULINOMA

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Case Presentation: A 58-year-old male was admitted to hospital for recurring episodes of altered mental status and low finger-stick glucose. History was notable for an insulinoma metastatic to liver that was managed with everolimus and diazoxide. At presentation, capillary blood glucose (CBG) was 54 mg/dL, plasma glucose 37 mg/dL, and mental status was altered. Insulin and C-peptide levels were 35.9 IU/L (< 3) and 8.7 ng/mL (< 0.6), respectively. Despite treatment with everolimus, diazoxide, and dexamethasone, 10% dextrose IV fluids were required to prevent hypoglycemia. An attempt at treatment with octreotide was stopped due to abdominal pain. Transarterial embolization of right hepatic lobe metastases was then performed with bland embospheres and Gelfoam slurry. Within 3-4 days of embolization, CBG was consistently > 300 mg/dL despite cessation of dextrose IV fluids and all medical therapies for hypoglycemia. Fasting insulin level was 2.8 IU/L (1.9-23.0) when fasting plasma glucose was 399 mg/dL. A low dose basal/bolus regimen of insulins lispro and glargine was initially required to keep CBG below 250 mg/dL, and the patient was discharged on metformin and acarbose to control hyperglycemia.

Discussion: Insulinomas are rare pancreatic islet tumors with an incidence of 1 per 250,000 person-years, and only 5-15% are malignant. Medical therapy is almost always required for malignant insulinomas due to inoperable metastases or primary tumors. Historically, streptozocin-based chemotherapy has been utilized, though everolimus, an inhibitor of mammalian target of rapamycin (mTOR), is a new treatment modality for patients with malignant insulinoma and refractory hypoglycemia. Diazoxide and somatostatin analogs are also utilized to control hyperinsulinemia. However, transarterial hepatic embolization or chemoembolization may be required in patients with liver metastases that are refractory to chemotherapy and other treatments to control insulin secretion. The rarity of malignant insulinomas limits reports of therapeutic outcomes, and rates of tumor responses to hepatic embolization vary widely (17-82%). This patient’s case appears unusual because hepatic embolization caused insulinopenia and severe hyperglycemia requiring pharmacotherapy for satisfactory control.

Conclusion: Transarterial hepatic embolization can be an effective treatment to reduce tumor mass and insulin secretion in patients with malignant insulinoma metastatic to liver and refractory hypoglycemia. Depending on the contribution of hepatic metastases to insulin production, this case illustrates that the response to treatment may lower insulin levels sufficiently to cause at least short term hyperglycemia.

Abstract #307

HYPOGLYCEMIA DUE TO A “CONCEPTION-ENHANCING” ORAL SUPPLEMENT

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Case Presentation: An 18 y.o. woman with DM-2, asthma and obesity came to the emergency department (ED) due to persistent hypoglycemia. Her medicines were Metformin, Aspart and Detemir daily. Two days prior, her fingerstick blood glucose (BG) was low. She held her medicines and still ate meals. One day prior, she became symptomatic post-breakfast with a BG of 31mg/dL. BG rose to 70mg/dL with food intake, then decreased. The night prior, her BG was 43mg/dL. In the ED, her plasma glucose was 58mg/dL after one ampule of D50. In the ICU, glucose was kept at about 100mg/dL with D10W. Endocrinology was called. She had a history of frequent prednisone use for her asthma. She denied fever, nausea, vomiting or diarrhea. She was morbidly obese. ACTH stimulation test was normal; A1c-
6.5%; anti-GAD and islet cell antibodies were negative. The glucose increased in 24 hours and she was discharged with Metformin, Aspart and a lower dose of Detemir daily. A second episode with BG in the 30s occurred 2 days later. She denied taking Metformin or insulin. Plasma glucose was 47mg/dL on D5W in the ED, and she was managed in the ICU with D10W. A 72 hour fast was done. Pro-insulin (50.5 pmol/L), Insulin (88 uIU/mL) and C-peptide (7.7ng/mL) levels were elevated pre-fast, and normalized during the test. Glucoses were normal during the fast. Blood sulfonylurea was negative. She revealed that prior to the episodes, she was taking pills from ConceiveEasy TTC Kit System to enhance her fertility. Three of the ingredients are reported to have significant effects on glucose homeostasis: Rehmannia Glutinosa; Planax Ginseng; Agnus Castus. She was instructed to stop this product, and was discharged with a lower Metformin dose without insulin. Four days later, she was readmitted for a similar episode. She admitted feeling unwell after taking ConceiveEasy.

Discussion: Our patient’s supplement intake was the most likely cause of her hypoglycemia. Rehmannia Glutinosa elevates plasma insulin, suppresses plasma corticosterone and decreases hepatic Glucose-6-phosphatase (G6P) activity. Planax Ginseng decreases fasting BG, decreases insulin resistance, and has a postprandial hypoglycemic effect by blocking hepatic G6P activity and inhibiting gastric acid secretion. Agnus Castus increases insulin secretion, stimulates regeneration of beta cells and improves insulin resistance. Her hypoglycemia resolved with cessation of ConceiveEasy.

Conclusion: Consumption of ConceiveEasy product can lead to severe hypoglycemia in susceptible individuals. A warning label to alert patients to this potential side effect should be used.

Abstract #308

PSEUDOHYPOGLYCEMIA ASSOCIATED WITH SCLERODERMA: A CAUTIONARY TALE

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Objective: Pseudohypoglycemia is defined by falsely low fingerstick capillary glucose measurement, which can lead to unnecessary intervention. Pseudohypoglycemia can occur in settings of impaired perfusion to the microvasculature. We present a case of pseudohypoglycemia in a patient with chronic idiopathic pulmonary fibrosis with Raynaud’s phenomenon and scleroderma.

Case Presentation: An eighty year old women with idiopathic pulmonary fibrosis, with no history of diabetes was admitted with dyspnea. Subsequent work up confirmed the diagnosis of scleroderma. Blood glucose of 60 mg/dL was found on routine fingerstick glucose testing on admission. Subsequent fingerstick glucose monitoring showed multiple readings below 55 mg/dL (even after changing glucometers). However, she had no hypoglycemic symptoms. This raised suspicion about these glucose levels, and concomittant venous blood glucose measurements never showed hypoglycemia. Insulin, proinsulin, C-peptide and cortisol ruled out organic causes of hypoglycemia. Upon further evaluation, it was noted that she had cyanotic fingertips, with features consistent with scleroderma.

Discussion: Although pseudohypoglycemia has been reported in the literature, few cases were reported with Raynaud syndrome or acrocyanosis. Decreased perfusion of the microvasculature of distal extremities or direct endothelial damage may result in increased glucose uptake from the blood due to increased transit time to extremities which may display falsely decreased levels of glucose in their distal extremities. In Raynaud syndrome and acrocyanosis, there is thought to be upregulation of alpha-adrenergic receptors leading to excessive peripheral vasoconstriction. In the case of circulatory shock, there is terminal vasoconstriction or probable true arterial insufficiency. Finally, peripheral vascular disease causes a physical decrease in peripheral blood flow. Pseudohypoglycemia can also be seen if there is an increase in in-vitro glycolysis, whereby increased numbers of cells in the serum will result in increased glucose consumption prior to laboratory analysis. This can be seen in myeloproliferative disorders such as leukemia and polycythemia.

Conclusion: In conclusion, clinicians should consider disease of the microcirculation when confronted with low fingerstick blood glucose results in asymptomatic individuals. While not ignoring emergent treatment of potential hypoglycemia, correlation with venous blood glucose is mandatory, if appropriate. Additional considerations include glucose measurement via earlobe stick, or fingerstick sampling of capillary blood glucose at more proximal levels before initiating costly lab work.
Abstract #309

PARANEOPlastic HYPOGLYCEMIA CAUSED BY A 20 CM PANCREATIC TUMOR, COMPLICATED BY COLONIC PSEUDO-OBSTRUCTION

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NYU Winthrop Hospital

Objective: To describe a case of paraneoplastic hypoglycemia caused by a large pancreatic tumor complicated by colonic pseudo-obstruction (Ogilvie Syndrome).

Methods: A clinical case with biochemical, histopathological, and imaging findings are discussed.

Case Presentation: A 92-year-old man with a known pancreatic head spindle-cell tumor and no history of diabetes was admitted with vomiting and inability to tolerate food. On physical examination, he had abdominal distension. CT of the abdomen revealed diffusely dilated loops of bowel without evidence of obstruction, consistent with Ogilvie Syndrome. The patient was made NPO, and dexamethasone was held out of concern for bowel perforation. He developed severe hypoglycemia, with fasting glucose levels as low as 42 mg/dL. He denied use of insulin or sulfonylureas. He reported previous episodes of hypoglycemia that were attributed to insulin secretion from the pancreatic mass, which was treated with dexamethasone, diazoxide, and frequent meals. Dextrose, octreotide and diazoxide were administered to treat hypoglycemia. Fasting laboratory evaluation revealed suppressed serum insulin and c-peptide levels with a correlating glucose of 42 mg/dL, which ruled out an insulinoma. The ratio of IGF-II to IGF-I ratio was elevated at 12:1 (normal: <3:1), and insulin-like growth factor binding protein 2 (IGFBP-2) was elevated to 1779 ng/mL. These findings were consistent with non-islet cell tumor hypoglycemia (NICTH). Neostigmine was given to treat Ogilvie Syndrome, with good effect. Diazoxide and octreotide were discontinued and glucocorticoids were restarted. The patient was able to maintain euglycemia without dextrose. He was ultimately discharged home on prednisone.

Discussion: Definitive management of hypoglycemia associated with NICTH consists of either surgical resection or systemic treatment of the culprit mass, or treatment with glucocorticoids. Based on our patient’s age and comorbidities, a surgical approach was unfavorable. Glucocorticoid therapy, which is the preferred medical treatment, was delayed because of risk of gut wall thinning and bowel perforation in the setting of Ogilvie Syndrome. Eventually, with the resolution of Ogilvie syndrome, glucocorticoids effectively prevented hypoglycemia. Our patient was initially misdiagnosed with insulin mediated hypoglycemia, and was treated with ineffective therapies.

Conclusion: NICTH is a rare cause of hypoglycemia. Treatment for NICTH can be challenging when faced with a condition such as Ogilvie Syndrome. This case also highlights the importance of performing a complete diagnostic workup for patients with hypoglycemia and a known pancreatic mass to avoid inappropriate therapies.

Abstract #310

CLINICALLY SIGNIFICANT HYPOGLYCEMIA: IMPACT OF THE GUIDELINE-BASED HYPOGLYCEMIA ALERT LEVEL ON INSULIN MANAGEMENT IN THE HOSPITAL

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Objective: Clinically significant hypoglycemia, defined by a blood glucose (BG) of <54 mg/dL, is a potentially life-threatening condition that most often occurs as a complication of diabetes management. Guidelines point to a BG level of ≤70 mg/dL as an alert level that should elicit the implementation of corrective measures to prevent a patient from experiencing clinically significant or severe hypoglycemia. This study investigated the occurrence of clinically significant hypoglycemic events in a general medicine service at a teaching hospital and examined physician adjustment of insulin therapy in the affected patients, in response to a preceding hypoglycemic alert level.

Methods: We reviewed all cases of hypoglycemia in patients with a diagnosis of diabetes who were admitted to the general internal medicine service during the period of December 2016 through February 2017. Hypoglycemia was identified using point of care and plasma BG testing contained within an electronic health record search tool that reports monthly inpatient glucose levels. We examined hypoglycemic event frequency by number of event days and analyzed insulin management prior to and in response to the events.

Case Presentation: Within a cumulative hospital length of stay of 335 days for patients with a recorded BG ≤70 (n=37), there were a total of 71 hypoglycemia event days (21% of their total hospital stay), of which 14 corresponded to clinically significant hypoglycemia (11% of hypoglycemic event days). Four patients suffered at least one clinically significant hypoglycemic event in the hospital after presenting earlier in their admission with a hypoglycemia alert level. Their mean age was 59 ± 12 years; hemoglobin A1c was 8.4 ± 2.3% and body mass index 25.3 ± 2.1 kg/m2. Three of the four patients...
had a history of type 2 diabetes and presented with acute and/or chronic renal impairment. Scheduled total daily insulin dose was reduced in only 43% of the cases after a preceding BG alert level of ≤ 70 mg/dL. The reduction of insulin varied from 0%-100%. Only half of the patients with recurring hypoglycemia had holding parameters included in their insulin orders. **Conclusion:** Failure to translate guideline hypoglycemia alert levels into meaningful changes in insulin therapy is a major contributor to the occurrence of clinically significant hypoglycemia in the hospital setting.

Abstract #311

**SEVERE HYPOGLYCEMIA- A CASE OF VON GIERKE’S DISEASE**

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**Case Presentation:** A 43-year-old male who presented to the emergency room with nausea, vomiting and severe hypoglycemia. Past medical history was significant for a history of type 1 glycogen storage disease type 1a that had been managed most of his life with daily corn starch to prevent the symptoms and consequences of hypoglycemia; however, he was unable to tolerate any oral intake on the day of presentation. Laboratory data showed severe hypoglycemia in association with significant metabolic acidosis and lactic acidosis. He had a serum glucose of 29mg/dL, anion gap of 26, carbon dioxide level of 6mmol/L, lactic acid level of 19.2mmol/L and beta hydroxy butyrate level of 2.9mmol.

**Hospital Course:** Hypoglycemia resolved over 24 hours in response to 10% intravenous dextrose for glucose infusion rate of ~2.3mg/kg/min. Lactic acidosis resolved gradually.

**Discussion:** Von Gierke’s disease, also known as glycogen storage disease (GSD) type 1a, is a rare autosomal recessive disorder of the metabolism in which there is an inability to break down glycogen into glucose due to the deficiency of enzyme glucose 6-phosphatase. Glycogen storage disorders type 1 have an incidence of 1 in 100,000 individuals. Patients with GSD type 1 usually present at infancy with hepatomegaly and signs and symptoms of hypoglycemia, and less commonly as adults. Severe hypoglycemia is potentially life-threatening and individuals with glycogen storage disease such as Von Gierke’s disease can present with severe hypoglycemia, when they are unable to maintain a steady source of exogenous glucose. Hypoglycemia at initial diagnosis or periods of acute stress or illness is common. Frequent small servings of carbohydrates must be maintained throughout life to prevent hypoglycemia, lactic acidosis, hypertriglyceridemia, hyperuricemia and other long-term complications.

**Conclusion:** Glycogen storage disorders are rare and a high index of suspicion for such disorders is warranted when severe hypoglycemia exists in combination with severe lactic acidosis, in the absence of sepsis. Prompt treatment of hypoglycemia is important to prevent significant morbidity and death.

Abstract #312

**SEVERE HYPOGLYCEMIA: A METABOLIC LIFE-THREATENING COMPLICATION OF OPIOID DEPENDENCE**

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UTMB

**Objective:** Opioid dependence has reached epidemic proportions in our country. We report a case of severe hypoglycemia in a patient without diabetes with undisclosed history of opioid use.

**Case Presentation:** A 58 year-old woman was transferred to our hospital after presenting to her local emergency room with severe hypoglycemia. Patient’s history was positive for hepatitis C and marijuana use. A family member found the patient experiencing a seizure-like episode, after which she became unresponsive. Paramedics were called to the scene and a blood sugar level of 30 mg/dL was documented. The patient was given a bolus of dextrose and started on dextrose infusion; her blood glucose increased to 300 mg/dL and she regained consciousness. Two hours after the paramedics left, her blood glucose dropped to 90 mg/dL and then to 27 mg/dL, despite intake of juices and snacks. Her family took her to the emergency room. The patient was on intravenous fluids with dextrose upon arrival to our hospital and was alert and oriented. A computed tomography scan of the head, thyroid function studies and cortisol levels were normal. Upon further questioning, she reported a similar episode of hypoglycemia 3 weeks prior to admission that had also resulted in loss of consciousness. Patient was taken to a local emergency room, and the episode resolved with dextrose administration and oral intake. Blood glucose monitoring at home had remained normal since the initial episode. Patient denied changes in appetite or weight. On hospital day 2, the dextrose was discontinued and a 72-hour fast was completed with normal results, including glucose, C-peptide, insulin and pro-insulin levels. A sulfonylurea screen, with glucose, insulin and C-peptide was requested on the sample obtained from her local emergency room at presentation. The sample revealed a blood glucose of 26 mg/dL, a C-peptide of 20.2 and an...
insulin level of 208; sulfonylurea screen was positive for glimepiride. Upon further questioning, she acknowledged acquiring what she thought were codeine-containing tablets and taking them prior to her hypoglycemic events.

Discussion: Street vendors may supply medications that appear similar to common opiates and that, in the case of sulfonylureas, may lead to severe neurological impairment or death.

Conclusion: The medical community should remain alert on the inadvertent use of sulfonylurea tablets by individuals with opioid abuse. It is important that patients with opiate dependence be warned about this potential life-threatening complication. Furthermore, physicians should retain a high level of suspicion for inadvertent sulfonylurea use and undisclosed opiate use in patients presenting with unexplained hypoglycemia.

Abstract #313

OUTPATIENT FAST TEST-A CASE OF INSULINOMA

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LSUHSC Shreveport

Objective: Insulinoma is a rare neuroendocrine tumor with incidence of 1-4 per million population per year.

Case Presentation: A 64 year old woman with history of hypertension presented to the endocrine clinic for evaluation of recurrent hypoglycemia. Patient reported symptoms of excessive sweating, weakness, shakiness and anxiety in the mornings for most days of the month for about 2-3 years prior to this visit that had prompted her to eat all the time and gain weight. She was otherwise healthy and took no medications.

On the day of her clinic visit she brought her blood glucose logs (POCT checks) with documented low values. We conducted an in clinic fasting test. Within 3 hours of starting the test, she reported not feeling well and progressed quickly to neuroglycopenic symptoms of confusion, slow conversation and inattention assessed by counting back from 20. After drawing labs (confirmatory plasma glucose of 39 mg/dL), she was treated with orange juice and crackers and her symptoms improved with patient returning to baseline alertness in about 5-10 minutes with repeat plasma glucose of 82 mg/dl.

Her other labs with BG of 39 mg/dl were-Insulin: 56 (<17uIU/ml), pro-insulin: 97 (1.7-12 pmol/l), c-peptide: 5.7 (0.4-21 ng/ml), Beta-hydroxybutyrate:1.3. Her Insulin antibodies were negative (<5.0) and sulfonyl urea screen was negative.

She had documented Whipple’s triad and labs were consistent with endogenous hyperinsulinemia causing hypoglycemia. Triple phase CT abdomen showed a subtle 1x1.2x1 cm area of arterial blush in the pancreatic tail consistent with Insulinoma. She was referred to surgical oncology and had distal pancreatectomy with splenectomy. Her surgical pathology showed a 1 cm well differentiated neuroendocrine tumor, Grade 1 and stained positive for Synaptophysin, CD 56 and Insulin, consistent with diagnosis of Insulinoma.

She had complete resolution of symptoms post operatively and was doing well at her 3 month follow up visit

Conclusion: Insulinomas are rare neuroendocrine tumors of the pancreatic islets which can cause severe hypoglycemia. Most are sporadic, some are associated with MEN 1 syndrome. Our patient had severe recurrent fasting hypoglycemia with a positive Whipple’s triad and lab work up Imaging consistent with Insulinoma. Post operatively she had complete resolution of her symptoms. She did not have any other features of MEN syndrome and we think this is a case of sporadic Insulinoma.

In evaluation of patients with hypoglycemia, based on clinical suspicion observed outpatient fast test can be considered with a plan for admission to hospital if needed for a longer 72 hr Fasting.

Abstract #314

COMBATTING PANCREATECTOMY DIABETES IN AN MEN1 PATIENT BY REGULATING TUMOR PRODUCTION OF INSULIN

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Objective: Patients requiring additional surgical treatment due to insulinoma recurrence or failed initial surgery have been reported an increased prevalence of MEN1 with multiple tumors and malignant insulinomas. We present a case of MEN1 with post pancreatectomy diabetes controlled by regulated insulin production by insulinoma recurrence - a narrative of successful titration of hyperglycemia generated by phenytoin against hypoglycemia caused by insulinoma in a hypopituitary patient.

Case Presentation: 67 year female with history of MEN1 diagnosed at age 20 with multiple pancreatic tumors and malignant insulinomas. We present a case of MEN1 with post pancreatectomy diabetes controlled by regulated insulin production by insulinoma recurrence - a narrative of successful titration of hyperglycemia generated by phenytoin against hypoglycemia caused by insulinoma in a hypopituitary patient.

Case Presentation: 67 year female with history of MEN1 diagnosed at age 20 with multiple pancreatic tumors s/p distal pancreatectomy, parathyroidectomy, diabetes insipidus and panhypopituitarism post pituitary surgeries, diabetes post pancreatectomy (A1C 9), bland embolization of liver metastases and CKD (Cr 1.5) was in remission for 20 years until she started experiencing recurrent episodes of hypoglycemia. Biopsy via EUS showed insulinoma recurrence. She responded well to Sunitinib but required cessation due to coagulopathy and hand-foot syndrome. Her symptoms are fatigue and hypoglycemia when blood glucose falls from 200s to 70 mg/dl. Lanreotide 120mg
monthly did not control hypoglycemia and was started on phenytoin, titrated up to 1000mg daily. CT abdomen revealed numerous abnormal hypervascular regions in pancreatic head, uncinate process and neck; Gallium DOTATOC showed 2 discrete somatostatin receptor positive foci at distal pancreatectomy site compared with prior Octreoscan, with focal radiotracer localization in portocaval space highly suspicious for metastatic lymph node. Labs-elevated: pancreatic polypeptide 1184(0-418 pg/mL), 5-HIAA 59(0-22 ng/mL), fasting insulin 69(0-17Uu/mL) and normal: pancreastatin 87(10-135 pg/mL), NKA 13(nl <40), dopamine, plasma metanephrines. She is under consideration for surgery which will condemn her to lifetime of diabetes vs. medical management with somatostatin analog (increasing Lanreotide dose), molecular targeted therapy (Everolimus known to suppress insulin production) and/or peptide receptor radionuclide therapy when available.

**Discussion:** With surgery considered curative for insulinoma, advent of newer agents for progressive and/or symptomatic disease provides alternate methods to treat with potential to control tumor growth and prolongation of progression-free survival. Phenytoin as a potent inhibitor of insulin secretion has been used to bring effective transient control of hypoglycemia in insulinoma patients.

**Conclusion:** For nonsurgical candidates, phenytoin serves as a potential treatment option thereby offering MEN1 patients an extended life free of pancreatectomy induced diabetes with all its consequences. However, its long-term efficacy needs to be further reported.

**Abstract #315**

**ANALYSIS OF HYPOGLYCEMIC EPISODES IN OUT PATIENT DIABETICS IN AFRICANS USING ADEMOLUS CLASSIFICATION OF HYPOGLYCAEMIA**

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**Objective:** The recent grading of severity of hypoglycaemia for use in clinical practice using Ademolus Classification of Hypoglycaemia (ACH) is opening new knowledge path and insight in hypoglycaemia complicating diabetes mellitus management. It is estimated that in 2017 about 726.7 billion U.S. dollars were spent worldwide on health care expenditure due to diabetes mellitus, out of this only 3.3 billion U.S. dollars was spent in Africa. In Africa, hypoglycaemia complicate diabetes mellitus management not only in in-patients but also in out-patients. This article aim to examine hypoglycaemia occurring in African diabetics on out patient pharmacologic management

**Methods:** This is a retrospective study of 200 hypoglycaemic episodes occurring in 88 diabetics attending the out patients of the Endocrinology Clinic of Lagos State University Teaching Hospital, Lagos, Nigeria, between February 2004 and November 2017 (13 years and 9 months). Hypoglycaemia was defined as a blood sugar level of 70mg/dl or below. Only documented hypoglycaemic episodes were used. A questionnaire was used to extract relevant information from the 88 casefiles. The inclusion criteria include known diabetics, documented hypoglycaemic episodes occurring during outpatient pharmacologic management. The analysis was done with the aid of SPSS Version 17.0

**Results:** Of the 200 hypoglycaemic episodes studied, 79.5% were grade 1, grade 2 were 18% while 2.5% were grade 3. (see figure 1)

In all type 2 diabetics (T2DM), 82.9% had grade 1 hypoglycaemia, 14.6% had grade 2, while 2.4% had grade 3. In all type 1 diabetics (T1DM) 66.7% had grade 1 hypoglycaemia, 30.6% had grade 2 while 2.7% had grade 3. The lowest hypoglycaemic episode among out patient T2DM was an asymptomatic value of 29mg/dl (grade 3 hypoglycaemia!).

**Discussion:** The majority of out patient hypoglycaemic episodes in African diabetics is grade 1 while only a minute proportion develop grade 3 as out patient. The majority of T2DM had mild hypoglycaemic episodes irrespective of whether they are on oral hypoglycaemic agents (OHA) alone or on OHA and insulin or on insulin only. Though the percentage of grade 1 hypoglycaemia in each category differ.

Among African T1DM, grade 1 hypoglycaemia is twice as common as grade 2 hypoglycaemia while severe hypoglycaemia is not common. Grade 4 hypoglycaemic episodes was not recorded over the 13 years and 9 months period of study in both T1DM and T2DM in Africans.

**Conclusion:** Mild (grade 1), moderate (grade 2) and severe (grade 3) hypoglycaemia can all occur in African diabetics on out patients basis but with the majority of the episodes occurring as grade 1. Asymptomatic grade 3 hypoglycaemia can occur in African T2DM as out patient. A similar study is advised in other regions of the world.
A STUDY ON THE CORRELATION OF LIPOPROTEIN (A) (LP(A)) LEVELS WITH SEVERITY OF ACUTE CORONARY SYNDROME

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Objective: To assess the plasma Lp(a) levels in patients with acute coronary syndrome
To assess the severity of the coronary lesion by syntax angiographic scoring.
To establish the association between Lp(a) levels and severity of the acute coronary event

Methods: A cross-sectional study was done in a tertiary care center attached to University in south India. Subjects were 108 patients with first acute coronary event undergoing the coronary angiogram. Patients with risks independently associated with Lp(a) elevations like previous cerebrovascular events, uncontrolled diabetes mellitus (HbA1c >9), renal failure (creatinine >1.2 mg/dl), hypothyroidism (TSH >5) were excluded. Syntax score was calculated on an online website. Lp(a) levels were assessed by an immunoturbidimetry based assay.

Results: There were 74 males and 34 females in our study. Females had a higher median Lp(a) levels of 43.7 mg/dl versus 34.6 mg/dl for males but values were not statistically significant (p=0.44). Younger subjects, age less than or equal to 40 years were found to have higher median Lp(a) levels as compared to subjects in the 41-60 years and above 60 age group but this difference was not statistically significant. Median Lp(a) levels were 21.2 mg/dl in the low-risk syntax group (score of 22 or less); 49 mg/dl in the moderate risk group (score between 23-32); 162.95 in the high-risk syntax group (score of 33 and more). p-value was <0.001; Spearman correlation coefficient was 0.66. Using ROC curve a cut off of 34 mg/dl was obtained above which were considered to be a medium to high-risk candidate based on grouping of syntax score with 91.48% sensitivity and 67.21% specificity.

Discussion: Lp(a) which is taken independently as a risk factor for cardiovascular diseases significantly correlates with the coronary artery disease severity. The PURE study conducted proved that despite the lower incidence of conventional CAD risk factors in the lower income countries, they were found to have a higher incidence of CAD as compared to higher and middle-income countries. In this study, 96% were from South Asia and 83% were from India. Angeline T et al, a south Indian study Lp(a) levels showed higher Lp(a) in younger patients.

Conclusion: Lp(a) levels significantly correlated with the severity of lesion as assessed by syntax scoring.

Abstract #401
CORRELATION OF VITAMIN D LEVELS WITH SEVERITY OF CORONARY ARTERY DISEASE BY CORONARY ANGIOGRAPHY CATEGORIES AND SYNTAX SCORING

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Objective: To determine the relationship of vitamin D deficiency with severity of coronary artery disease.
To compare vitamin D levels in coronary artery disease and non coronary artery disease group & correlate vitamin D levels with severity of coronary artery disease by coronary angiography categories and syntax scoring

Methods: case control study. Patients diagnosed as CAD by coronary angiogram were included in the study as cases and matched controls were taken into study. The angiography findings was reported as single vessel disease (SVD), double vessel disease (DVD), triple vessel disease (TVD), multi vessel disease (MVD). Vitamin D was measured in cases and controls. Serum vitamin D level was graded as, normal (>30ng/ml), insufficiency (20-30ng/ml) and deficiency (<20ng/ml)

Results: 71% cases found to have low vitamin D levels(<30ng/ml) compared to controls (59%). Vitamin D deficiency (<20ng/ml) was more common in cases(32%) compared to controls(16.9%).

In coronary angiographic categories, vitamin D deficiency was significantly more in MVD(83.3%), followed by TVD(80%), DVD(23.07%), then SVD(22.72%). There is statistically significant relation exists between coronary angiography categories and vitamin D levels with p value < 0.001. Relationship between vitamin D levels and syntax scoring was evaluated by using spearman's rank correlation coefficient analysis, which showed a negative correlation with -0.339. Multiple linear regression analysis performed to determine the relationship between Coronary artery disease and multiple variables (vitamin D deficiency, Diabetes Mellitus, Hypertension, Dyslipidemia). Stepwise regression revealed CAD status and severity of Coronary artery disease is related to diabetes and vitamin D deficiency (p =0.014) but not to Dyslipidemia and Hypertension.

Discussion: Vitamin D had a skewed distribution with median
of 24 with range of 15.18 in cases, and 27 with range of 10.14 in controls. Results showed that there was no statistically significant difference between two groups (p value = 0.229). Varying levels of vitamin D levels in Indian population, severe vitamin D deficiency in cases and small sample size, may be the reasons for the skewed distribution. Earlier studies by Bakthir et al, S Karur et al & Lee et al have shown significant correlation between severity of coronary artery disease and vitamin deficiency.

**Conclusion:** Vitamin D deficiency is more commonly seen in CAD subjects. Vitamin D deficiency is more common in TVD compared to DVD and SVD. Vitamin D as an independent risk factor of Coronary artery disease

**Abstract #402**

**ACHIEVEMENT OF PRE-DEFINED LIPID GOALS IN INDIVIDUALS WITH TYPE 2 DIABETES RANDOMIZED TO ALIROCUMAB OR EZETIMIBE**

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**Objective:** Lipid profiles of individuals with type 2 diabetes (T2DM) often display a mixed dyslipidemia phenotype associated with elevated levels of triglycerides, non-high-density lipoprotein cholesterol (non-HDL-C), and apolipoprotein (Apo) B, and increased cardiovascular (CV) risk. We assessed achievement of risk-based goals for calculated low-density lipoprotein cholesterol (LDL-C), non-HDL-C, and ApoB measurements, all 3 lipid parameters) may reflect discordance between calculated LDL-C, non-HDL-C, and ApoB measurements, for example those often observed in individuals with mixed dyslipidemia and T2DM.

**Methods:** The pooled studies enrolled individuals with high/very-high CV risk who had hypercholesterolemia, despite background statin therapy (COMBO II) or background statin therapy ± other lipid-lowering therapies (OPTIONS I & II). Individuals were randomized to ALI 75 mg every 2 weeks (Q2W) (with possible dose increase to 150 mg Q2W at W12) or EZE (10 mg/day), each in addition to background statin therapy.

**Results:** Baseline characteristics were comparable between groups (Table 1). At W24, a significantly higher proportion of ALI-treated individuals achieved LDL-C <70/100 mg/dL, depending on CV risk, versus those who received EZE (P=0.0005; Table 1). ALI treatment also resulted in higher proportion of individuals reaching non-HDL-C <100/130 mg/dL or ApoB <80/90 mg/dL versus EZE (P=0.0086; Table 1). The combined threshold for LDL-C, non-HDL-C, and ApoB was achieved by 75.0% of ALI-treated and 56.7% of EZE-treated individuals (P=0.0003 vs EZE; Table 1). Levels of glycated hemoglobin and fasting plasma glucose were similar at baseline and W24 in each treatment group (Table 1). The proportion of individuals with treatment-emergent adverse events were similar between the ALI and EZE groups (Table 1).

**Discussion:** ALI enabled more individuals with T2DM to achieve their goals for LDL-C, non-HDL-C, and ApoB compared with EZE; in addition, the safety profile was similar in individuals treated with ALI or EZE. These results suggest that ALI is a more effective lipid-lowering therapy for this population. Small differences between the proportions of individuals achieving each lipid goal type (vs the slightly lower proportion achieving goals for all 3 lipid parameters) may reflect discordance between calculated LDL-C, non-HDL-C and ApoB measurements, for example those often observed in individuals with mixed dyslipidemia and T2DM.

**Conclusion:** In individuals with T2DM on background statin therapy, alirocumab demonstrated superiority in reaching LDL-C <70/100 mg/dL, non-HDL-C <100/130 mg/dL and ApoB <80/90 mg/dL (depending on CV risk) versus ezetimibe, and was generally well tolerated.

**Abstract #403**

**ELEVATED TRIGLYCERIDES (≥150 MG/DL) AND DIABETES MELLITUS ARE SIGNIFICANT PREDICTORS OF MAJOR CARDIOVASCULAR EVENTS AND INCREASED HEALTH CARE COSTS IN STATIN-TREATED PATIENTS: A REAL-WORLD ANALYSIS**

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**Objective:** Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality in individuals with diabetes. Although cardiovascular (CV) risk can be reduced with statin therapy, residual CV risk may remain, and epidemiologic, clinical, and genetic evidence suggests that elevated triglycerides (TG) are in the causal pathway of ASCVD. This analysis investigated
the real-world impact of elevated TG and diabetes on CV outcomes and cost in high-risk, statin-treated patients.

Methods: This retrospective administrative claims analysis of the Optum Research Database included patients aged ≥45 years with diabetes and/or ASCVD who had a statin prescription filled in 2010, had continuous medical/pharmacy coverage (index date in 2010), and were followed for ≥6 months (or less if due to death) up to March 2016. Patients with TG ≥150 mg/dL (n=27,471) and a comparator cohort with TG <150 mg/dL and high-density lipoprotein cholesterol (HDL-C) >40 mg/dL (n=32,506) were included in this analysis. Exclusion criteria included a day’s supply of niacin on the index date and other medical conditions. Hazard ratios (HR) and cost ratios were calculated from multivariate analyses (controlled for patient characteristics and comorbidities).

Results: Multivariate analyses revealed a 26% higher rate of occurrence of composite major CV events per unit time in the cohort with TG ≥150 mg/dL versus the comparator cohort (HR 1.258, 95% confidence interval [CI] 1.185–1.335, P<0.001), 12% higher total health care costs (HR 1.118, 95% CI 1.080–1.159, P<0.001), and 13% greater risk of inpatient hospital stay (HR 1.134, 95% CI 1.101–1.169, P<0.001). Multivariate analyses of the diabetes mellitus covariate revealed diabetes mellitus to be a significant predictor of composite major CV events, higher average monthly health care costs, and risk of inpatient hospital stay while controlling for other covariates (Table).

Discussion: Elevated TG and diabetes mellitus are known and important CV risk factors in high-risk patients. Although statin therapy is known to reduce CV risk, residual risk remains, leaving patients vulnerable to CV events and increased health care costs. To better understand the potential real-world burden and impact of elevated TG and diabetes mellitus, this retrospective administrative claims analysis evaluated risk for occurrence of CV events and health care costs and resource utilization.

Conclusion: In statin-treated patients with high CV risk, elevated TG and diabetes mellitus were found to be significant predictors of worse CV and health economic outcomes in a real-world setting.

Abstract #404

COMPARATIVE FASTING LIPID PROFILE IN RELATION TO TIME SINCE LAST MEAL IN SUBJECTS WITH TYPE2 DIABETES MELLITUS: AN OBSERVATIONAL STUDY FROM A TERTIARY HOSPITAL IN INDIA

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Objective: Lipid profile is traditionally measured after twelve hours of fasting. Measurement of lipid profile after ten hours fasting state would be more convenient, particularly in diabetic subjects. This study was done to evaluate the extent of alteration of serum lipid profile parameters in relation to time since the last meal in subjects with type 2 diabetes mellitus.

Methods: Sixty adult subjects with type 2 diabetes satisfying inclusion criteria were included in this study. Fasting blood samples were drawn at the outpatient clinic at 8 am and 10 am. Fasting lipid profile were measured by fully automated chemical analyser. Total cholesterol, triglyceride, were measured by enzymatic – colorimetric method. LDL-C and HDL-C were estimated by direct specific enzymatic analysis following pre-treatment to remove unintended interfering lipoprotein particles. Descriptive statistics were presented in the form of mean, standard deviation, median, inter quartile range for data on continuous scale depending on the distribution of data. Significance is assessed at 5 %.

Comparison of ten hours fasting lipid profile values with those of 12 hours values were done by paired sample t-test and Wilcoxon signed rank test.

Results: Mean serum fasting total cholesterol, high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) at ten hours were 186.45(±44.05) mg/dL, 45.28(±12.25) mg/dL, 112.38(±35.28) mg/dL respectively and at 12 hours were 185.90(±45.61) mg/dL, 45.03(±12.44) mg/dL, 112.07(±36.91) mg/dL respectively with no statistically significant difference (P=0.61,0.69,0.47 respectively).

There is no statistically significant difference between median (interquartile range) triglycerides (TG) levels of 143(96-214) mg/dL and 150(103-226) mg/dL at 10th and 12th hours respectively (P=0.57).

Discussion: We observed no significant difference in 10 hours and 12 hours value of triglyceride, total cholesterol, HDL cholesterol and LDL cholesterol. This observation...
THE EFFECT OF NICOTINE AND HIGH-DEXTROSE ON ENDOPLASMIC RETICULUM STRESS IN HUMAN CORONARY ARTERY ENDOTHELIAL CELLS

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Objective: Endoplasmic reticulum (ER) stress has been shown to be an important component in promoting cardiovascular disease and type 2 diabetes. Recent chemical screening in our laboratory suggested that nicotine induces endoplasmic reticulum stress in human coronary artery endothelial cells. However, due to the supra-physiological level of nicotine we used we wished to clarify this further.

Methods: Human coronary artery endothelial cells were obtained from ATCC. ER stress was measured using the ER stress secreted alkaline phosphatase (ES-TRAP) assay. Expression and/or phosphorylation of the ER stress mediators inositol-requiring enzyme 1a (IRE1a), phospho-IRE1a, protein kinase R (PKR)-like endoplasmic reticulum kinase (PERK), phospho-PERK, and activating transcription factor 6 (ATF6) expression were measured by Western blot. Cell viability was measured using the MTT assay, crystal violet staining, and trypan blue exclusion.

Results: In cells transfected with the secreted alkaline phosphatase (SAP) expression plasmid, treatment with 0.1, 1.0, 10, 100 nM and 1 and 10 mM nicotine resulted in a dose-dependent decrease in SAP expression with no noticeable toxicity as determined with the MTT assay. ER stress induced by 10 nM nicotine was inhibited by the addition of the ER stress inhibitors 4-phenylbutyrate and taurodeoxycholic acid. Nicotine (10 nM) also increased IRE1a and PERK phosphorylation, and increased ATF6 expression. Since high-dextrose increases ER stress in HCAEC, we examined the effect of combining nicotine with high-dextrose. Treatment of HCAEC with 10 nM nicotine and 13.8 mM dextrose (250 mg/dl) for 24-hours resulted in lower SAP activity as expected, but when combined, SAP activity was even lower. However, significant toxicity was observed in cells treated with both nicotine and high-dextrose, relative to the control cells as well as the cells treated with either nicotine or high-dextrose alone.

Discussion: Our studies indicate that nicotine treatment significantly increases ER stress in HCAEC at very low doses. Maximal inhibition of SAP activity occurred between 1 and 10 nM nicotine, without any toxicity up to 10 mM. Like other ER stress inducers, treatment with nicotine induced IRE1a and PERK phosphorylation as well as ATF6 expression. Interestingly, significant toxicity was observed in HCAEC treated with both nicotine (10 nM) and high-dextrose (13.8 mM), which by themselves have no associated toxicity.

Conclusion: These results suggest that smokers or those who use electronic cigarettes may be at increased risk for developing cardiovascular disease. Future studies are in the process to identify the type of cell death involved.
improvement in liver and kidney function. Lovaza was discontinued on discharge. Triglyceride levels checked at 15 and 28 days post discharge, were 309mg/dl and 197 mg/dl, respectively.

**Conclusion:** Propofol infusion syndrome (PRIS) can present as a complex of rhabdomyolysis, acute kidney injury, high anion gap metabolic acidosis, hyperlipidemia, cardiac dysfunction and elevated liver enzymes. The occurrence of PRIS increases with longer duration and higher infusion rate. However, it may also occur even after short infusion duration and with moderate doses (<4 mg/kg per hour), which can delay the diagnosis as most of the typical symptoms may be missing. The etiology of PRIS is complex. Inhibition of both mitochondrial electron transport chain and fatty acid oxidation leading to accumulation of fatty acids in various organs, and blockage of calcium channels in the heart are some of the commonly proposed mechanisms. Hypertriglyceridemia in PRIS could be an epiphenomenon caused by fat overload. Given the lack of specific signs and symptoms, physicians should remain aware of this diagnosis as its presentation may overlap with other underlying disease processes like shock and sepsis. The best management for PRIS is prevention, by limiting the duration of propofol infusion to less than 48 hours and the dose to less than 4mg/kg/hour. The management of established PRIS includes immediate discontinuation of propofol infusion and aggressive supportive management.

**Abstract #407**

**PCSK9 INHIBITORS - DOUBLING HEMOGLOBIN A1C: A DILEMMA**

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**Objective:** To describe a case of uncontrolled hyperglycemia induced by proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9I) therapy.

**Case Presentation:** A 70 year old man with history of stroke, hyperlipidemia, type 2 diabetes mellitus (DM), and non ischemic cardiomyopathy, was admitted with polyuria, polydipsia and weight loss. Uncontrolled hyperglycemia with a serum glucose level of 585mg/dL and elevated levels of AST and ALT, at 703 U/L and 779 U/L, respectively, were present on admission. DM was diagnosed 4 years ago and was managed with glipizide 10mg daily. Hemoglobin A1C (HbA1C) levels were in the range of 6.4 to 7.3% over that time. A history of persistently elevated low-density lipoprotein (LDL) levels of greater than 200mg/dL was present, and intolerance to four different statins, ezetimibe and colesevelam had been reported. Two years prior to admission, HbA1C was 6.7% and total cholesterol was 314mg/dL, triglycerides were 200mg/dL, high density lipoprotein was 69mg/dL, and LDL was 217mg/dL. Evolocumab 140mg biweekly was initiated. HbA1C increased to 7.8% and then 7.7%, 4 and 9 months later, respectively. Therapy was changed to alirocumab 150mg due to insurance reasons, and HbA1C increased to 8.1% and then 13.7%, 3 and 6 months later, respectively. There was no change in diet, physical activity or concomitant medications. Insulin was initiated and total daily insulin dose of about 70-80 units was required to maintain euglycemia. Alirocumab was discontinued. Three months later, daily insulin requirements have decreased to 25 units and HbA1C has decreased to 7.6%.

**Discussion:** New onset DM and worsening of glycemic control is a reported consequence of lipid lowering agents such as statins and is a key safety concern with PCSK9I therapy. The data on the effects of PCSK9I therapy on glycemic control is conflicting. Pooled analyses of phase III studies have reported no significant glycemic effect of alirocumab in patients with and without diabetes. No significant changes in HbA1C, fasting plasma glucose levels, total daily insulin dose and number of antihyperglycemic agents in patients with type 1 and type 2 DM were shown in a 24 week trial. Similarly, HbA1C levels were reported to be similar between evolocumab and placebo over 2.2 years. Recently, a Mendelian randomization study, using PCSK9 genetic variants as representation of pharmacological inhibition of PCSK9, showed a higher risk of DM. No cases of severe hyperglycemia after initiation of PCSK9I have been reported previously to our knowledge.

**Conclusion:** Close monitoring for dysglycemia is warranted in patients being treated with PSCK9I therapy and long-term safety data is needed regarding their glycemic and metabolic effects.

**Abstract #408**

**METABOLIC SYNDROME IN A LEAN PATIENT**

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**Objective:** Lipodystrophy are heterogenous disorders characterized by selective loss of body fat. These conditions may be genetic or acquired. There is considerable heterogeneity related to the pattern and extent of fat loss among various types of lipodystrophies. Partial and generalized lipodystrophies in addition to fat loss predispose patients to insulin resistance and complications such as diabetes mellitus, hypertriglyceridemia, hepatic steatosis, polycystic ovaries, and acanthosis nigricans. We
present a patient with partial lipodystrophy.

**Case Presentation:** 25 year old female with PCOS and adolescent-onset type 2 diabetes. In December 2014, she was referred by her PCP for papillary thyroid cancer diagnosed in the Dominican Republic. During the evaluation of thyroid cancer, she was noted to have pauciity of fat in the lower extremities as well as arms with central and upper body fat distribution, severe acanthosis nigricans over the neck, axillae and chest wall under the axillae. She was noted to be hirsute under the chin and abdomen. Biochemical evaluation showed elevated HbA1c >7.5%, elevated free testosterone level of 12.1, hypertriglyceridemia which have been as high as 6000s, all suggesting severe insulin resistance. She underwent a liver ultrasound which showed fatty infiltration, and measured 23.3 cm. She had multiple admissions for pancreatitis in the setting of hypertriglyceridemia. In the setting of decreased peripheral subcutaneous fat, a diagnosis of partial lipodystrophy was made. She met criteria for Dunnigan’s type familial partial lipodystrophy.

**Discussion:** Lipodystrophies should be considered in differential diagnosis of patients presenting with early diabetes, severe hypertriglyceridemia, hepatic steatosis, hepatosplenomegaly, acanthosis nigricans, and polycystic ovarian syndrome. A thorough physical examination particular in lean patients with these metabolic complications to look for evidence of fat loss should clinch the diagnosis. These patients can develop acute pancreatitis, cirrhosis μ/macrovascular complications of diabetes. Many patients die of coronary artery disease or cardiomyopathies therefore diagnosis early in life is important. Treatments are challenging and include high carbohydrate/low fat diets, increased physical activity to lower insulin resistance, thiozolidinediones, and even leptin therapy for generalized lipodystrophy.

**Conclusion:** Lipodystrophic syndromes are a group of congenital or acquired disorders that are characterized by either a complete or partial lack of adipose tissue. As these patients may develop hepatic cirrhosis, diabetes and complications, and pancreatitis and other catastrophic complications, early diagnosis and treatment is necessary.
improved and is categorized as “mild”. He has not had any cardiovascular problems and reports feeling less fatigued and much healthier.

**Discussion:** This patient presents with the typical comorbidities associated with hypogonadism: (abdominal) obesity and T2DM, accompanied by the symptoms ED and loss of energy. The hypogonadal state contributes to his inability to lose weight despite making efforts to do so. Restoration of normal testosterone levels changes the complex situation.

**Conclusion:** While hypogonadism is a major cardiometabolic risk factor, TTh improves all established cardiovascular risk factors and may profoundly improve cardiometabolic health in hypogonadal men.

**Objective:** Vitamin D plays a role in cardiovascular health by regulating blood pressure, healthful endothelial and smooth muscle functions. It also has effects on improving islet cell functions, insulin release and sensitivity thereby preventing the development of Diabetes mellitus. The objective of the study was to determine the prevalence of Hypovitaminosis D and its relationship with cardiovascular risk factors among adults in Kano.

**Methods:** The study was a community-based cross-sectional descriptive study. The study population was adults 18 years and above that have consented. A multistage sampling method was used to select a sample of 500 participants. A questionnaire was used to collect the information of each patient. The anthropometric measurements were determined using stadiometer, weighing scale and a tape. Plasma glucose, total serum cholesterol and its components and above that have consented. A multistage sampling method was used to select a sample of 500 participants. A questionnaire was used to collect the information of each patient. The anthropometric measurements were determined using stadiometer, weighing scale and a tape. Blood pressure was taken using sphygmomanometer. Vitamin D was assayed using ELISA technique. Fasting plasma glucose, total serum cholesterol and its components were estimated using enzymatic reactions methods.

**Results:** The mean age of the participants was 44.9±12.7 years, and 59.4% of them were females. Vitamin D insufficiency was found in 10.6% and deficiency among 31.3%. The proportion of those with adequate vitamin D was 58.1%. The factors that were significantly associated with Hypovitaminosis D include female gender, Body mass index ≥25kg/m2, increased waist circumference, hypertension, fasting blood glucose ≥6mmol/l, dyslipidemia and high parity among females (p<0.05). On multiple logistic regression, it was found that hypertension p=0.00 (95% C.I 0.332-0.810), female gender p=0.01 (95% C.I 0.337-0.884) and dyslipidaemia p=0.04 (95% C.I 1.009-2.399) were significantly related to Hypovitaminosis D. Studies have shown that living in abundant sunlight areas is not the only determinant of vitamin D status among human beings; other factors also contribute which include extremes of age, dark skin pigmentation, malnutrition, lack of sun exposure e.t.c. Women in Kano tend to be at risk of low vitamin D levels because of religious and cultural reasons which prevent them from staying outdoors or covering their body entirely when outside (burqah). The significant relationship between low vitamin D levels and cardiovascular risk factors among the participants is not surprising as several epidemiological and clinical studies have proved that.

**Conclusion:** The inhabitants of the tropics are at increased risk of Hypovitaminosis D in spite of the abundant sunshine. This deficiency could increase their risk of cardiovascular events.

**Objective:** Endoplasmic reticulum (ER) stress as well as oxidative stress have been shown to play important roles in metabolic and cardiovascular disease, and drugs that counteract the effects of ER and oxidative stresses maybe clinically useful.

**Methods:** To identify novel compounds that ameliorate ER and oxidative stresses, we screened two drug libraries purchased from Evotec, San Francisco, CA; the NIH clinical collection 1 (446 compounds) and the NIH clinical collection 2 (281 compounds). Human coronary artery endothelial cells (HCAEC) were tested for ER and oxidative stress. ER stress was measured with an ER stress-sensitive secreted alkaline phosphatase (SAP) assay. The cells were transfected with the plasmid pSEAP2-Control, expressing a heat-resistant form of SAP, and treated with the ER stress inducer tunicamycin in the presence or absence
of each of the various compounds for 24-hours, at which time SAP activity was measured. Compounds exhibiting significant increases in SAP activity (41 compounds out of a total of 727 tested; 5.6%) were then assayed for their ability to suppress superoxide (SO) anion generation in cells treated with 27.5 mM dextrose. SO generation was measured using the superoxide-reactive probe 2-methyl-6-(4-methoxyphenyl)-3,7-dihydroimidazo[1,2-A]pyrazin-3-one hydrochloride chemiluminescence.

**Results:** Out of 727 compounds tested, only 41 compounds exhibited a reduction in ER stress (5.6%). Of the 41 compounds identified as ER stress reducers, only 33 (80.5%) suppressed dextrose-induced SO anion generation. Interestingly, 51% of the compounds found to be dual-stress modifiers consisted of cardioprotective drugs, including statins, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors as well as beta-blockers.

**Discussion:** Only a limited number of agents had ER stress reducing capacity and even fewer were dual-stress modifiers. Fifty one percent of the compounds found to be dual-stress modifiers consisted of cardioprotective drugs, including statins, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors as well as beta-blockers.

**Conclusion:** Overall, this study shows that there is a paucity of pharmaceutical agents that have dual antioxidative and ER stress reducing capacity. Only 4.5% (33 of 727) of the drugs tested had these properties and of this group 51% were agents proven to have cardioprotective properties. Future studies should screen libraries of novel pharmaceutical compounds to identify candidate drugs for the prevention of cardiovascular disease.

**Abstract #412**

**IMPACT OF HIGH FIBRE DIET ON CARDIOVASCULAR RISK MARKERS IN COMORBIDITY OF HYPERTENSION AND TYPE 2 DIABETES**

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Care Well Heart and Super Speciality Hospital

**Objective:** Markers of subclinical cardiac injury are elevated in individuals with T2DM compared to healthy individuals. Dietary factors are associated with severity of coronary artery disease. Low intake of protein, fiber, vitamins, minerals and high intake of carbohydrate and fat was associated with higher probability of having severe CAD. Increase consumption of dietary fiber is widely recommended to improve health, but knowledge of relation between high fiber diet and cardiovascular disease risk factors in limited. Comprehensive evaluation of etiologic effects of dietary factors on cardiometabolic outcomes, their quantitative effects, and corresponding optimal intakes are not well-established. We aim to investigate whether diet changes in diabetes patients can control hypertension and associated cardiovascular risk factors

**Methods:** The patients were included if they were known hypertensives with T2DM (n=200) with BMI > 26kg/m2 and excluded if there were diagnosed with diabetic retinopathy, diabetic nephropathy or coronary artery disease. The planned intervention was the low fat and high fiber diet and all participants received behavioral and nutritional education, including recommendations for increasing the consumption of high fibre vegetables, fruits, cereals and legumes. Brachial-ankle pulse wave velocity (baPWV) measured along with lipid profile, fasting blood glucose. HbA1c, Lipid profile, baPWV, BMI, waist-hip ratio (WHR) monitored at start, after 3 & 6 months

**Results:** The mean age was 49.8 ±12.1 years. High fiber and Low – Glycemic Index diet intake were associated with significant improvement of baPWV, (p<0.0001) and hypertension, both SBP (p= 0.0068), DBP(p <0.0001). Serum cholesterol (p<0.0001), LDL-C (p<0.0001), WHR (p<0.0001) which are strong cardiovascular risk markers, also improved significantly. All diabetic demonstrated improvement in HbA1C (p=0.0001) and fasting glucose (p= 0.0017)

**Discussion:** High fiber diet is inversely related with several cardiovascular factors in the study which supports its protective role against cardiovascular disease and recommends for its increase consumption

**Conclusion:** High fibre diet has strong positive corroboration for the cardiovascular risk reduction in patients with hypertension and type 2 diabetes

**Abstract #413**

**CARDIOVASCULAR RISK ASSESSMENT BY UTILISING MICROALBUMINURIA AS A BIO-MARKER IN TYPE 2 DIABETES**

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**Objective:** Microalbuminuria is a marker for Diabetic Nephropathy (DN) and cardiovascular disease in patients with type 2 diabetes mellitus as well as in general population. Microalbuminuria, a complication of diabetes, is closely related to cardiovascular events. A fragmented QRS (fQRS) in the electrocardiogram (ECG) is strongly associated to cardiovascular morbidity and mortality. Microalbuminuria serves as an early indicator of DN risk and a predictor of its progression as well as cardiovascular disease risk in diabetes. We aim to determine the prevalence of microalbuminuria and its association with Cardiovascular risk markers

**Methods:** 4788 Type II diabetes patients attending
the endocrine outpatient clinic were screened. Microalbuminuria in all the subjects was estimated and the albumin to creatinine ratio (A:C) determined. Cardiovascular risk parameters: BMI, WHR, HbA1c, baPWV, Blood Pressure, ABI, LDL, HDL, TGs of all the subjects were also measured. baPWV was measured with VP-2000/1000-Colin Corporation, (Hyayashi Komaki Japan). Microalbuminuria was measured Clinitek status Analyzer. (Bayer Health Care)

Results: The overall prevalence of microalbuminuria was 48.4% (54.4% M /42.4% F). The longer the duration of diabetes, the greater the prevalence of microalbuminuria. Microalbuminuria had a highly significant correlation with duration of diabetes (p<0.001), HbA1c and BMI (p<0.05), Systolic and Diastolic Blood Pressure (p<0.01). Positive correlation was found with PWV, ABI, Cholesterol, LDL & TG.

Discussion: Regular screening for microalbuminuria is recommended for all diabetic patients, as early treatment is critical for reducing cardiovascular risks and slowing the progression to late stages of diabetic nephropathy (overt proteinuria and end-stage renal disease) patients.

Conclusion: The screening method with high sensitivity and negative predictive value, can be considered as a valid and reliable method for microalbuminuria screening in patients with HTN with/without T2DM.

Abstract #414

AMBULATORY BLOOD PRESSURE MONITORING AND CORRELATION WITH CARDIOVASCULAR RISK MARKERS IN TYPE 2 DIABETES IN ASSOCIATION WITH THE PREVALENCE OF NON-DIPPERS

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Objective: Ambulatory blood pressure monitoring is regarded as the gold standard for monitoring Nocturnal Blood Pressure (NBP) and is usually performed out of office. The widely used manual BP monitoring procedure has the potential to monitor NBP and estimate the prevalence of non-dippers and further estimate their relationship with cardiovascular risk markers. We aim to evaluate the prevalence of non-dippers in T2DM

Methods: We studied the prevalence of non-dippers among 80 T2DM patients in OPD setting, all of whom underwent 24-hour ambulatory BP monitoring. Uric Acid, HbA1c, Duration of Diabetes, BMI (Body mass Index), Lipids, Heart Rate, percent time elevation (PTE), Hyperbaric Index (HBI) and BP Variability of all the subjects were measured

Results: The measurements at 22:00, 02:00 and 06:00 h were defined as night-time and the others as daytime. ABPM was programmed to measure at 30-min intervals between measurements. 31.2 % patients were found to be non-dippers and 7.5% were found to be reverse dippers. There was no significant correlation of non-dippers with cardiovascular risk marker. Significant correlation of ABPM parameters was found among the reverse dippers with HbA1c (p<0.01) and SBP (p<0.01). 66% patients were hypertensives with 80% of BP variability

Discussion: The results of the present study indicate high prevalence of non-dipping phenomenon among T2DM patients.

Conclusion: 24-h ABPM monitoring is useful as an early predictive tool in assessing future cardiovascular risk, guiding treatment and management of these patients.

Abstract #415

PERIPHERAL ARTERIAL DISEASE AND ITS ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS IN TYPE 2 DIABETES

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Objective: Studies primarily from the European population have demonstrated the association of cardiovascular risk in patients with peripheral arterial disease in association with or without diabetes. Mechanistic insights also demonstrate the association of endothelial dysfunction. Landmark study from Italy (PANDORA Study) has demonstrated the factorial risk grading of CV risk in patients with peripheral arterial disease. In type 2 diabetics PAD has been defined as ankle-brachial pressure index (ABPI)<0.9. There is paucity of data from the Indian setting for the assessment for the corelates for CV risk association and grading in peripheral arterial disease in T2DM. We aim to evaluate the prevalence of PAD by means of ankle-brachial index (ABI) in T2DM patients-stage I grade 0 category 0 (Fontaine’s stages and Rutherford categories classification of PAD) in North Indian population

Methods: Between winter 2012 and summer 2016, 8734 asymptomatic (no complaints pertaining to PAD) Type II Diabetes patients were enrolled. Blood pressure, BMI, baPWV, HbA1c, Cholesterol, HDL, LDL & Triglycerides values were analysed. The ABI was measured with VP-2000/1000-Colin Corporation, Hyayashi Komaki, Japan. PAD was considered when ABI measured was <0.9 in either leg

Results: We studied 8734 patients (5201 men and 3533 women. The mean age 48.3 ±7.0 years, the mean duration of diabetes (8.2± 4.3 years). The prevalence of PAD was 15.3% with men having a slightly higher prevalence
(15.9%), as compared to women (14.8%). ABI was found to be significantly correlated with age (r=0.05), duration of diabetes (r=0.06), PWV (r=0.07 for left and r=0.08 for right) and DBP (r=0.06). We did not find a significant correlation between measures of obesity (WHR) and PAD.

**Discussion:** Using ABI, we found prevalence of PAD in 15.3% of type 2 diabetics which is comparable to western population. Risk factors significantly associated with PAD were - age, duration of diabetes, PWV and DBP. The contribution of blood pressure as an independent contributor to the risk score needs further exploration. The reduction of blood pressure would also have implications for the reduction of events, which needs an independent evaluation. ABI should be evaluated and promoted as an ideal tool for predicting mortality in diabetic patients.

**Conclusion:** Considering ABI as a significant future CV risk marker, routine screening of diabetic population is advisable for future CV risk prevention.
The obesity epidemic continues unhindered and the rate of bariatric surgery rises, clinicians must be familiar with common and uncommon nutritional deficiencies that may be exacerbated by bariatric surgery.

**SEVERE REPERCUSSIONS OF ROUX-EN-Y SURGERY**

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**Objective:** A growing body of literature has documented several micronutrient deficiencies more prevalent in obese individuals. Patients undergoing bariatric surgery often develop nutritional deficiencies or exacerbate established deficiencies requiring lifelong supplementation. Bariatric surgery leads to severely reduced caloric intake, leading to decreased intake of macro- and micronutrients. Adequate nutrition can be provided through parenteral administration. This case highlights the repercussions of fat-soluble vitamin and mineral deficiencies leading to severe malnutrition.

**Case Presentation:** The patient, a 57-year-old female, presented with chronic malnutrition. She had Roux-en-y gastric bypass surgery (RYGB) in 1988 and subsequently developed many nutritional complications: osteomalacia, peripheral myelopathy (copper deficiency), pellagra dermatitis (vitamin B3 deficiency), iron deficiency anemia, and retinal degeneration (vitamin A deficiency). Given her deterioration, she was started on total parenteral nutrition (TPN) through a peripherally inserted central catheter. DEXA scan showed hip T score of -3.49. MRI of her thoracic spine revealed chronic loss of height at multiple levels. Treatment with vitamin and mineral supplementation yielded suboptimal results. After one year, the PICC had to be removed due to infection; TPN was discontinued resulting in unintentional weight loss, worsening myelopathy, and vision impairment from worsening mineral and vitamin deficiencies. After failing outpatient management and undergoing severe malnutrition, surgery is planning on reversing RYGB.

**Conclusion:** Bariatric surgery has become a popular option to tackle the rising prevalence of obesity. Prior to surgery, obese individuals are, paradoxically, privy to metabolic and nutritional derangements that could be further exacerbated by bariatric surgery. RYGB develops deficiencies in fat-soluble vitamins and minerals. Screening for nutritional deficiencies is critical in obese individuals before and after bariatric surgery. The American Society for Metabolic and Bariatric Surgery recommends assessments every three to six months in the first year after bariatric surgery. Patients may require continued reminders on how to adapt to their new body. This case emphasizes the importance of counseling sessions with a registered dietitian experienced with bariatric patients. As the obesity epidemic continues unhindered and the rate of bariatric surgery rises, clinicians must be familiar with common and uncommon nutritional deficiencies that may be exacerbated by bariatric surgery.

**HYPERPHOSPHATAEMIC FAMILIAL TUMORAL CALCINOSIS: A RARE CASE**

Tania Tofail, MRCP, Mohammed Fariduddin, MD, Shahjada Selim, MD, Tahniyah Haq, MRCP, MD, MSc, Sharmin Jahan, FCPS, MD, Mursheed Khan, MD, Hirjahan Banu, FCPS, Marufa Mustari, FCPS, Mohammad Abul Hasanat, MPhil, MD

**BSMMU**

**Objective:** To describe a rare case of Hyperphosphatemic familial tumoral calcinosis (hFTC) which is an autosomal recessive (AR) disorder characterized by deposition of calcium phosphate crystals in periarticular space and soft tissues.

**Methods:** We present the clinical, laboratory and imaging findings and a review of the literature.

**Case Presentation:** A 16-year girl, second issue of a consanguineous couple presented with painless symmetrical bony swellings around hips for 3 years. She lost 25 kg weight due to profound anorexia in the first year of illness and developed secondary amenorrhea. Last 7 months she had repeated GTCS due to hypocalcaemia. The bony swellings were located in both gluteal regions and were 30x35 cm², hard and non tender. Mobility of hip joints were restricted. Except for severe wasting as a part of generalized cachexia, other systemic examination was unremarkable. Investigations revealed anaemia (Hb-E trait), low albumin, low corrected calcium (during convulsions) otherwise normal, persistently high phosphate & vitamin-D level, normal iPTH & ALP, low serum ascorbic acid, normal ESR & CRP. X-ray & CT scan of pelvis showed large calcified mass in periarticular soft tissues. Biopsy confirmed presence of dystrophic calcification. Diagnosis of tumoral calcinosis was based on biochemical parameters, imaging and biopsy findings. Phosphate restricted diet and phosphate lowering agent improved biochemical parameters. Vitamin C supplementation has led to gradual reduction of tumour size. Surgical excision has been planned. Discussion: hFTC is a rare entity that we encounter in our clinical practice. Around 100 cases has been reported in English literature so far. hFTC is characterized by periarticular calcified masses in the hip, elbow or shoulder. The calcinosis occurs by deposition of basic calcium phosphate crystals in periarticular spaces, soft tissues & bone. Hallmark of tumoral calcinosis is hyperphosphatemia. Other findings include elevated serum vitamin D. Serum calcium, parathormone and ALP levels are usually normal. Radiographic features are typical rounded multiple opacities separated by radiolucent lines. Complete excision of the tumor is the treatment of...
choice. Reduction of serum phosphate is also helpful. Our case presented with bilateral tumoral calcinosis on the hip. The anemia, hypoalbuminemia, marked weight loss; osteoporosis can be explained by malabsorption resulting in malnutrition of the case. Low vitamin C in hFTC and shrinkage of the size of the masses in the response of vitamin C supplementation has not been discussed in any literature.

**Conclusion:** Contemporary manifestation of hFTC and Hb E trait; two disease of AR inheritance in an individual makes it extremely rare.

**Abstract #502**

**INTERESTING CASE OF BONE PAINS AND FRACTURES**

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**Objective:** To present a case of a patient with multiple bone pains and fractures and to review the diagnosis and treatment of underlying disease.

**Case Presentation:** A 58-year-old female with no past medical history with ongoing multiple bone pains for years. In 2014 had a stress fracture in the right foot. Bone scan done showed multiple focal areas of increasing uptake involving bilateral ribs, distal right tibia and the left femur neck representing previously healed fractures. MRI lower extremities showed stress fracture of the anteromedial cortex of the right tibia and inferior cortex of left femoral neck. CT chest showed multiple rib fractures. No history of falls, kidney stones or family history of osteoporosis. Started on Teriparatide 20mcg daily. Evaluation of secondary causes was negative. The only abnormalities were phosphorus 1.9 (2.0-4.0mg/dl) and alkaline phosphatase of 179 (25-110 U/L). Bone Density in 2015 showed T score spine -0.7 and the hip -2.3. Repeat bone density in 1 year showed T score spine -0.3 and hip -0.6 so teriparatide stopped. In 2016 due to hip pain, imaging was done which showed right pubic ramus fracture so teriparatide restarted. In 2017 again had rib pain, CT chest showed a development of several new rib fracture deformities with nonunion. Bone Density at that time showed T score spine -0.5, hip -1.0 with a decline of 3.9% in the hip. Secondary causes of osteoporosis ruled out again however phosphorus noted to be 2.0 mg/dl. Concern for tumor-induced osteomalacia given the low phosphorus levels, repeat phosphorus levels after stopping teriparatide for 1 month was 1.5mg/dl, and FGF-23 was 243 RU/ml (<50). NMPET/CT Trunk Ga 68 DOTATATE showed 1.6x 1.2cm soft tissue density nodule with central calcific density in the soft tissue of right heel. Biopsy consistent with a phosphaturic mesenchymal tumor, positive for FGF-23 mRNA. Final pathology showed phosphaturic mesenchymal tumor. After surgery had a resolution of symptoms and phosphorus normalized.

**Discussion:** Tumor-induced osteomalacia (TIO), also known as oncogenic osteomalacia, is a rare paraneoplastic syndrome characterized by bone pain, muscle weakness and fractures associated with persistent hypophosphatemia. Tumoral overproduction of FGF23 acts primarily at the proximal renal tubule to inhibit phosphate reabsorption and 1α-hydroxylation of 25-hydroxyvitamin D, leading to hypophosphatemia and osteomalacia. Symptoms are nonspecific and hypophosphatemia is often overlooked and patients are misdiagnosed with variety of other diseases.

**Conclusion:** TIO is rare and easily missed as identification is difficult. Once identified complete resection leads to restoration of normal mineral metabolism and dramatic resolution of symptoms.

**Abstract #503**

**A RARE CASE OF NON-UREMIC CALCIPHYLAXIS IN A PATIENT POST-ROUX-EN-Y GASTRIC BYPASS SURGERY: ROLE OF VITAMIN K DEFICIENCY**

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University of Texas Southwestern Medical Center

**Objective:** Calciphylaxis is a rare disorder characterized by calcifying cutaneous arterioles and rapidly progressive painful skin ulcerations. It occurs primarily in patients with end stage renal disease, and is associated with high mortality as there is no known effective treatment. Early identification of calciphylaxis can be helpful in the overall prognosis of patients. We present a rare case of non-uremic calciphylaxis occurring post- Roux-en-Y Gastric Bypass surgery (RYGB), and the possible underlying etiology.

**Case Presentation:** Case presentation: A 41 year old woman was referred to our clinic due to history of recurrent calciphylaxis. Her past medical history was significant for RYGB in 2003 and heavy alcohol use between 2012-14. She initially presented with painful skin lesions on her thighs and breasts in 2014 (Figure A). A skin biopsy showed calcific/thrombotic angiodysplasia suggestive of calciphylaxis with fat necrosis (Figure B). At presentation, serum creatinine, calcium, vitamin D, and PTH levels were within normal limits, and no definitive etiology for calciphylaxis could initially be identified. She received hyperbaric oxygen therapy, multiple sodium thiosulfate infusions, wound debridement and care with improvement in her skin lesions. Skin lesions recurred in 2016, requiring repeat sodium thiosulfate infusions with eventual resolution of her open wounds. When she
was evaluated in our clinic in March 2017, we ruled out connective tissue disease, protein C/S deficiency, malignancy, warfarin use, and other known causes of non-uremic calciphylaxis. However, her serum vitamin K levels were at the lower limit of the reference range (0.15 and 0.18 ng/ml, reference: 0.1-2.2 ng/ml).

**Discussion:** Literature search reveals hyperparathyroidism, malignancy, alcoholic liver disease, and connective tissue disease as major causes of non-uremic calciphylaxis. Warfarin (Vitamin K inhibitor) has also been associated with calciphylaxis. Vitamin K deficiency may have a role in pathogenesis of calciphylaxis as it can cause a reduction in carboxylated matrix gla protein, a potent inhibitor of vascular calcification. We therefore speculate that vitamin K deficiency from malabsorption (RYGB-related) and alcohol abuse may have caused and/or contributed to calciphylaxis in our patient. One previous case of calciphylaxis as a fatal delayed complication of RYGB has been reported, although vitamin K level was not measured in that report.

**Conclusion:** Vitamin K deficiency from RYGB with/without alcohol abuse could have contributed to non-uremic calciphylaxis in our patient. Treatment of vitamin K deficiency after gastric bypass may be relevant to prevent this rare but potentially under-recognized complication of RYGB.

**Abstract #504**

**HYPERCALCEMIA AND ELEVATED PTH IN A PATIENT WITH CKD: HYPERPARATHYROIDISM OR FAMILIAL HYPOCALCIURIC HYPERCALCEMIA**

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**Objective:** In patients with hypercalcemia, it is important to distinguish between primary hyperparathyroidism and Familial hypocalciuric hypercalcaemia (FHH) as the treatment protocols vary. The diagnosis becomes exceptionally difficult when the patient has underlying chronic kidney disease (CKD). Although secondary hyperparathyroidism is the most common cause of elevated PTH in CKD, this case highlights the need for high clinical suspicion for other causes.

**Case Presentation:** A 41-year-old male with past medical history of congenital cardiac disease (s/p Left Blalock-Taussing Thomas shunt), CKD stage 3 presented to the clinic for evaluation of hypercalcemia and hyperparathyroidism. Patient denied history of kidney stones, bone pain, abdominal pain, osteoporosis. At presentation, his labs showed Creatinine 1.7, Ca 10.2, PTH 149.4 (Normal 11.1-79.5 pg/mL). His primary nephrologist recommended a low phosphorus diet and a trial of calcitriol 0.25mcg once weekly for the working diagnosis of chronic kidney disease-mineral bone disorder (CK-MBD). At the start of the trial, labs showed PTH 237.7, Ca 9.6, Phos 2.8; after three months PTH 188.2, Ca 10.7, Phos 3.6. The elevation of calcium prompted the discontinuation of the calcitriol and work up for primary hyperparathyroidism. Sestamibi scan of the parathyroid glands were negative. DEXA Bone density scan did not reveal osteoporosis. Subsequently, endocrinology referral for primary hyperparathyroidism was made. Given the clinical suspicion of FHH, 24-hour urine calcium and spot urine calcium/creatinine ratio were measured with the patient off diuretics for a week. Spot urine calcium and 24-hour urine calcium was undetectable confirming the diagnosis of FHH in the setting of CKD.

**Conclusion:** While hyperparathyroidism in patients with chronic kidney disease (CKD) is very common, it rarely manifests with hypercalcemia in the absence of aggressive vitamin D suppression. Traditionally hypercalcemia in patients with FHH (a defect in calcium sensing receptor (CaSR) the parathyroid gland and renal tubules) presents with mild elevations in PTH but in the setting of CKD, we hypothesize that CKD with attendant elevation in FGF23 drives PTH secretion which is not blunted by hypercalcemia due to defect in CaSR in the parathyroid gland. Also during the work up diuretic use can cause calciuria which may mask the diagnosis of FHH, therefore it is ideal to check while off diuretics1. It is important to make the distinction between primary hyperparathyroidism and FHH because parathyroidectomy surgery or calcimimetics are usually highly effective in the former but not the latter.

**Abstract #505**

**VITAMIN D STATUS AMONG ADULTS BANGLADESHI FEMALE WITH DIABETES AND USING MUSLIM RELIGIOUS GOWN**

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**Objective:** To evaluate Vitamin D status among the diabetic and non-diabetic adult female subjects and to find out status of vitamin D level subjects using Muslim religious gown or not.

**Methods:** A cross-section observational study was conducted among adult female Bangladeshi subjects during the period of 2015 January -2017 July attending an urban endocrine OPD Clinic with the complaints of
myalgia, fatigueability etc. Diabetic subjects were selected as per A1C and or clinical history. Vitamin D status was defined as deficient (≤20 ng/ml), insufficient (20.01-29.9 ng/ml) and normal (30-100 ng/ml). A total of 354 female adult subjects were studied.

**Case Presentation:** Among studied subjects, 332 (94.1%) female were urban dwellers, 163 (46.2%) were diabetic and rest 53.8% were non-diabetic. As mean ± SD, subjects had age (years): 40.66 ±13.80 and vitamin D level (ng/ml): 17.27±7.47. 253 had vitamin D deficiency and 80 subjects were insufficient. Age was not different among groups [p.01]. 277 (78.5%) subjects had adequate exposure to sunlight and rest (21.5%) had less exposure. Vitamin D levels were not significantly different among these two groups [17.33±7.37 vs 17.08±7.87 ng/ml, p .70]. According to glycemic status, subjects were grouped as diabetic (n=163, 46.2%) and non-diabetic (n=190, 53.8%). Residence status (urban vs rural) was not different among groups [p.824]. Diabetic subjects were older than non-diabetic subjects [47.06±11.76 vs 35.19±13.08 years respectively, p.001]. Vitamin D levels were not significantly different among groups [deficiency: 111 vs 142 subjects, insufficiency 40 vs 40 subjects respectively, p.28]. Among studied subjects, 32.9% (n=116) female never used muslim religious gown and they were of mostly urban dwellers (n=111) with mean age o39.80±13.67 years and mean vitamin D level 17.04±7.77 ng/ml. 30.3% (n=107) subjects used gown more than 15 years with mean age 49.79±11.52 years and mean vitamin D level 18.52±8.07 ng/ml; mean age was more in subjects who used gown [p.001] but difference of vitamin D levels was not significant [p.16].

**Discussion:** Most of the studied subjects were urban dwellers, 253 (71.67%) had vitamin D deficiency and 80 (22.66%) subjects were insufficient. 21.5% had less exposure to sunlight. Vitamin D level and status were similar among subjects with or without diabetes. Most of urban dwellers never used Muslim religious gown. Vitamin D level was not significantly different among gown user and non-user.

**Conclusion:** Urban dwellers in Bangladesh had vitamin D deficiency and insufficiency and levels were not significantly influenced by glycemic status and using Muslim religious gown.

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**Abstract #506**

**PTHRP AND 1-α HYDROXYLATION OF VITAMIN D CAUSING HYPERCALCEMIA IN A CASE OF METASTATIC CLEAR CELL OVARIAN CANCER**

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**Objective:** Humoral hypercalcemia of malignancy, HHM, occurs due to various reasons. The major causative agent is PTHrP related; however, activation of vitamin D by 1-α hydroxylation also appears to be an important etiology. PTHrP plays crucial roles not only in development and in various physiological events associated with normal life, but also in a number of pathological conditions such as cancer. Granulomatous diseases include infectious etiologies, such as mycobacteria, and non-infectious mechanisms, as observed in certain lymphomas and sarcoidosis,…, and, through the activation of 1-α hydroxylase in macrophages, result in hypercalcemia. This is a case of HHM, both PTHrP and 1-α hydroxylase mediated, in a patient with metastatic clear cell ovarian cancer.

**Case Presentation:** The patient is a 47-year-old Asian female who was recently diagnosed with metastatic clear cell carcinoma of ovarian origin after a right thigh mass biopsy. She had presented with complaints of constipation, fatigue, weakness and was found to have Calcium 15.7, albumin 3.3, Phosphorous 1.7 with PTH 4.0 and PTHrP 8.7; she was started on denosumab 120 mg weekly for a total of three doses then every four weeks afterwards. The calcium initially improved to 13.2 but then stabilized in the 13s range. Moreover, she was noted to have 1,25 dihydroxyvitamin D of 241 in the setting of 25, hydroxyvitamin D of 10 indicating an additional etiology to her HHM through 1-α hydroxylation of vitamin D. Therefore, she was started on prednisone 20mg daily later increased to 30 mg daily and her calcium trended down now to the 10s range. Furthermore, the patient has reported improvement in her fatigue and energy levels and has been having regular bowel movements. She is also being followed up by Oncology and treated with cisplatin based chemotherapy for her ovarian cancer.

**Discussion:** This is an interesting case of an individual diagnosed with clear cell ovarian cancer with symptomatic hypercalcemia in the setting of elevated PTHrP and 1,25 vitamin D indicating the presence of two pathological mechanisms responsible for the HHM. It was only after we had addressed both pathologies, through denosumab, inhibiting RANK-L and therefore inhibiting the action of PTHrP, and prednisone, inhibiting the activation of vitamin D through 1-α hydroxylation, that we were able to correct this hypercalcemia.
Conclusion: This case highlights the importance of overactivation of vitamin D as one of the more common pathologies of HHM which can also be an accompanying mechanism to PTHrP as in our case. This might be of significant importance for further treatment and normalization of calcium levels.

Abstract #507

OCCURRENCE AND PREDICTORS OF OSTEOBONE DISEASE IN YOUNG EUGONADAL INDIANS WITH HIV INFECTION

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Objective: Data on skeletal health among people living with HIV in India is not available. This study aimed to determine occurrence and predictors of osteoporosis in premenopausal women and eugonadal men with HIV

Methods: 220 men and 214 women with HIV were screened, of which 115 men (30–50 years-age) and 103 women (25–45 years-age), clinically stable, having >1-year follow-up at the anti-retroviral therapy clinic, underwent hormonal and DXA analysis. 40 male and 75 female matched controls were evaluated

Results: HIV males and females had significantly lower BMD and Z-scores at all sites. Osteoporosis was diagnosed in 64.35% males; commonest site being radius total (RT) (49.56%), followed by radius 33% (45.21%), radius ultra distal (RUD) (36.52%), lumbar spine (LS) (19.13%), neck of femur (NOF) (17.39%), total femur (TF) and greater trochanter (GT) (7.82% each). Osteoporosis was diagnosed in 34.95% HIV females, commonest site being RUD (24.27%), followed by radius 33% (17.48%), RT (15.53%), GT, NOF and LS (6.80% each). HIV males and females had significantly lower fat mass (FM), lean mass (LM), fat% (FP), bone mineral content (BMC), gynoid (G) fat,% skeletal muscle mass (PSMM) (sarcopenia), compared to controls. LM and FM was -15.65% and -11.54% lower in HIV. Sarcopenia was observed in 40% males and 17.5% females with HIV (controls none). HIV males with osteoporosis had higher HAART use, immune reconstitution inflammatory syndrome (IRIS), tuberculosis, lower FM, LM and sarcopenia. Logistic regression revealed PSMM, age and delta (Δ) CD4 count (change in CD4 count at 1 year of HAART, compared to pre-HAART) were best predictors of osteoporosis. Greater PSMM was associated with decreased osteoporosis, without adjusting for any variable (Model-1), adjusting for disease duration, tuberculosis and IRIS (Model-2), and adjusting for model-2 plus gonadotropins and sex steroids (Model-3). Greater ΔCD4 count and age were associated with increased osteoporosis after adjusting for models 1 and 3, and models 2 and 3 respectively. HIV females with osteoporosis had significantly higher use of HAART, lower LM, FM and FP. On logistic regression, LM followed by A/G ratio and BMI were best predictors of osteoporosis

Discussion: Patients with osteoporosis had higher use of HAART. A more severe immunodeficiency at disease onset, greater ΔCD4 count, and IRIS are associated with higher systemic inflammation, which may contribute to bone mineral loss.

Conclusion: Osteoporosis and sarcopenia are major problems in young eugonadal men and women with HIV. Decreased skeletal mass, age, lower baseline CD4 count and rapid improvement in immune function were predictors of osteoporosis

Abstract #508

FRACTURE RISK ASSESSMENT IN THE SETTING OF BILATERAL ATYPICAL FEMORAL FRACTURES AFTER LONG-TERM BISPHOSPHONATE USE AND SEVERE LUMBAR DEGENERATIVE DISEASE

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Objective: Atypical femoral fractures, with specific clinical and radiographic criteria for diagnosis, have been seen in patients on long-term bisphosphonate therapy. We present the clinical challenges involved in evaluating fracture risk in a postmenopausal female with sequential bilateral femoral fractures after long-term bisphosphonate use, and severe degenerative spine disease.

Case Presentation: A 79 year old Caucasian female presented for follow-up care for osteoporosis. She has a history of compression fracture of the T10 thoracic vertebra in 1998. At that time, her DXA revealed T-score -3.3 at the right femoral neck and -3.1 at the left femoral neck consistent with osteoporosis. She was begun on alendronate 70 mg weekly shortly thereafter, along with supplemental calcium and vitamin D. Interval monitoring with DXA in 2001 revealed T-score -3.3 at the right femoral neck and -3.1 at the left femoral neck consistent with osteoporosis. She was begun on alendronate 70 mg weekly shortly thereafter, along with supplemental calcium and vitamin D. Interval monitoring with DXA in 2001 revealed T-score -3.3 at the right femoral neck and -3.1 at the left femoral neck consistent with osteoporosis. She was begun on alendronate 70 mg weekly shortly thereafter, along with supplemental calcium and vitamin D. 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pain followed by a sensation of leg “giving way” prior to the fall and fracture. Laboratory studies at the time of the second fracture revealed corrected calcium 8.8 (8.4 – 10.4 mg/dL), PTH 61 (12 – 67 pg/mL) and low 25-OH vitamin D 23.7 (>30.0 ng/dL).

**Conclusion:** The clinical history and radiographic findings of the femoral fractures in this patient are consistent with sequential atypical femoral fractures secondary to long-term bisphosphonate therapy. Both fractures were low-energy with delayed healing of the left femur due to bisphosphonate-related supression of bone turnover and alteration of bone strength. Our patient has multiple risk factors for recurrent osteoporotic fracture: prior fragility fracture, advanced age, female gender, Caucasian ethnicity and long-term corticosteroid use. DXA scanning is of no utility as two valid sites are not available due to bilateral hip replacements, and severe degenerative disease of the spine. Osteoporosis is a clinical diagnosis that warrants vigilant monitoring in this patient at high risk for recurrent fracture.

**Abstract #509**

**ORBITAL INFLAMMATION ASSOCIATED WITH ZOLEDRONIC ACID**

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University of Kansas Medical Center

**Objective:** To increase awareness of orbital inflammation as a potentially serious early complication following Zoledronic acid infusion.

**Methods:** Case report of orbital inflammation following Zoledronic acid infusion including clinical presentation, imaging findings, management, outcome, and literature review

**Case Presentation:** A 60-year-old female with history of breast cancer in remission following therapy with Tamoxifen. Patient developed left humeral fracture after a fall from standing height and bone density confirmed osteoporosis. She poorly tolerated Alendronate 70mg weekly due to reflux symptoms and was switched to intravenous Zoledronic acid 5mg yearly infusion. Within 48 hours after her first infusion she developed left eye throbbing pain, painful eye movements, and upper eyelid edema. Symptoms worsened over the next two days so she presented to emergency room where her left eye exam showed ptosis, proptosis and up gaze movement restriction. No fever or leukocytosis to suspect orbital cellulitis. Orbital MRI showed left pre-septal soft tissue edema and inflammation extending to retro-bulbar fat with proptosis. Ophthalmology evaluation ruled out eyeball involvement and was diagnosed with orbital inflammation or (Orbital Pseudo tumor) secondary to Zoledronic acid. Patient received prednisone 80mg daily which was tapered over 28 days which resulted in complete resolution of her eye symptoms.

**Discussion:** Bisphosphonate associated orbital inflammation is rare but serious complication of Zoledronic acid infusion that have been reported to result in permanent vision damage if not recognized and treated promptly. This medication carries the highest risk for such complication among the Bisphosphonates accounting for 75% of cases in one series. All reported cases were seen after first Zoledronic acid infusion. Symptoms usually develop within 3 to 5 days of the infusion and range from mild eye burning to sudden vision loss. Ocular inflammation has mainly been reported in patients with an underlying malignancy whether current or in remission as in our case. It is unclear if malignancy predisposes to this side effect. Mechanism of ocular inflammation is considered part of an acute-phase response to bisphosphonates given the onset of symptoms and response to steroids. Glucocorticoids whether intraocular or systemic are the treatment of choice with excellent prognosis for full resolution of symptoms but needs ophthalmology evaluation first.

**Conclusion:** Orbital Inflammation is a rare and a serious side effect associated with zoledronic acid use and patients should be counselled to monitor for signs and symptoms during therapy.

**Abstract #510**

**MINERAL METABOLISM AND BONE MINERAL DENSITY IN PATIENTS WITH NEUROENDOCRINE TUMORS**

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**Objective:** Some papers have recently described an association between neuroendrocrine tumors (NET) and both vitamin D deficiency (VDD) and low bone mineral density (BMD). The ten-year risk of osteoporotic fractures can be calculated with the FRAX algorithm. Aim of this study was evaluating BMD, VDD and FRAX scores in a cohort of NET patients.

**Methods:** The study included 30 consecutive unselected patients (mean age 65.5±11.0 years; males 56.7%) with a diagnosis of NET. All the patients underwent dual X-ray absorptiometry scan (DXA). FRAX was calculated in the whole sample and mineral metabolism serum indices were measured.

**Results:** Osteopenia and osteoporosis were found in the 60% and 20% of the patients respectively. Only 20% of the patients had normal bone mineral density (BMD). VDD
was found in 80% of the patients. Subjects with VDD had higher BMI (P=0.037), higher FRAX scores (P=0.003), higher PTH (P=0.024), than patients with normal serum vitamin D. No difference in bone mineral density values was observed between these two groups. After exclusion of hip BMD values, calculated FRAX scores remained significantly different between normal and VDD patients (P=0.019). Cromogranin-A (CgA) showed a negative correlation with hip BMD (r=-0.297; P=0.002) and a positive correlation with FRAX Major score calculated without hip BMD (r=0.45; P=0.014).

Discussion: Both low BMD and VDD were common findings in our NET population. No association was found between VDD and low BMD. According to literature, VDD was associated with higher BMI and lower PTH. Surprisingly VDD was higher in patients with a higher FRAX risk, even after exclusion of BMD. A higher risk of osteoporosis and fractures was found in NET patients with higher CgA.

Conclusion: Low bone mass and hypovitaminosis D seem to be a common finding in NET patients. A correct screening for both these conditions is highly advisable in this population.

Abstract #511

COMPARISON OF 3-YEAR ESTIMATED GLOMERULAR FILTRATION RATES BETWEEN RECOMBINANT HUMAN PARATHYROID HORMONE (1-84) (RHPTH[1-84])-TREATED PATIENTS WITH CHRONIC HYPOPARATHYROIDISM AND A HISTORICAL CONTROL COHORT

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Objective: Chronic hypoparathyroidism (HPT) is associated with increased incidence of renal complications including nephrolithiasis, nephrocalcinosis, and renal dysfunction. In this study, estimated glomerular filtration rate (eGFR) was assessed over a 3-year period among patients participating in a study evaluating recombinant parathyroid hormone [rhPTH(1-84)] treatment and in a historical control cohort not treated with rhPTH(1-84).

Methods: rhPTH(1-84)-treated HPT patients were selected from the single-arm, open-label, long-term, phase 3 RACE trial (NCT01297309). Historical control patients not treated with rhPTH(1-84) were identified from the MedMining database using similar enrollment criteria to RACE. All patients were required to have ≥2 eGFR tests that were 3 years apart after HPT diagnosis.

Index date was defined as the baseline visit in the rhPTH(1-84)-treated cohort and as the 1st eligible eGFR test date in the historical control cohort. Change in eGFR (calculated using CKD-EPI formula) for both groups was summarized and comparisons were performed using a multivariable regression model, adjusting for age, sex, history of hypertension, type 2 diabetes mellitus, cardiac disorders, nephrotoxic concomitant drug use, baseline serum calcium, and baseline eGFR.

Results: A total of 119 patients were included, 43 with and 76 without rhPTH(1-84) treatment. At baseline, rhPTH(1-84)-treated patients were younger (49.2 vs. 55.4 years); a higher proportion were female (79.1 vs. 75.0%) and a lower proportion had a history of hypocalcemia, hypertension, type 2 diabetes mellitus, cardiac disorders and nephrotoxic concomitant drug use. eGFR at index was lower in the rhPTH(1-84)-treated cohort (77.0 vs. 82.9 mL/min/1.73mm2). Body mass index, race, and serum calcium were comparable between cohorts. In the multivariable analysis adjusting for confounders, predicted change in eGFR at year 3 was +4.4 vs. -5.6 mL/min/1.73mm2 in the rhPTH treated vs. non-treated cohort. rhPTH(1-84) was associated with a significantly lower rate of annual eGFR decline compared to the historical control cohort over the 3 years of follow-up (difference in annual eGFR change=3.1; p<0.01).

Discussion: This non-randomized post hoc analysis is hypothesis generating and further research is warranted.

Conclusion: Over a 3-year timeframe, the historical control cohort of patients with chronic HPT not treated with rhPTH(1-84) exhibited significantly greater decline in mean eGFR than the rhPTH(1-84) treatment cohort after taking known confounders into account.
Abstract #512

A PHASE 3 RANDOMIZED, PLACEBO-CONTROLLED STUDY INVESTIGATING BUROSUMAB FOR ADULT X-LINKED HYPOPHOSPHATEMIA (XLH)

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Objective: In adults with XLH, inappropriately elevated circulating fibroblast growth factor 23 (FGF23) causes hypophosphatemia with consequent osteomalacia, musculoskeletal pain, stiffness, pseudofractures, osteoarthritis, entheseopathy, muscle dysfunction, and impaired physical function. Burosumab, an investigational fully human monoclonal antibody, binds FGF23 and inhibits its activity. UX023-CL303 is an ongoing, Phase 3, double-blind, multicenter study examining the efficacy and safety of burosumab in adults with XLH.

Methods: Eligible participants (pts) had fasting serum phosphorus (Pi) levels <2.5 mg/dL and skeletal pain (Brief Pain Inventory [BPI] – Question 3, Worst Pain Score ≥4 on an 11-point scale). Pts (N=134) were randomized 1:1 to receive burosumab 1 mg/kg or placebo subcutaneously every 4 weeks for 24 weeks. Changes in pharmacodynamic measures, stiffness, physical functioning, and pain were evaluated. Fracture healing was assessed radiographically using a baseline skeletal survey and follow-up target x-rays of regions identified with active fractures/pseudofractures (Fx/PFx).

Results: Results from the 24 week primary analysis are presented here. At baseline, groups were comparable for sex, age, and disease severity. A significantly greater percentage of burosumab-treated pts attained the primary endpoint of mean serum Pi levels above the lower limit of normal at the midpoint of the dosing intervals through week 24 compared with placebo-treated pts (Table 1). For secondary endpoints, burosumab-treated pts had significantly greater decreases in WOMAC stiffness scores compared with placebo-treated pts and there were numerically greater changes in WOMAC Physical Function and BPI Worst Pain severity with burosumab. A greater percentage of baseline Fx/PFx were fully healed with burosumab (43.1%) compared with placebo (7.7%) at week 24. Serious AEs were reported in 2 pts from each group, none of which were drug-related. There were no meaningful changes from baseline, or differences between groups, in serum or urine calcium, serum iPTH, or nephrocalcinosis severity scores. The overall safety profile of burosumab was similar to placebo; 12% of pts in each group experienced injection site reactions.

Conclusion: Burosumab was well tolerated, restored serum Pi homeostasis, reduced stiffness, improved physical functioning, increased markers of bone remodeling, and was associated with improved healing of Fx/PFx in adults with XLH.

Abstract #513

HYPER PARATHYROIDISM PRESENTING WITH SEVERE WEIGHT LOSS IN YOUNG MALE.

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Objective: Primary Hyperparathyroidism often has an unusual clinical presentation. Inability to locate the adenoma in an ectopic parathyroid gland may delay the diagnosis. Parathyroid hormone (PTH) increases Serum Calcium(Ca) by increasing release of Ca and phosphate from bone matrix, increasing Ca reabsorption by kidney and intestine. We report an unusual case of a young patient presented with severe weight loss in the background of severe 1° hyperparathyroidism.

Case Presentation: 24 M presented with severe anorexia, generalised weakness, weight Loss (20 kg) since 6 wks. P/E- average built, BMI 22, BP-150/100 mmHg, had small lump on right side of neck. Lab results- Hb 11(14-18), WBC 9000, Platelets 356,000, Total Bil. 0.50 mg/dl, ALT 22 IU/L, Alkaline phosphatase 1692 (110-310), Ser.Cr 1.5 mg/dl (0.4-0.8), Uric acid 6.6 mg/dl, Ca-16.2 mg/dl (8.8-10.2), Ph- 4.0(2.5-5.0),
Serum PTH >1900 pg/ml (14.0-72.0), Na-136, K-3.5, T4-3.9 (4.5-12.0), TSH-2.25, FBS-71 mg/dl, ECG normal, USG abdomen-nephrolithiasis, Protein electrophoresis normal. USG neck-large solid nodule posterior to right lobe of thyroid. Parathyroid adenoma suspected and parathyroidectomy was done. Excised parathyroid section showed small parathyroid acini, cells containing small oval nuclei and clear cytoplasm with intact fibrous capsule (parathyroid adenoma). S.Ca decreased to 9.1 mg/dl and PTH 70 pg/ml postoperatively. Patient discharged in stable condition after 5 days of surgery. Within a month of discharge, patient gained 10 kg, calcium and PTH remained normal.

Discussion: 1° hyper parathyroidism causes metabolic bone disease, hypercalcemia and diffuse bone resorption. May present with subtle manifestations, leading to misdiagnosis in early stage. Excess PTH causes involvement of skeletal system and the kidneys, leading to increased bone resorption causing osteitis fibrosa cystica, subperiosteal resorption of distal phalanges, bone cysts and brown tumours. More than 15% of cases of 1°hyper parathyroidism have renal involvement 2° to hypercalciuria causing nephrocalcinosis and nephrolithiasis. Diagnosed by hyperCa, hypophosphatemia, Increased bone specific ALP and raised PTH. Anterior neck mass maybe palpable in parathyroid tumour. USG has sensitivity and specificity of 73% and 100% respectively. FNAC may help supplement diagnosis. Surgical excision is the only permanent cure for 1°hyperPTH. Bisphosphonates (Alendronate) are given in low bone mineral density and if surgery is not feasible.

Conclusion: 1°hyperPTH is known to pose diagnostic dilemma as seen in our patient who had severe weight loss at young age. An ectopic location may further complicate the issue. Once diagnosed, disease is curable with surgery.

Abstract #514

SEVERE VITAMIN D DEFICIENCY PRESENTING AS KYPHOSCOLIOSIS.

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Objective: Vitamin D deficiency causes poorly mineralized bone matrix. Patients present with diffuse or migratory pain in shoulder and pelvic girdle, ribcage and lower back. We report 2 cases presented with kyphoscoliosis due to severe Vit. D deficiency.

Case Presentation: 30 years F presented with difficulty in walking, getting up from sitting position, severe pain in chest and limbs, routine activities performed by crawling only. Symptoms worsened after 3rd delivery (2 years ago). P/E- BMI 34, severe tenderness in ribcage, pelvic girdle and thighs, proximal weakness, power 3/5-shoulders and 2/5- pelvic girdle, dorsal kyphosis, had stooped forward gait. Lab tests- Hb 10.5, other routine tests Normal including TFT, Ca- 7.8, Ph- 4.3, alkaline phosphatase-1000. S.25 OH D-undetectable (30-70 ng/ml). X-ray spine- anterior wedging of thoracic vertebrae and CT spine-severe osteoporosis with anterior wedging. Diagnosed to have severe Vit. D deficiency causing osteoporosis. Treated with oral Ca, inj. Vit.D3 (600,000 units weekly for 5 weeks) followed by oral D3 60,000 units weekly. 6 weeks of therapy improved power to 4/5. Pain subsided gradually and started walking with support. She continued to improve, but gait didnot.


Discussion: Vit.D deficiency results from Inadequate sun exposure, malabsorption, medications (phenytoin, phenobarbital and rifampicin), specially in elderly. The high prevalence of hypovitaminosis D in India, mandates early diagnosis. Widespread pain is a prominent manifestation, but nonspecific. RDA of Vit.D in children and adults-600-2000 IU. A 25(OH) D level <30ng/mL is considered Vit.D insufficient. Ergocalciferol is the widely available form of Vit.D. In severe deficiency, given daily/weekly (60,000 IU weekly for 6-8 weeks), followed by increase in daily dose, it decreases risk of hip and non-vertebral fractures. A meta-analysis in postmenopausal F& in Males >50 years reported a daily intake of Vit. D reduces hip fractures by 18%.

Conclusion: Vitamin D deficiency is common in post-menopausal women, leading to multiple musculoskeletal disorders and if not treated early, can cause irreversible deformity. As patients usually visit primary care physicians first, our study will help them recognize its deficiency early.
Abstract #515

PITFALLS OF PTHRP TESTING

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Objective: Humoral hypercalcemia of malignancy (HHM) mediated by PTHrP is the commonest cause of hypercalcemia in malignancy, accounting for up to 80% of cases. Different immunoassays have been developed that are capable of measuring PTHrP concentrations, including immunoradiometric assays (IRMA) and immunoochemiluminometric assay (ICMA). Of note, all of these assays documented the instability of PTHrP in plasma.

Case Presentation: An 83 year old man with hypertension, type 2 diabetes mellitus and congestive heart failure presented to the hospital with altered mental status. He was found to have elevated total calcium at 15.52 mg/dl. Initial labs showed low PTH (5.1 pg/ml), low PTHrP (0.3 pmol/L), normal 25 hydroxy vitamin D (26.4 ng/ml) and normal 1,25 dihydroxy vitamin D (26 pg/ml). Patient was started on vigorous intravenous fluid infusion, furosemide, bisphosphonate and calcitonin. CT chest showed right upper lobe paramediastinal mass. Biopsy showed small cell carcinoma.

Upon reviewing the literature, we discovered that PTHrP is unstable at room temperature and false negative results can happen if the sample was not handled properly. Therefore, PTHrP was repeated with proper specimen handling, and the result was elevated (7.2 pmol/L), confirming the paraneoplastic etiology of the patient’s hypercalcemia.

Discussion: As stated above, different immunoassays have demonstrated the instability of PTHrP concentrations in the blood at room temperature. In 1992, Pandian et al documented the instability of PTHrP in plasma of patients with HHM using the IRMA test. He found that immunonoactivity decreased at room temperature but it was improved with the addition of protease inhibitors. Newer ICMA test showed no decrease in PTHrP levels up to 8 hours either at room temperature or at 4°C. However, there were progressive decreases of PTHrP at 24, 48 and 72 hours at the same temperatures. It indicates that PTHrP will degrade in EDTA treated plasma after prolonged storage at room temperature or 4°C, and immediately frozen EDTA treated plasma is adequate to preserve the specimen. Further addition of protease inhibitors may not be necessary, but they are not harmful.

Conclusion: PTHrP is unstable at room temperature and the result can be falsely negative if the blood sample was handled incorrectly. Therefore it is recommended to repeat the test if the biochemical value was inconsistent with the patient’s clinical picture. We believe that such situations are not uncommon in clinical practice and might be overlooked. This needs a whole team education and coordination including physicians, phlebotomists, nurses and the lab technicians to avoid such errors which can affect further management.

Abstract #516

A CALCIUM CONUNDRUM: A RARE CONFOUNDING CASE OF COINCIDENT PAGET’S DISEASE OF BONE AND PRIMARY HYPERPARATHYROIDISM

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Objective: To present a case of Paget’s disease of bone and primary hyperparathyroidism with evaluation confounded by iatrogenic hyperthyroidism, hyperalbuminemia, vitamin D deficiency, and osteoporosis.

Case Presentation: A 60 year old woman with a history of Hashimoto’s thyroiditis, depression, and untreated surgical menopause since age 40 presented for evaluation of diabetes mellitus. Recent labs also revealed a low TSH, elevated calcium, and elevated alkaline phosphatase which she clarified was longstanding and previously fractionated to bone. Her diabetes mellitus was addressed and additional labs showed a calcium of 10.9, albumin of 5.1, alkaline phosphatase of 510, 25-hydroxy vitamin D of 12, and PTH of 55. In light of these findings and comorbid depression, thyroid hormone doses were gradually reduced and vitamin D repleted. After 14 months of de-escalation, euthyroidism was restored with labs revealing a TSH of 0.810, calcium of 9.9, albumin of 4.8, alkaline phosphatase of 384. Eventually a nuclear medicine bone scan was performed with uptake in the sacrum and L5 vertebral body. X-ray showed a destructive sclerotic process with L5 height loss and sacral osteopenia. MRI revealed an L5 compression fracture and Paget’s disease at L3 and L5. Zoledronic acid was infused and alkaline phosphatase normalized to 55. Six months post-treatment, calcium was 10.7, albumin 4.9, and DXA scan T-scores were -2.6 at the left femoral neck, -2.1 at the left total hip, and -0.8 at the total spine. Further labs collected having verified the patient was off calcium supplements showed a calcium of 11.0, albumin of 5.0, PTH of 43, creatinine 0.64, and 24 hour urine calcium of 449.5 mg with fractional excretion of calcium of 2.65%. Ultrasound and sestimibi scan localized a parathyroid adenoma. Parathyroidectomy within months removed a left sided adenoma. Labs six months later revealed normocalcemia.

Discussion: Coincident primary hyperparathyroidism
ABSTRACTS – Metabolic Bone Disease

in Paget’s disease is rare with a prevalence of 2.2-6%. Confounders exist in evaluation. Thyrotoxicosis may cause increased bone resorption, hypercalcemia, and along with vitamin D deficiency elevated alkaline phosphatase. Persistent alkaline phosphatase elevation after restoration of euthyroidism and vitamin D repletion in a background of premature menopause raises concern for osteoporotic fractures, malignancy, primary hyperparathyroidism, and Paget’s disease. Moreover, albumin affects calcium levels with primary hyperparathyroidism associated with varying hypercalcemia and hypercalciuria. The presence of these findings in treated Paget’s disease suggests primary hyperparathyroidism.

Conclusion: One must be methodical in evaluating bone and calcium disorders.

Abstract #517

REFRACTORY HYPERCALCEMIA IN A PATIENT WITH MULTIPLE MYELOMA CAUSED BY HISTOPLASMOsis

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Case Presentation: A 75 year-old man with history of IgG kappa multiple myeloma status post autologous stem cell transplant 7 years ago was on Carfilzomib-based chemotherapy on presentation. Blood work and bone marrow biopsy 4 months before were consistent with complete remission. He presented in the clinic with poor appetite, generalized weakness, and confusion, and was found to have hypercalcemia with albumin-corrected calcium level of 12.3 mg/dL and ionized calcium of 1.42 mmol/L. He was admitted to the hospital and received intravenous fluid resuscitation, calcitonin injections for 3 days and discharged with zoledronic acid infusions every 2 weeks. His calcium level was normalized within 2 weeks.

Discussion: Although hypercalcemia is one of the most common clinical presentations of multiple myeloma, this case illustrates the importance of a thorough investigation to rule out other causes in patients with multiple myeloma in remission. Histoplasma Capsulatum is the most common mycosis in the United States. However, very few cases have been reported in the medical literature in which multiple myeloma and histoplasmosis have coexisted. Detection of Histoplasma antigen in the urine or blood is a rapid diagnostic test for histoplasmosis. Tissue cultures are the gold standard, but take several weeks to grow. Although less sensitive, fungal staining of the tissues also provides a rapid diagnosis. Immunosuppressive disorders or medications are recognized as risk factors for disseminated histoplasmosis. Treatment with steroids and Itraconazole can resolve the refractory hypercalcemia.

Conclusion: This case of concurrent multiple myeloma with disseminated histoplasmosis illustrates the importance of prompt investigation for other causes of refractory hypercalcemia in patients with multiple myeloma.

Abstract #518

ATRAUMATIC PELVIC FRACTURES ASSOCIATED WITH BISPHOSPHONATE THERAPY

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Case Presentation: Introduction: Atypical fractures are a complication of long-term bisphosphonate therapy. By suppressing osteoclast activity, bisphosphonates inhibit bone resorption. While data supports the effect of bisphosphonates on prevention of osteoporotic fractures, there is concern that prolonged therapy (median therapy seven years or more) can lead to suppression of bone turnover, increased skeletal fragility and increased risk of atypical fractures. Cases of atypical fractures are traditionally subtrochanteric and mid-shaft femoral fractures.

Case presentation: A 69 year old woman known with osteoporosis for 16 years was referred with increasing pelvic and groin pain plus a recent finding of pelvic fractures on imaging. She had been on 5 years of hormone replacement therapy (HRT) after reaching menopause at age 50. She was then diagnosed with breast cancer and HRT was stopped. She also had lumpectomy and 5 years of Tamoxifen therapy. She was on Alendronate for 6 years followed by Risedronate for 10 years. After the
age of 40, she had a fracture of left humerus at age 48
due to fall while skiing; and a L1 vertebra compression
fracture detected on imaging. There was no history of
malabsorption, thyroid or parathyroid disorders, treatment
with steroids, antiepileptic or heparin medications. Her
presenting complaint was 1 month of persistent pain to
the right pelvis and left groin with no preceding history
of trauma. CT imaging of the pelvis revealed fracture to
left inferior and superior pubic rami as well as fracture of
right sacral ala. Bone mineral density scan demonstrated
L1 to L4 T score -3, femoral neck T score -1.9, and total
hip T score -2.2. Calcium was 2.53 mmol/L (2.15-2.60)
and 25-hydroxy vitamin D level was 96 nmol/L (75-250).
TSH and myeloma screen were negative. In the context of
16 years of bisphosphonate therapy, an atypical fracture of
the pelvis was suspected. Bisphosphonates were stopped.
Treatment with Teriparatide was initiated alongside
continuation of calcium and vitamin D supplementation.

Discussion: Patient gave no history of trauma. She had
ongoing groin and gluteal/thigh pain for a month before
presentation. Initial pelvic X-rays did not show any
fractures. As the pain was persistent, CT scan of the
pelvis was done and this picked up the fractures. Patient
had treatment with anti-resorption agents for a total of 21
years (HRT 5 years and bisphosphonates 16 years)

Conclusion: Atraumatic pelvic fractures have been noted
in this patient after prolonged bisphosphonate therapy for
osteoporosis. Bisphosphonate related fractures of the pelvis
have previously been reported. This case adds to the current
body of evidence around non-femoral atypical fractures.

Abstract #519

TREATMENT OF LOW BONE DENSITY IN RARE
DISEASE: ALAGILLE SYNDROME

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Objective: Alagille Syndrome is an autosomal dominant
disorder characterized by reduced interlobular bile ducts
and resultant nutritional deficiencies. It affects multiple
organs such as the heart, liver, kidney and eyes. In greater
than 90 percent of cases, the cause of the disease is related
to mutations in the JAG1 gene. We present a young patient
who presented to us to discuss his bone health and Vitamin
D deficiency.

Methods: Case study: an 18 year old African-American
male transitioned from pediatric to adult endocrinology
at our medical center in October 2017. The patient had
been diagnosed with Alagille syndrome at age 7 weeks.
No family history was available as he was adopted. He
denied suffering any fragility fractures, but he sustained
vertebral compression fractures from 2 major trauma-
related accidents. His wrist and hand x-rays showed he
did not have rickets. He has had persistent vitamin 25-OH
D levels at <4 ng/mL (30-100). He took variable amounts
of elemental calcium (1000-1800 mg) daily. As he had
persistently low vitamin 25-OH D levels despite taking
cholecalciferol 12,000 IU twice a day through liquid and
tablets, he was also prescribed calcitriol. It is unclear if
there was a component of medication non-compliance.

Case Presentation: In June 2009, a bone density study
(DXA) revealed the following Z Scores: L1-L4: -3.0, right
femoral neck: -3.9, and hip: -2.9. A repeat DXA in October
2017 showed a deterioration: Z scores L1-L4: -4.4, right
femoral neck: -4.4, right femoral neck: -1.8, and total hip: -2.3.

Discussion: Patient’s have difficulty absorbing fat
and develop fat-soluble vitamin deficiencies if they do
not receive proper supplementation. Childhood and
adolescence is an important period of time for bone
growth. Different genetic diseases, limited physical
activity, poor nutrition and hormonal deficiencies can
negatively affect bone strength and quality. There is
limited research on interpreting low bone density scans
or treating secondary osteoporosis in young adults with
anti resorptive medications. As these children grow into
adulthood, bone quality should be monitored to assess
for progression to osteoporosis. According to Wood and
Ahmed (2017), there is not enough evidence to recommend
bisphosphonate treatment as a standard treatment in
children and adolescents with secondary osteoporosis.

Conclusion: Alagille Syndrome is a rare autosomal
dominant genetic disorder associated with the inability to
absorb fat soluble vitamins such as vitamin D. Patients
are at risk for secondary osteoporosis and rickets/
osteomalacia. Treatment should include ensuring adequate
calcium and vitamin D intake, monitoring for vitamin D
deficiency, monitoring for fragility fractures, and avoiding
trauma-related accidents.

Abstract #520

SEVERE HYPERCALCEMIA AND ACUTE PANCREATITIS IN A POSTPARTUM WOMAN

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Case Presentation: A 32 year-old postpartum woman
presented to the emergency department with a two-day
history of headache, nausea and vomiting. Admission
chemistry showed a markedly elevated calcium level of
18.3 mg/dL, creatinine of 2.1 mg/dL and a bicarbonate of 33 mEq/L. Her 25-hydroxyvitamin D (41 ng/mL) and albumin levels were normal. Parathyroid hormone (PTH) was low (8.6 ng/mL). Aggressive hydration with IV fluids and a dose of calcitonin were administered. On day 2 of admission she developed severe epigastric abdominal pain and an elevated lipase level (1629 U/L) consistent with acute pancreatitis. Other causes of pancreatitis were ruled out indicating hypercalcemia was the most likely cause. Within 48 hours of initiation of hydration and one dose of calcitonin, her calcium level decreased to 6.7 mg/dL and she developed perioral paresthesias and a positive Trousseau’s sign. Further information obtained from the patient revealed she had ingested up to 12 grams of calcium carbonate daily for 3 days prior to admission for severe heartburn. She was diagnosed with the milk-alkali syndrome. Due to the acute hypocalcemia symptoms, she received IV calcium boluses and was then transitioned to calcium citrate repletion to maintain calcium levels in the low normal range. On day 7 of admission, her abdominal pain resolved, PTH level was elevated (246 ng/mL), and calcium level normalized (9.2 mg/dL).

**Discussion:** This is a rare case of severe hypercalcemia and pancreatitis in the setting of excessive oral intake of calcium products (milk-alkali syndrome) and demonstrates the classic triad of hypercalcemia, alkalosis and acute kidney injury. Hypercalcemia and pancreatitis are unusual findings in the postpartum period, thus their development should lead to the suspicion of other causes such as the milk-alkali syndrome. Additionally, in this patient calcium levels were difficult to maintain following abrupt discontinuation of high dose calcium at home pending appropriate rise in PTH. This may have been exacerbated by saponification of fatty acids with calcium sequestration in the actively inflamed pancreas. In this setting, intermittent calcium repletion may be required to prevent serious complications.

**Conclusion:** In patients with severe hypercalcemia, etiologies such as the milk-alkali syndrome and its potential life-threatening complications, such as acute pancreatitis and severe hypocalcemia, should be considered, especially when there is a rapid decrease in calcium levels with only mild interventions. This case demonstrates the critical importance of reviewing the patient’s history to aid diagnosis.

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**Abstract #521**

**A CASE OF GENERAL LYMPHATIC ANOMALY TREATED WITH RADIATION AND BISPHOSPHONATE**

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**Objective:** General lymphatic anomaly (GLA), also known as lymphangiomatosis, is a rare disease featuring multifocal lymphatic malformations affecting bone, skin, soft tissue, and viscera. We present a unique case treated with surgery, radiation, and bisphosphonate.

**Case Presentation:** A 34 year-old woman developed back pain while training for a marathon in 2010. CT revealed a 12.1 x 9.6 x 11.4 cm multi-loculated cystic retroperitoneal mass and a destructive L4 vertebral lesion with epidural compression. She underwent staged resection of the abdominal mass and L4 corpectomy and discectomy. Pathology of the abdominal mass showed large, irregular lymphatic channels lined with endothelium staining for lymphatic marker PROX-1. The vertebral lesion pathology revealed thin-walled vascular channels lacking smooth muscle and round vascular channels with endothelium staining for lymphatic markers PROX-1 and D2-40 and vascular endothelial marker CD31. The histologic differential diagnosis included arteriovenous malformation, hemangioma, and lymphangioma.

In 2015, surveillance imaging revealed growth of the L4 mass. In 2016, she received 45 Gy proton beam radiation to the lumbar spine. She presented to our endocrinology office in October 2016 for consideration of medical therapy. Laboratory evaluation revealed normal calcium 8.8 mg/dL and PTH 42 pg/mL. Vitamin D-25 was 20 ng/mL. Bone turnover markers were normal, including bone specific alkaline phosphatase 16.1 mcg/L, C-telopeptide 253 pg/mL, and osteocalcin 16 ng/mL. Vitamin D was replenished, and she received 5mg IV zoledronic acid. Imaging in October 2017 showed stability of the L4 mass.

**Conclusion:** GLA is a type of angiomatosis similar to Gorham Stout Disease (GSD), but more likely to include visceral involvement. Our patient has histologic and clinical features consistent with GLA. There are several reported cases of successful use of bisphosphonates to treat GLA involving bone. Radiation treatment, which has been used to treat GSD, has not been efficacious in GLA. Our case uniquely reports use of both radiation and bisphosphonate therapy years after surgery to achieve stabilization of a vertebral GLA lesion.
Abstract #522

HYPOCALCEMIA-HYPERCALCEMIA PATTERN AFTER SEVERE TRAUMA AND PROLONGED IMMOBILIZATION IN A YOUNG MAN

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Objective: Severe illness and trauma may be associated with hypocalemia. Conversely, hypercalcemia may be a feature of prolonged immobilization, especially in young bedbound individuals. We describe a case of prolonged hospital stay after serious injuries in a young male where initial hypocalemia was followed by progressive symptomatic calcium elevation.

Case Presentation: A 29-year-old male was hospitalized for 4.5 months after suffering motor vehicle trauma with multiple fractures and bilateral upper extremity amputations. The calcium level on admission was 6.8 mg/dl (normal range 8.5-10.2), while peak serum ionized and total calcium values during hospital stay reached 1.98 mmol/L (1.1-1.3), and 15.8 mg/dl respectively. The albumin level was 3.2 g/dl (3.5-4.0) and alkaline phosphatase was 88 IU/L (44-147). Renal insufficiency ensued, with serum creatinine reaching a peak of 6 mg/dl 2 days after admission, and stabilizing at 0.87 mg/dl at discharge. Additional laboratory investigations showed parathyroid hormone (PTH) level 13.9 pg/ml (10-65), 25-Hydroxyvitamin D 17.8 ng/ml (20-60), 1,25-Dihydroxyvitamin D <5.0 pg/ml, 24-hour urinary calcium 470 mg (100-300). The patient was treated with intravenous fluids and calcitonin with a reduction in the calcium level to between11-12 mg/dl, and eventually required intravenous pamidronate administration as an outpatient (Fig. 1).

Discussion: Our patient manifested hypocalemia at admission. As the patient stayed in a prolonged bedridden state, the calcium level rose gradually and transitioned into the hypercalcemic range approximately six weeks into hospitalization (>10.2 mg/dl), reaching peak values >15 mg/dl after 4 months of hospital stay, accompanied by symptoms of irritability and confusion. Investigations pointed to a non-PTH mediated etiology compatible with hypercalcemia of immobilization.

Conclusion: Prolonged immobilization in young individuals with high bone turnover may lead to significant, symptomatic hypercalcemia. A preceding hypocalemic state may be seen in patients who present with hemodynamic instability and renal failure. Normal or low PTH, low 1,25-Dihydroxyvitamin D, normal alkaline phosphatase, and high urine calcium excretion in the appropriate clinical setting help to exclude other etiologies and support the diagnosis of immobilization-related hypercalcemia. Early mobilization with physical and occupational therapy is the mainstay of treatment, while pharmacologic agents including calcitonin, bisphosphonates, or denosumab can be used for calcium-lowering in recalcitrant situations.

Abstract #523

SYMPTOM BURDEN AND HRQOL REPORTED AMONG PATIENTS WITH CHRONIC HYPOPARATHYROIDISM: IMPACT OF TREATMENT WITH RHPTH (1-84) AND WITH STANDARD THERAPY

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Objective: Chronic hypoparathyroidism (HypoPT) is a rare disease associated with a variety of symptoms and diminished health-related quality of life (HRQoL). This study aimed to characterize and quantify the symptom burden, HRQoL, and overall disease impact in patients (pts) receiving recombinant human parathyroid hormone [rhPTH(1-84), Natpara®] for inadequately controlled HypoPT, and in symptomatic pts receiving standard therapy (ST, calcium and/or vitamin D supplements).

Methods: A web-based pt survey was developed with input from members of the Hypoparathyroidism Association and from physician experts. Eligibility criteria included receiving rhPTH(1-84) or having symptoms of HypoPT while on ST. All respondents were ≥18 years old, diagnosed with HypoPT, and currently taking prescription and/or over-the-counter therapies to manage their condition. The surveys were completed at one point in time and focused on pt characteristics, recall of symptom burden from prior to and while taking their current treatment, impact of HypoPT on life and work, and HRQoL evaluated by SF-36 v2.0.

Results: 90 adult pts (mean age 54, women 83%) with HypoPT (mean duration 8.8 years) currently on rhPTH(1-84) (mean duration of therapy 19 months) and 47 adult pts (mean age 50, women 93%) with HypoPT (mean duration 16.3 years) currently symptomatic on ST completed the survey. Pts on rhPTH(1-84) (mean duration 16.3 years) currently symptomatic on ST experienced an average of 9.1 symptoms (range 0-34) and pts on ST experienced an average of 20.2 symptoms (range 1-39) over a recall period of up to 12 months. Pts currently on rhPTH(1-84) recalled experiencing an average of 17.0 symptoms (range 3-40) prior to rhPTH(1-84) therapy.
A numerically greater proportion of pts on ST reported disease-associated interference with their lives (49%) and impact on work responsibilities (31%) vs pts on rhPTH(1-84) (27% and 15%, respectively). rhPTH(1-84) pts scored numerically higher HRQoL (SF-36v2 domain scores range 44.8-49.8) vs ST pts (range 33.9-40.9).

**Discussion:** The cross-sectional real-world non-interventional study does not control for unobserved treatment selection bias and underlying clinical differences that may impact treatment effectiveness between treatment groups. Retrospective reporting of baseline symptoms and other questions, which depend on pt recall, represent additional limitations.

**Conclusion:** HypoPT is associated with significant symptom burden. Pts on rhPTH(1-84) recalled a reduction in symptoms after starting therapy, while most pts on ST reported minimal improvement of their HypoPT-related symptoms. Pts on rhPTH(1-84) reported numerically higher physical and mental domain scores as measured by SF-36v2 (higher score indicating better HRQoL) compared to ST pts.

**Abstract #524**

**WOMAN OF 28 YEARS WITH SEVERE PRIMARY HYPERPARATHYROIDISM AND MULTIPLE BROWN TUMORS**

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**Objective:** Present an interesting case on severe primary hyperparathyroidism (PHPT) and multiple brown tumors.

**Methods:** The clinical and paraclinical findings of the patient are presented.

**Case Presentation:** A 28-year-old woman with a thyroid nodule history of 8 years of evolution, asymptomatic until 1 year ago, in which she presented weight loss (18kg) and painful maxillary tumors, with progressive growth. Upon physical examination: Mass of 5.0x2.5cm at the level of LTL, delimited edges, indurated. Others in upper right maxilla region, mental region, lower maxilla and superior palatine. Analytical: Corrected calcium: 16.5 mg/dl; Intact PTH: 1600 pg/ml; Hb: 7.4g/dl. Treatment of severe hypercalcemia and anemia was initiated. Cervical USG: Thyroid nodule in LTL of 47x17x17 mm with signs of moderate risk, nodular formation adjacent to the left lower pole. FNAB: papillary carcinoma variant of oxyphilic cells. Bethesda VI. Immunocytochemistry: TG (-), TTF1 (-), Calcitonin (-), CgA (-). Conclusion: parathyroid origin. CT: Parathyroid carcinoma. Patient is discharged without complications, receiving treatment with calcium and calcitriol at high doses when developing hungry bone syndrome.

**Discussion:** While renal calculi have been reported in 10-25% of the primary hyperparathyroidism cases, the frequency of bone disease has been reported to be around 10-20%. The Brown tumor is a localized bone cyst. In histological perception, it is a benign lesion. Although bone findings are rarely seen in PHPT, they are frequent in the carcinomas or in the case of secondary HPT. The Brown tumor may cause swelling, pathological fracture, and bone pain in the skeletal system. Multiple Brown tumors in the setting of PHPT is very rare. Only six cases have been reported in the English medical literature.

**Conclusion:** Parathyroid carcinoma is a rare cause of PTH-dependent hypercalcemia, its etiology still unknown. The clinical findings are due to the excessive secretion of PTH, rather than to the tumoral infiltration of organs. It is characterized by the presence of a palpable mass in the neck and unlike other causes of PHPT, it presents with severe hypercalcemia (over 14mg/dl) and PTH increased by 3-10 times over the normal limit. The definitive treatment is surgical.

**Abstract #525**

**BUROSUMAB FOR X-LINKED HYPOPHOSPHATEMIA (XLH): RESULTS FROM TWO PEDIATRIC PHASE 2 TRIALS**

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**Objective:** In X-linked hypophosphatemia (XLH), excess circulating fibroblast growth factor 23 (FGF23) causes hypophosphatemia and consequent rickets, skeletal...
deformities, and growth impairment. We evaluated the efficacy and safety of burosumab, a fully human monoclonal antibody against FGF23, in two Phase 2 trials in children with XLH.

**Methods:** In the UX023-CL201 study, 52 children with XLH (baseline ages 5-12 years, Tanner ≤ 2 at baseline) were randomized 1:1 to receive subcutaneous (SC) burosumab every two (Q2W) or four (Q4W) weeks for 64 weeks. Doses were titrated up to a maximum of 2 mg/kg to achieve fasting serum phosphorus levels within 3.5-5.0 mg/dL. In the UX023-CL205 study, 13 children with XLH (baseline ages 1-4 years) received SC burosumab 0.8 mg/kg Q2W; the dose was increased to 1.2 mg/kg if serum phosphorus remained low. Previously treated subjects discontinued oral phosphate/active vitamin D before starting burosumab. In each study, change in rickets severity was a key efficacy endpoint, assessed radiographically by blinded readers using two scales: Thacher Rickets Severity Score (RSS) and Radiographic Global Impression of Change (RGI-C). Changes in pharmacodynamic measures and safety were also assessed. We report data for 39 subjects from both studies treated Q2W through week 40.

**Results:** Thirty-six of the 39 subjects had received prior treatment with oral phosphate and active vitamin D before starting burosumab. In each study, change in rickets severity was a key efficacy endpoint, assessed radiographically by blinded readers using two scales: Thacher Rickets Severity Score (RSS) and Radiographic Global Impression of Change (RGI-C). Changes in pharmacodynamic measures and safety were also assessed. We report data for 39 subjects from both studies treated Q2W through week 40.

**Conclusion:** In children 1-12 years old with XLH, ~1.0 mg/kg burosumab administered Q2W significantly improved phosphate homeostasis and healed rickets.

**Abstract #526**

**PARATHYROID CARCINOMA IN A PATIENT WITH CHRONIC RENAL DISEASE IN HEMODIALYSIS WITH TERTIARY HYPERPARATHYROIDISM.**

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**Objective:** To describe an infrequent case of parathyroid carcinoma in a young patient in long-standing HD

**Methods:** The clinical and paraclinical data of the patient are presented

**Case Presentation:** A 29-year-old man on HD therapy for approximately 13 years due to ESRD secondary to mesangial glomerulonephritis refractory to corticosteroids, VHB and HTN for 9 years. Pathological intertrochanteric fracture of the left femur 1 year ago. It was controlled in nephrology, where iPTH levels were observed above 2000 pg/dL for 8 years, receiving calcium carbonate, calcitriol 1 mg EV in each session of HD and subsequently sevelamer, suspended calcitriol to develop hypercalcemia for two years (corrected serum calcium of 11 mg/dL). USG of the neck: nodule of 8x5 mm with peripheral vascularization in the lower pole of the RTL, and nodule with thick calcifications at the edge of the lower pole of the LTL, in addition to the 14.9x8.6 mm nodule posterior to the upper pole of LTL, with partially calcified edges that would correspond to parathyroid glands. Scan with Tc Sesta-MIBI: parathyroid adenomas at lower poles of both thyroid lobes. Bone scan: Multiple foci in the skull, thorax, pelvis and extremities, the largest in the spine (D6 to L4), to rule out pathological fractures. He underwent cervical exploration with total parathyroidectomy with autograft of ¼ of the right inferior parathyroid gland. The pathological study reported: a nodule of 1.1x1 cm is observed in the left upper parathyroid gland, which was reported as partially encapsulated in microscopy, exhibits marked fibrosis and dystrophic calcification, with histological evidence of lymphatic and vascular tumor embolism, with endothelin studies (+) in the IHQ. The surgical margins were free, and the rest of the glands with signs of pseudonodular hyperplasia. In the PO period, he presented with a hungry bone syndrome: Corrected calcium: 6.84 mg/dL, PO4: 2.9 mg/dL, Mg: 2.37 mg/dL; iPTH: 244 pg/mL, Osteocalcin: 23.8 ng/mL; Alkaline Phosphatase: 551 U/L.

**Discussion:** Parathyroid carcinoma is a disease with a considerably low incidence, occurring in less than 1% of all patients diagnosed with primary hyperparathyroidism (PHPT). According to data from the US SEER, the incidence is from 0.4 to 0.6 per million inhabitants, and there is no institution worldwide with a series of cases
reported with more than 50 patients.

**Conclusion:** The etiology of parathyroid carcinoma is still unknown. Several reports on concurrence between carcinoma, adenoma and hyperplasia in the same parathyroid gland suggest that adenoma and parathyroid hyperplasia can lead to carcinoma. However, these conclusions are controversial and unclear due to the low incidence of this entity.

**Abstract #527**

**A CONSULT FOR DISH (DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS): WHAT CAN THE ENDOCRINOLOGIST OFFER?**

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Advocate Christ Medical Center

**Objective:** Diffuse idiopathic skeletal hyperostosis (DISH), a non-inflammatory disease characterized by ossification of the ligaments and entheses of the spine, has no known clear etiology but may be associated with the metabolic syndrome. We report herein a patient referred to an endocrinology clinic for evaluation of DISH findings by X-Ray and discuss potential endocrine causes and implications.

**Case Presentation:** A 48 year old lady with history of chronic back pain was referred to the Endocrinology clinic for further evaluation and management of incidental radiographic findings of DISH on chest X-ray. Her only reported medication is amlodipine for hypertension. Physical exam was significant for obesity (BMI of 49 kg/m2). No acromegalic features and no decreased spinal range of motion were appreciated. Further testing demonstrated a normal fasting glucose (83mg/dL), IGFI level (88 ng/mL [94-252 ng/mL]), and lipid panel, elevated fasting insulin of 23 µIU/mL with a HOMA-IR score (Homeostatic Model Assessment for Insulin Resistance) of 4.7, and a mildly elevated HbA1c at 6.1%

**Discussion:** DISH is a skeletal disease characterized by ligamentous ossification, most often of the anterolateral thoracic spine. Abnormal osteoblastic differentiation and activity results in the distinctive features of DISH. It is primarily seen in middle-aged and elderly patients. In addition to spinal involvement, DISH is frequently reported in association with obesity, metabolic syndrome, hypertension, diabetes mellitus, hyperinsulinemia and dyslipidemia. Our patient has metabolic syndrome features including severe obesity, hypertension, a HOMA score of 4.7, suggestive of insulin resistance and a HbA1c level consistent with prediabetes. Biological anthropology studies confirmed that persons of high social standing, likely enjoying a more indulgent diet of animal fats and alcohol, had a higher prevalence of DISH compared to their lower social status counterparts. While normal in our patient, IGF-1 levels require testing since 20% of patients with acromegaly have associated DISH.

**Conclusion:** DISH is typically diagnosed on radiographic findings alone. However, given the metabolic abnormalities associated with DISH, it may be better defined as a systemic disease, rather than solely a skeletal condition. With the obesity epidemic and the higher rates of metabolic syndrome, endocrinologists need to be aware of the occurrence of DISH with such conditions.

**Abstract #528**

**AN AGGRESSIVE CASE OF POLYOSTOTIC FIBROUS DYSPLASIA AND THYROID CANCER: A POSSIBLE ASSOCIATION**

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**Objective:** We report a rare case of isolated polyostotic fibrous dysplasia in a patient with papillary thyroid cancer.

**Case Presentation:** A 52-year-old woman with type 2 diabetes, hypertension, and papillary thyroid cancer status post total thyroidectomy and radioactive iodine ablation, presented to the emergency department with severe right leg and groin pain. The pain had acutely worsened over a period of weeks, rendering her unable to bear weight on her right leg. She had no history of pathological fractures, precocious puberty, soft tissue growths, or change in shoe/ring size. Physical examination was notable for limited range of motion in the right hip due to pain. Skin exam was unremarkable and she had no clinical signs of hormonal hypersecretion. Alkaline phosphatase was elevated at 108 (32-91U/L). Radiographs demonstrated cortical thickening and an abnormal trabecular pattern within the right tibia, diffuse abnormal heterogeneous appearance of the right femoral interosseous matrix with interspersed areas of sclerosis, raising concern for malignancy. Bone scan revealed intense abnormal tracer uptake in multiple bones including the right superior pubic ramus, right femur, right tibia, right first metatarsal, both humeri and mandible. Serum protein electrophoresis did not show a monoclonal spike. Pathology from the needle biopsy was consistent with fibrous dysplasia (FD). Given the dramatic findings on bone scan and ongoing concern for malignancy, she underwent a fluoroscopy guided open biopsy with extensive sampling and removal of most of the right pubic bone lesion. Intra-operatively, no gross signs of malignancy or infection were
noted. Surgical pathology confirmed FD. Further work up revealed normal bone mineral density, C-telopeptide, bone specific alkaline phosphatase, osteocalcin and vitamin D 25 OH. Our patient received zoledronic acid infusion for symptomatic relief.

Discussion: The triad of FD, Café au lait spots and hyperfunctioning endocrinopathies constitute McCune Albright Syndrome (MAS). One case of thyroid cancer has been reported in association with MAS and two cases have been reported in association with Mazabraud’s Syndrome, which is defined by the association of intramuscular myxoma with FD. To our knowledge, this is the first case report of isolated, aggressive polyostotic FD in a patient with papillary thyroid cancer.

Conclusion: Mutations in the GNAS1 gene have been linked to both FD and thyroid cancer and could be a possible common denominator. However, further genetic and molecular studies are needed to clarify any existing association between the pathogenesis of FD and papillary thyroid cancer.

Abstract #529

OSTEOPOROSIS AMONG PATIENTS WITH CORONARY ARTERY DISEASE.

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Objective: Coronary Artery Disease (CAD) and Osteoporotic fractures are important public health problems which carry high morbidity and mortality. Both diseases are important from developing countries point of view where they occur a decade earlier and are common in the elderly. The studies are limited on their interaction. The present study was conducted to find any association between these two common diseases.

Methods: We studied 279 patients in age range of 51-75 years (135 females & 144 males) during 2014-2015. While they were being evaluated for CAD, Osteoporosis workup was done. CAD was confirmed by CT and/or catheter coronary angiography. Diagnosis of CAD was made when ≥ 1 arteries showed > 50% stenosis in angiogram or presence of past history of myocardial infarction. CT coronary angiography was done on 64 slice CT using non–ionic (ioversol) dye. Diagnosis of osteoporosis was made with a value of BMD > 2.5 SD below the young adult mean or presence of fragile fracture. A detailed drug history including estrogen,bisphosphonates and steroids, comorbidities including diabetes, hypertension, smoking, physical inactivity, clinical examination, BMI and laboratory workup including nutritional hormonal and lipids etc. were done. A BMD that lies between 1 and 2.5 SD below the young adult mean was considered as having osteopenia. BMD within 1 SD of young adult mean was considered normal. BMD was measured using Dual energy X-ray absorptiometry (DEXA) scan done for bilateral femoral neck, lumbar spine and both wrists on whole body DEXA machine.

Results: The 279 patients were divided into two groups based on presence or absence of CAD. The prevalence of osteoporosis in the two groups was observed as follows - GROUP CAD(n=185) No CAD(n=94)

- Normal BMD 42.7% 70.2%
- Osteopenia 17.8% 11.7%
- Osteoporosis 39.5% 18.1%

Discussion: Our study showed that patients with CAD are ~1.7 times more likely to have low BMD versus group with no CAD, having a major difference for fracture risk. Potential links underlying in the calcification process and mineralization by non-collagen bone related proteins mediating bone resorption and calcification of vascular intima and may involve estrogen deficiency mediated RANKL and OPG system on osteoclast. Drug treatment for osteoporosis like few bisphosphonates have also shown to modify the cholesterol biosynthesis, vascular inflammation and calcification.

Conclusion: Patients with CAD are more likely to have osteopenia and osteoporosis.
1. Group with CAD had low BMD in 57%
2. Group with no CAD had only low BMD in 30%
These results highlight that the presence of one disease should prompt an investigation for the other.

Abstract #530

EFFECT OF ABALOPARATIDE VERSUS ALENDRONATE ON FRACTURE RISK REDUCTION IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS

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Objective: Abaloparatide (ABL) is a selective activator of the PTH1 receptor signaling pathway that stimulates bone formation. In the 18-month (mo) Phase 3 ACTIVE study ABL significantly decreased the risk of vertebral and nonvertebral fractures vs placebo (PBO) in postmenopausal women with osteoporosis. In the 24-mo ACTIVExtend extension study, treatment (tx) with alendronate (ALN) following ABL resulted in sustained
fracture risk reduction vs ALN following PBO. The purpose of this post hoc analysis was to assess the relative anti-fracture efficacy of ABL and ALN by comparing the average monthly vertebral fracture incidence in patients who received ABL in ACTIVE with the average monthly vertebral fracture incidence in patients who received ALN in ACTIVExtend (after 18 mos PBO in ACTIVE).

Methods: In ACTIVE, patients were randomized 1:1:1 to double-blind ABL 80 µg, PBO, or open-label TPTD 20 µg SC for 18 mos. Following 1 mo for reconsent, ABL and PBO patients who entered ACTIVExtend were provided ALN 70 mg weekly for 24 mos. Average monthly vertebral fracture incidences were calculated for ABL and PBO during 18 mos of tx in ACTIVE, and during 24 mos of ALN tx in ACTIVExtend. Average monthly fracture incidences for ABL in ACTIVE were compared with ALN in the PBO/ALN ACTIVExtend using the Z-test; no adjustment was made for patients receiving ALN 19 mos after randomization into ACTIVE as there was no interaction between tx and age.

Results: A total of 558 ABL/ALN and 581 PBO/ALN patients in ACTIVExtend were evaluated. Consistent with the expected effect of ALN, the average monthly incidence of vertebral fractures in the PBO/ALN group in ACTIVE and ACTIVExtend was 0.234% and 0.117%, respectively, representing a 50% decline after transition to ALN (P=0.024). For the ABL/ALN group, the average monthly incidence of vertebral fractures was 0.032% in ACTIVE and 0.015% in ACTIVExtend (P=0.443). A cross-group comparison of the average monthly vertebral fracture incidence of ABL in ACTIVE (0.032%) and the average monthly fracture incidence of ALN in the PBO/ALN group in ACTIVExtend (0.117%) corresponds to a 73% lower incidence with ABL vs ALN (P=0.014) (Figure).

Discussion: Consistent with the expected effect of ALN, a significant decline in fracture incidence was observed as patients transitioned from PBO to ALN. Transitioning from ABL to ALN was associated with continued anti-fracture efficacy. A cross-group comparison demonstrated that ABL may provide greater vertebral fracture risk reduction vs ALN; confirmation of these results is warranted.

Conclusion: ABL may provide benefits in terms of vertebral fracture risk reduction vs ALN.
were observed. Results were similar for TPTD vs PBO.

**Discussion:** Among postmenopausal women with osteoporosis enrolled in ACTIVE, in a subpopulation with type 2 DM, ABL-SC resulted in numerical reduction in risk of vertebral, nonvertebral, clinical, major osteoporotic, and wrist fractures, as well as in significant improvements in BMD, compared with PBO. Results are consistent with the significant fracture risk reduction observed in the overall ACTIVE population, confirmation of these findings is warranted.

**Conclusion:** Results from this post hoc analysis suggest ABL-SC may provide a valuable treatment option for women with postmenopausal osteoporosis and type 2 DM at high risk for fracture.

Abstract #532

FIVE-YEAR EFFICACY AND SAFETY OF RECOMBINANT HUMAN PARATHYROID HORMONE 1-84 (RHPTH[1-84]) FOR THE TREATMENT OF ADULTS WITH CHRONIC HYPOPARATHYROIDISM

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**Objective:** The primary aim of the ongoing RACE study is to assess the long-term safety and tolerability of recombinant human PTH 1-84 (rhPTH[1-84]) for the treatment of hypoparathyroidism in adults (NCT01297309).

**Methods:** Patients initially received 25 or 50 µg/day of rhPTH(1-84) subcutaneously, with increases in 25-µg increments to a maximum of 100 µg/day. rhPTH(1-84) could be titrated and oral calcium (Ca) and calcitriol doses adjusted at any time during the study to maintain serum Ca levels within the optimized target of 8.0–9.0 mg/dL. A composite efficacy endpoint was the proportion of patients who achieved a ≥50% reduction from baseline (BL) in oral Ca dose (or Ca ≤500 mg/day) and a ≥50% reduction from BL in calcitriol dose (or calcitriol ≤0.25 µg/day) while maintaining albumin-adjusted serum Ca between 7.5 mg/dL and the upper limit of normal for the central laboratory. We now present 5-year, open-label efficacy and safety data with descriptive summary statistics (mean±SD).

**Results:** The study cohort consisted of 49 patients enrolled at 12 centers (age 48.1±9.78 years; 81.6% female); 40 patients (81.6%) completed 60 months (M60) of treatment with rhPTH(1-84) as of May 8, 2017. Oral Ca and calcitriol doses were reduced by 53.4% and 75.7%, respectively, while albumin-adjusted serum Ca levels were maintained within the target range (M60, 8.5±0.78 mg/dL, n=40; BL, 8.4±0.70 mg/dL, n=49). At M60, the efficacy composite endpoint was achieved by 28 of 40 patients (70.0%). Urinary Ca excretion showed a numerical reduction (M60, 246.3±132.21 mg/24 h, n=40; BL, 356.7±200.37 mg/24 h, n=48), as did serum P levels (M60, 3.9±0.66 mg/dL, n=40; BL, 4.8±0.58 mg/dL, n=49), and Ca-P product levels (M60, 34.2±5.55 mg2/dL2, n=40; BL, 42.1±6.35 mg2/dL2, n=49). Serum creatinine levels remained stable (M60, 0.9±0.23 mg/dL, n=40; BL, 1.0±0.21 mg/dL, n=49), as did estimated glomerular filtration rate (M60, 108.1±42.32 mL/min, n=40; BL, 108.2±36.36 mL/min, n=41). Treatment-emergent adverse events (TEAEs) were reported in 48 of 49 patients (98.0%). The most common TEAEs (>25% of patients) reported included symptoms of the underlying disease (ie, hypocalcemia [36.7%], muscle spasms [32.7%], paresthesia [30.6%]), sinusitis (30.6%), and nausea (30.6%). Serious TEAEs occurred in 13 patients (26.5%).

**Discussion:** Hypoparathyroidism is an uncommon disorder of mineral homeostasis due to deficiency of PTH. Conventional treatment with oral Ca and calcitriol can help to maintain serum Ca levels, but does not replace other physiologic effects of PTH.

**Conclusion:** Continuous use of rhPTH(1-84) over 5 years has an acceptable safety profile, was well tolerated, efficacious, and improved key measurements of mineral homeostasis.
Abstract #533

THE IMPACT OF VITAMIN D STATUS ON PREOPERATIVE ULTRASOUND FINDINGS AND PARATHYROIDECTOMY OUTCOMES IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Objective: Impaired vitamin D status may lead to an aggressive phenotype of primary hyperparathyroidism (PHPT) due to persistent stimulation of parathyroid glands. In this study we aimed to determine whether 25-hydroxyvitamin D (25[OH]D) levels impact preoperative ultrasound findings and outcomes following parathyroidectomy.

Methods: Retrospective analysis of 81 patients who had a parathyroidectomy for PHPT from January 2008 to October 2016. Patients were grouped according to their (25[OH]D) levels (GrpA-deficient [<30 nmol/L], GrpB-insufficient [≥ 30 and < 50 nmol/L], GrpC-sufficient [≥ 50 nmol/L]). All patients had preoperative ultrasound scans (USS) and pre and post-operative biochemistry and pathology results were obtained from hospital clinical portal.

Results: Our patients were predominantly females(80.2%). Preoperatively, there was no statistically significant difference in parathyroid hormone (PTH) (p=0.19) and adjusted calcium (p=0.91) levels in different vitamin D subgroups. Parathyroidectomy was an effective cure as post-operative PTH, adjusted calcium, phosphate, alkaline phosphatase and creatinine levels improved significantly [p < 0.00001]. USS didn’t show any significant difference in localizing single gland disease (SGD) in vitamin D subgroups (sensitivity in GrpA, GrpB and GrpC were 57.1%, 62.5% and 55.8% respectively) (Table 1) and the chances of finding a negative scan was fairly identical in all groups (~44.5%). USS couldn't detect any multi-gland disease (MGD) but we observed that the inferiorly located glands were more involved when 25[OH]D levels were in the deficient or insufficient range. Postoperatively, patients had higher adenoma weight in GrpA (1.42 ± 1.35 gm) and in GrpB (1.11 ± 1.39 gm) vs. GrpC (0.58 ± 0.48 gm) for SGD and trend was identical for the combined weight of glands in MGD (1.81 ± 2.79 gm; 0.93 ± 0.58 gm and 0.59 ± 0.33 gm respectively). Linear regression analysis showed an inverse association of 25[OH]D level with adenoma weight for SGD ([r: -0.006; p=0.008]) but a similar relationship could not established when multiple glands were resected ([r: -0.0007; p=0.54]).

Conclusion: Preoperative vitamin D status doesn’t significantly influence biochemical severity of disease in PHPT. USS is a reliable tool for localization of parathyroid glands in SGD but ineffective for MGD and the sensitivity, specificity and accuracy of scan results are not influenced by 25[OH]D levels. Patients with hypovitaminosis D have higher adenoma weight and an inverse relationship exists between the two in single gland disease.

Abstract #534

SEVERE HYPOPHOSPHATEMIA DUE TO DENOSUMAB IN METASTATIC PROSTATE CANCER

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Objective: Denosumab monoclonal antibody is used for prevention of skeletal-related events in bone metastases from solid tumors. Hypophosphatemia and hypocalcemia are known side effects of Denosumab; we present here a case of severe hypophosphatemia due to denosumab in metastatic prostate cancer.

Case Presentation: A fifty nine year old male with adenocarcinoma of prostate with extensive bone metastases was initially treated with Lupron, Casodex, Taxotere later with Cabazitaxel, Casodex along with Denosumab(Xgeva). Calcium was checked periodically was normal. Received radiation therapy to thoracic, lumbar spine. Two days after completion of second cycle of chemotherapy was admitted for nausea, vomiting, diarrhea thought secondary to neutropenic enteritis. He was noted to have persistently low hypophosphatemia <1 along with mild hypocalcemia 6.5 dispite resolution of diarrhea and several days of high doses of IV phosphorus and oral calcium. He also had Vit D deficiency ~8 which was corrected. Urine phosphorus 26 and PTH 482.

Discussion: Denosumab approved by FDA for prevention of skeletal-related events in bone metastases under the trade name XGEVA. The recommended dose for XGEVA is 120 mg subcutaneously every four weeks c.f. PROLIA (Denosumab) used for osteoporosis is 60mg subcutaneous every six months.Therefore, the side effects of Hypophosphatemia and Hypocalcemia are more severe and common with Xgeva. The XGEVA prescribing information recommends the administration of calcium and vit D as necessary to prevent hypocalcemia, but does not recommend checking phosphorus and vit D levels prior to or while giving the drug. As previously observed We also observed Denosumab along with vit D deficiency...
may be more resistant to treatment for hypophosphatemia and hypocalcemia.

**Conclusion:** We strongly advice checking and supplementing phosphorus and vit D levels along with calcium in patients recieving Xgeva. Routine comprehensive panel do not include serum phosphate levels which can result in considerable delay in diagnosis with sometimes devastating consequences.

**Abstract #535**

**IMPLEMENTATION OF A FRACTURE-LIASON PROGRAM AT A UNIVERSITY MEDICAL CENTER: A CHART REVIEW**

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**Objective:** Patients who sustain fragility fractures are at high risk of refracture, but osteoporosis treatment rates are low. Our objectives were to determine if 25(OH)D was checked, Vitamin D and calcium supplements started, DXA scan ordered and osteoporosis medication started.

**Methods:** From May 2016 to May 2017, patients with fragility fracture were identified at the time of fracture. Inclusion: >19 years old, seen by academic orthopedic s, and identified as having a fragility fracture. Exclusion: traumatic fracture.

**Results:** Of 271 patients, 47.2% (n=128) had no previous fracture or osteoporosis diagnosis; 20.3% (n=55) had a previous fracture and osteoporosis diagnosis; 18.5% (n=50) had a previous fracture but no osteoporosis diagnosis or treatment; and 14% (n=38) had no previous fracture, but had a osteoporosis diagnosis. 228 patients were admitted and 43 were seen in the ER. Of those admitted, 71.9% were seen by the inpatient endocrinologist and 58.3% had inpatient vitamin D levels checked. Prior to admission, 29.9% of patients were treated with calcium, and 33.6% treated with vitamin D. In the inpatient setting, 51.8% were started on calcium and 59.9% were started on vitamin D. At discharge, 45.1% were discharged on calcium and 56.6% were discharged on vitamin D. At the time of follow-up, 80.2% of patients had a diagnosis of osteoporosis, 81% had a DXA done, 59.5% were on calcium, 73.3% were on vitamin D and 52.6% were started on osteoporosis medication. This is compared to the year prior to the FLS implementation, when 80% of patients carried a diagnosis of osteoporosis, 47% had a DXA done, 67% were on calcium, 60% were on vitamin D, and 40% were on osteoporosis medication. There was a statistically significant difference in number of DXAs done (p=0.002). When comparing endocrine vs. primary care, significantly more patients were treated with osteoporosis medication by endocrine.

**Discussion:** 20% of fracture patients had previously fractured and were without a prior diagnosis or treatment. Vitamin D and calcium prescriptions were not carried over to discharge. However, there was an increase in DXAs performed and osteoporosis medication prescribed since 2016. Education of primary care physicians is a key part of ensuring these patients are being treated, since a majority follow-up with them on discharge.

**Conclusion:** This study showed that many patients have fractures and are not diagnosed or treated appropriately for osteoporosis. A FLS that has increased the number of DXA scans and osteoporosis medication prescribed. However, there is still room for improvement in capturing more inpatients admitted for fractures, and ensuring calcium on discharge.

**Abstract #536**

**PHYSICIAN- AND PATIENT-REPORTED DISEASE SEVERITY IN ADULTS WITH OSTEOPOROSIS: A US CROSS-SECTIONAL SURVEY**

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**Objective:** Osteoporosis (OP) is a leading cause of morbidity and mortality in the US, yet there is limited understanding of its severity in clinical practice. The objective of this study was to evaluate the association between physician (MD)- and patient-rated OP disease severity and concern.

**Methods:** Data were taken from the 2016 Adelphi US Osteoporosis Disease Specific Programme, a cross-sectional survey of MDs and their patients with OP; patients were invited to complete a questionnaire. Current disease severity (mild/moderate/severe/very severe) and concern about OP (not at all/slightly/very/extremely) were based on patient reports and were independently rated by their MDs. The weighted kappa statistic identified level of agreement between MDs and their patients.

**Results:** Overall, 1,848 patients were included 1,690 [91.5%] were women, 1,245 [67.4%] were ≥65. Most patients were identified by their MDs as having either mild (549 [29.7%]) or moderate (944 [51.1%]) and fewer as severe (304 [16.5%]) and very severe (51 [2.8%]) OP. Overall, 128 (14.0%) patients rated their disease as more severe than did their MD, and 182 (19.9%) rated it as less severe. Patient and MD agreement on disease severity was moderate (kappa=0.4977) for all MDs, with similar rates
of agreement between MD and patient ratings based on specialty: primary care (0.4974) and specialists (0.4567). When evaluating concern about OP, 268 (29.3%) patients reported greater concern about their OP than did their MD while 188 (20.6%) patients reported lower concern. Agreement on concern about OP between MDs and their patients was fair (kappa=0.3786), with slightly lower agreement for specialist (0.3193) vs primary care (0.4161).

Discussion: Some patients may perceive OP severity differently from their MDs and have different concerns regarding the disease and its management.

Conclusion: Communication between MDs and their patients regarding disease severity and future fracture risk may facilitate shared treatment decision making.

Abstract #537

MONOSTOTIC PAGET’S DISEASE OF THE MANDIBLE

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Objective: Paget’s disease is a common disorder of bone metabolism; with most estimates of prevalence ranging between 1-3% of adults over age 40. The most commonly reported symptoms include pain and deformity. Other associated features include fractures, hearing loss and osteosarcoma. Paget’s disease may be monostotic or polyostotic.

Methods: Monostotic Paget’s disease is rare in the mandible, with few reports in the literature. Herein we describe the clinical course of a patient with monostotic disease of the anterior mandible.

Case Presentation: An 81-year-old male presented to our Endocrinology clinic for an evaluation in December 2016. He reported that for the past 6 months, he had been suffering from gradual inability to bite and eat solid foods. He reported his jaw was enlarged and painful. He had also been suffering from headaches and had difficulty turning his head to the left side. Additionally, he reported hearing loss that had gradually worsened over the past 6 months. Review of the CT scan of maxillofacial bones from November 2016 showed that the mandible was diffusely exhibiting areas of cortical thickening & trabecular thickening. Radionuclide bone scan was suggestive of increased uptake in jaw and ethmoid bones. Lab work showed a Bone-specific Alkaline phosphatase (Bs-ALP) of 45.5 mcg/L (7.6-14.9) & Insulin like Growth Factor-1 was 116 ng/mL (34-246). The patient was recommended to proceed with a bone biopsy to rule out an underlying infection or malignancy. Biopsy from the anterior mandible in January 2017 revealed fragments of bone with irregular, thickened trabecula consistent with Paget’s disease. Patient was then offered treatment with 5 mg of Intravenous Zoledronic acid. He tolerated this well and gained relief from his jaw pain and started eating solid foods again. Bs-ALP was down to 15.5 mcg/L and 12.3 mcg/L at 3 and 6 months post therapy respectively.

Discussion: Some patients may perceive OP severity differently from their MDs and have different concerns regarding the disease and its management.

Conclusion: Communication between MDs and their patients regarding disease severity and future fracture risk may facilitate shared treatment decision making.

Abstract #538

MALIGNANT HYPERCALCEMIA IN SEMINOMA: AN EXTREMELY RARE PRESENTATION

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Objective: Malignant hypercalcaemia associated to seminoma is extremely rare, accounting for less than 10 cases reported in the literature.

Case Presentation: A 44-year-old man with history of left testicular seminoma diagnosed when he was 31-years old, treated with left orchiectomy and 30 cycles of carboplatin, was consulted to the endocrinology service for severe hypercalcaemia. The patient was lost to follow-up until 3 weeks before hospitalization, when he noticed fatigue, lack of energy, polyuria, generalized abdominal pain and occasional palpitations. Physical exam was remarkable for an enlarged, non-tender right testicle, without palpable lymphadenopathy. Initial laboratories showed normocytic normochromic anemia, acute kidney injury and severe hypercalcaemia (corrected serum Ca: 15.7 mg/dL, reference 8.5 – 10.5 mg/dL). EKG showed no abnormal QT-interval. Abdominopelvic CT scan revealed extensive retroperitoneal lymphadenopathies...
The diagnosis is often delayed due to failure to check serum phosphorus levels. Surgical resection is curative, but the tumors are typically small and difficult to locate. Treatment with phosphorus and calcitriol supplements requires monitoring for associated complications.

**Abstract #540**

**A CASE OF LITHIUM INDUCED SEVERE HYPERCALCEMIA**

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**Objective:** Hypercalcemia has been associated with long term use of Lithium carbonate but is often under recognized. Symptoms may progress insidiously and can be similar in presentation to the underlying psychiatric illness which may cause delay in diagnosing Lithium induced hypercalcemia (LIH). We report a case of a patient on Lithium therapy for bipolar disorder who presented with depression-like symptoms which were found to be secondary to hypercalcemia, requiring discontinuation of Lithium.

**Case Presentation:** A 46 year old woman who presented to the hospital with complaints of abdominal pain, nausea, vomiting and weakness for 1 week. She was on Li 300 mg
three times daily for 7 years. She complained of anorexia, confusion, decreased concentration and fatigue for several weeks which were concerning for an exacerbation of depression. Admission laboratory values revealed an elevated serum Lithium level of 2.3 (0.5-1.2 mmol/L) and corrected calcium of 13.69 (8-10.5 mg/dL). Serum phosphate and magnesium were normal. Further testing revealed parathyroid hormone (PTH) level of 56.2 (10-65 pg/ml) and total 25-hydroxy vitamin D level of <10 (25-80 ng/ml). Her eGFR was 90 (>90 ml/min). Chest and abdominal imaging ruled out sarcoidosis or malignancy as possible etiologies. Intravenous fluids and Calcitonin were initiated. Her hypercalcemia progressively resolved, with concomitant clinical improvement. Lithium was discontinued and replaced by Topiramate.

Discussion: The exact pathophysiology of LIH is not fully known. Lithium may cause increased calcium reabsorption in the loop of Henle. Lithium can also alter feedback mechanisms in the Calcium sensing receptor preventing PTH suppression normally produced by hypercalcemia. It may further unmask a previously unrecognized primary hyperparathyroidism. There are no clear predictors to establish which patients are at risk for LIH. The rates of LIH are reported to be 5-40%. Signs and symptoms of LIH can be misinterpreted in the context of mood disorders. As in our case, evaluation of such symptoms should include assessment for hypercalcemia.

Conclusion: As per recent American Psychiatric Association Practice Guidelines, although the interval has not been established, it is recommended to periodically monitor serum calcium given the relatively non familiarity with LIH. An exacerbation of mood symptoms may be the initial manifestation of emerging hypercalcemia. Symptomatic cases may be managed with lithium discontinuation along with use of hydration and diuretics resulting in prompt resolution of symptoms. Recently, Cinacalcet, a calcimimetic agent has been used without discontinuation along with Lithium. Parathyroidectomy may be warranted in refractory cases.

Abstract #541

DENOSUMAB-INDUCED SEVERE HYPOCALCEMIA IN A PATIENT WITH HTLV-ASSOCIATED ADULT T-CELL LEUKEMIA / LYMPHOMA (ATLL)

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Objective: Review the pathophysiology of hypercalcemia in malignancy, specifically ATLL. Understand the mechanism of RANK-L monoclonal antibody therapy, and of post-therapy hypocalcemia.

Case Presentation: A 54-year-old female from Trinidad with no significant past medical history presented with abdominal pain, vomiting, and unintentional weight loss. She denied medication or supplement use. Physical examination was not relevant. Initial laboratory studies showed: Ca 19.7 mg/dL, Cr 0.89 mg/dL, ALP 338 U/L, normal GGT, AST 104 U/L, ALT 15 U/L, total bilirubin 3.7 mg/dL, negative gamma gap, 25-OH vitamin D 16.4 pg/mL, 1,25-OH vitamin D 15 pg/mL, PTH 4.2 pg/mL, PTH-RP 40 pg/mL, LDH 1185 U/L, euthyroid indices, and normal ACE. Imaging showed normal skeletal survey and CT chest / abdomen / pelvis. CBC was initially normal, but had progressive monocytosis with aberrant T-cells on flow cytometry. HTLV serologies were positive, and liver biopsy showed an atypical lymphocytic infiltrate. Initial treatment was IV fluids, furosemide, pamidronate, and calcitonin. However, hypercalcemia persisted for 1 week. Denosumab was given and within days, serum calcium decreased to 5.1 mg/dL and magnesium to 1.1 mg/dL. Treatment with calcium and magnesium was given to resolution. She underwent chemotherapy for her HTLV-associated ATLL.

Discussion: This case illustrates the possibility of rapid and severe hypocalcemia after denosumab therapy. Hypercalcemia occurs in up to 80% of HTLV-associated ATLL. The mechanism involves PTH-RP expression, hematopoietic stem cell differentiation into osteoclasts, molecular mimicry between gp46 peptide and anti-osteoprotegerin, and RANK-L secretion. Denosumab, a RANK-L monoclonal antibody, prevents osteoclastic resorption of bone. It is indicated for bisphosphonate-refractory hypercalcemia of malignancy. Post-marketing occurrences of symptomatic hypocalcemia are reported as 1-2%, and up to 3% in patients with renal impairment. Given our patient was vitamin D deficient and had malignancy, the multiple calcium-lowering therapies along with denosumab resulted in profound hypocalcemia. Denosumab blunted the typical compensatory mechanisms for hypocalcemia: PTH secretion and osteoclastic activity. As her malignancy predisposed to high bone turnover, denosumab therapy effected a phenomenon similar to hungry bone syndrome - it inhibited osteoclastic activity, but not new matrix deposition. Also as its long half-life averaged 25 days, this resulted in the severe hypocalcemia.

Conclusion: Denosumab therapy can cause profound hypocalcemia, especially in patients with conditions that cause high bone turnover. Close monitoring and repletion with calcium, magnesium and vitamin D is key to treatment.
Abstract #542

AN UNUSUAL INITIAL PRESENTATION OF ACTIVE PULMONARY TUBERCULOSIS: SEVERE HYPERCALCEMIA WITH ALTERED MENTAL STATUS AND RENAL FAILURE

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Objective: Hypercalcemia is most commonly due to primary hyperparathyroidism or malignancy. Severe hypercalcemia, with renal failure and altered mental status (AMS), is not the usual initial presentation of active pulmonary TB in the US. We describe herein an unusual such presentation.

Case Presentation: A 77-year-old male presented with AMS, anorexia, generalized weakness, polydipsia, polyuria, and weight loss. He denied respiratory symptoms. History was remarkable for HTN and smoking. Vital signs were stable. Examination revealed a cachectic male in no distress, alert and oriented only to self - a marked change from baseline. Lungs were clear. He was mildly tachycardic with a regular rhythm.

Labs revealed hypercalcemia (corrected Ca2+ 17.2 mg/dL), AKI (Scr 2.18 mg/dL, up from 0.73 mg/dL one month prior), and elevated total protein (8.6 g/dL). CBC revealed a normocytic anemia (Hgb 10.2 g/dL). CT-chest demonstrated left upper lobe consolidation. Given his severe hypercalcemia, elevated protein gap, renal insufficiency, and anemia, there was high suspicion for multiple myeloma vs. PTHrp-driven hypercalcemia. PTH was suppressed (16 pg/mL) and PTHrp was low (0.4 pmol/L). 25-OH vitamin D was normal (31.7 ng/mL) and 1,25-(OH)2 vitamin D was elevated (92.5 pg/mL). TSH was normal (2.15 U/mL). Inflammatory markers, including procalcitonin, ESR, and CRP, were all highly elevated. Fungal serologies were negative. SPEP revealed a small M-spike (0.5 g/dL IgG lambda monoclonal protein). Bone marrow biopsy revealed 3% plasma cells, consistent with MGUS; a lymphoma panel was negative. A BAL was performed: cytology was negative for malignancy and mycobacterial and AFB smears were negative. The cause for severe hypercalcemia remained elusive, as MGUS precludes myeloma-related organ dysfunction. Treatment with IV fluids, calcitonin, and zoledronic acid, led to resolution of hypercalcemia, improvement in renal function, and restoration of cognition. A repeat PTH after treatment was markedly elevated at 357 pg/mL. Several days after discharge, AFB cultures came back positive for mycobacterium TB. The patient was notified and started on appropriate anti-TB therapy.

Conclusion: While an unlikely cause of severe hypercalcemia, it is important to consider the possibility of pulmonary TB when other causes have been ruled out, especially with an elevated 1,25-(OH)2 vitamin D level. Given the fastidious nature of TB, AFB staining may be negative, but the culture may come back positive after several weeks. We are the first to describe elevated PTH in association with treatment of severe hypercalcemia with bisphosphonates. The prevalence of this observation, as well as underlying mechanism, deserves further investigation.

Abstract #543

TERIPARATIDE-INDUCED HYPERCALCEMIC CRISIS IN A PATIENT ON LITHIUM: OVERWHELMING THE CALCIUM SENSING RECEPTOR

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Objective: To describe the potentially serious drug interaction of teriparitide in a patient on lithium (Li) and to review the biochemical interactions.

Case Presentation: A 69 year-old woman with bipolar disorder on Li for 40 years, with central motor neuron disease “Parkinson’s disease”, osteoporosis, and vitamin D (Vit D) deficiency was admitted for weakness and confusion. Past history included fractures of the left femoral neck, right pubic ramus, and lumbar spine. Physical examination was notable for bilateral hand tremors, cogwheel rigidity of the upper extremities, and lead pipe rigidity of the lower extremities. She had a serum calcium of 11.9 mg/dL with an elevated iPTH (Table, Time 1). She was hydrated, Li discontinued and mentation improved (Time 2). At a two-month follow-up visit, she revealed although she had been taking alendronate for osteoporosis since 2011 she was switched by her physician to teriparatide due to worsening of her DEXA score. She had been on teriparatide for the 2 weeks before the current clinic visit, at which time (3) the serum calcium was elevated, but the iPTH now suppressed. Teriparatide and Vit D supplements were discontinued with resolution of the hypercalcemia (Time 4, Time 5).

Discussion: The initial presentation was felt to be due to Li-induced hyperparathyroidism with abrupt recovery with the discontinuation of the offending Li. Li antagonizes the Ca-sensing receptor (CASKR) in the parathyroid glands and the renal thick ascending limb, resulting in a higher Ca threshold required for suppression of serum PTH secretion.
and in inappropriately low urinary calcium (Time 1). At time 3, after institution of teriparatide, hypercalcaemia now occurred with a low measured intact PTH presumably due to the fact that the 1-34 amino acid teriparatide does not have the entire 1-84 amino acid chain necessary for detection by the iPTH dual antibody assay.

**Conclusion:** Although the patient was considered a treatment failure on bisphosphonates by worsening DEXA scores, the teriparatide may have provoked underlying hyperparathyroidism. Many of the effects of Li persist after discontinuation, causing permanent damage (e.g. nephrogenic DI, neurological tremors) and the patient may have residual hypersensitivity at the CASR. Teriparatide and Li must be considered as a potential for serious drug interactions.

**Abstract #544**

**THE MANY GUISES OF PRIMARY HYPERPARATHYROIDISM: AN UNCHANGED SCENARIO**

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**Objective:** To study the causes, characteristics and outcome of treatment of patients with primary hyperparathyroidism (PHPT).

**Methods:** This retrospective cohort analysis was conducted at the Jinnah Postgraduate Medical Centre, Karachi, and comprised data of patients with primary hyperparathyroidism between 2004 and 2014.

**Case Presentation:** Of the 25 patients, 1(4%) was male and 24(96%) were female. The overall mean age was 41.72±15.9 years, with a mean duration of symptoms of 4.1±3.3 years. The mean pre-operative parathyroid hormone level was 879.48±793.51 pg/ml. Skeletal manifestations were reported in 17(68%) patients, whereas 4(16%) patients had renal stone disease. Besides, 2(8.0%) patients presented with severe abdominal pain, 1(4%) had asymptomatic hypercalcaemia and 1(4%) patient presented with headache and was diagnosed as parathyroid adenoma in the context of multiple endocrine neoplasia type 2A. All patients underwent parathyroidectomy. A solitary adenoma was reported in 23(92%) patients, carcinoma in 1(4%) and an adenoma with hyperplasia of other glands in 1(4%) patient.

**Discussion:** A striking discrepancy exists with respect to incidence, clinical manifestations and complications of PHPT across the globe. There are wide variations in the clinical spectrum of PHPT in our geographical region. Here, it involves considerably younger age group, with symptomatic hyperparathyroidism; hence recurrent calculi and overt bone disease are still the predominant forms of the disease. Crippling skeletal manifestations mainly account for the morbidity associated with the disease. Most of our patients had some form of skeletal disease, indicating a substantial delay in diagnosis. The severe form of disease seen in this study may in part be related to the delay in seeking medical care due to lack of awareness and paucity of adequate health care facilities for low socio-economic group patients in this country.

**Conclusion:** A high index of suspicion is required for clinching the early diagnosis of primary hyperparathyroidism. Concomitant vitamin D deficiency masks the hypercalcaemia, related to elevated PTH levels, thus leading to a delay in diagnosis. Therefore, hypercalcaemia must not be used alone as a screening tool for PHPT. In addition, long-standing vitamin D deficiency may cause hyperplasia and/or adenoma of parathyroid glands due to PTH dysregulation.

**Abstract #545**

**EARLY RECURRENT OF ELEVATED THYROID HORMONE AFTER SUCCESSFUL REMOVAL OF PARATHYROID ADENOMA**

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**Objective:** To study the characteristics of patients who had elevated parathyroid hormone (PTH) levels despite successful removal of parathyroid adenoma.

**Methods:** A retrospective cohort analysis of prospectively collected data in a subset of patients with primary hyperparathyroidism.

**Case Presentation:** A total of 26 patients (F=25, M=1) presenting from 2004 to 2017 were analyzed; of these, 9 patients had recurrent PTH elevation. All 9 were female with a mean age of 46.22±18.8 years and a mean duration of symptoms of 18.8 months. There were no clinical or hormonal indicators of MEN syndrome in these 9 patients. The mean post-operative PTH level was 162.42±91.02 pg/ml (max. 378 pg/ml). The mean post-operative vitamin D level was 21.86±15.45 ng/ml (min. 4.04 ng/
ml). All patients were supplemented with vitamin D 2000 IU daily, although the compliance was variable. The commonest presenting symptom was body aches, reported in 4 (44.4%) patients. PTH normalized over an extended period of time in 2 patients. Fluctuating levels were seen in 7 patients who had erratic vitamin D intake; of these, 2 had a recurrent parathyroid adenoma. Both underwent repeat parathyroidectomy.

**Discussion:** Early recurrence of PTH elevation after removal of parathyroid adenoma poses a medical dilemma. Whereas residual tumour could be a possibility, histopathology showed complete excision of the adenoma in all cases. A close follow up over an extended period of time, unravelled different possibilities. The most common cause of recurrence of PTH elevation appears to be a functional overshoot of the remaining parathyroid glands, which had been relatively dormant during the course of hypersecretion from the parathyroid adenoma. Persistence of vitamin D deficiency and lack of inhibition of PTH secretion by vitamin D, may be a factor for the recurrent and persistent PTH elevation. PTH levels normalized over an extended period of time in 2 patients with vitamin D supplements only.

**Conclusion:** Lack of exposure to sunshine and inadequate nutritional supplementation with vitamin D, are responsible for severe and widespread vitamin D deficiency. Prolonged D deficiency leads to secondary and possibly tertiary hyperparathyroidism. Adequate vitamin D supplements are essential in the post-operative period as well as long term in order to prevent dysregulation in the remaining glands. Elevation of PTH levels post-operatively should be monitored carefully.

**Abstract #546**

**GLYCEMIC AND BONE PROFILE IN POST-MENOPAUSAL WOMEN WITH AND WITHOUT PREVALENT FRAILTY FRACTURES**

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**Objective:** The frailty fracture is the most important complication of osteoporosis in postmenopausal women, with increased risk of morbidity and mortality. Current studies support the association of hyperglycemia and even obesity (metabolic syndrome) with deterioration of bone microarchitecture resulting in increased fragility and susceptibility to fracture.

**Objective:** We evaluated the glycemic and bone profile in postmenopausal women, with and without prevalent frailty fractures.

**Methods:** We conducted a cross-sectional study in a Tertiary Endocrine Center, East Europe on postmenopausal women without known prior bone pathology or anti-osteoporotic drugs exposure. Evaluation included: fasting plasma glucose, glycosylated hemoglobin (HbA1c), the levels of parathyroid hormone (PTH), 25 hydroxy vitamin D (25(OH)D) and bone markers (CrossLaps-bone resorption marker, and osteocalcin and Procollagen Type 1 N-Terminal Propeptide (P1NP) -bone formation markers). Bone mineral density (BMD) was determined in the lumbar spine and femoral neck (GE Lunar), along with trabecular bone score assessment (TBS). For data analysis we used Student’s t-test (statistical significance at p<0.05).

**Results:** Were enrolled 80 postmenopausal women of which 14 women (62.21 ± 10.77 years) with frailty fracture and 66 without fracture (60.78 ± 9.15 years). Between the 2 groups, there were no differences in body mass index (29.31 vs 29.19 kg/m2), 25(OH)D (19.36 vs 19.23 ng/ml) or HbA1c (6.37 vs 6.32 %). The patients with frailty fractures showed a lower PTH level (46.14 vs 50.91) and a lower bone mineral density at the lumbar and femoral neck (1.001 vs 1.046 g/cm^2; 0.813 vs 0.860 g/cm^2), with a smaller trabecular bone score (1.244 vs 1.288). Regarding the bone markers, there was a higher level of both cross-laps and osteocalcin and P1NP(0.439 vs 0.402 ng/ml; 21.65 vs 20.79 ng/ml; respectively 52.20 vs 47.50 ng/ml) among patients with fragility fractures. (p>0.05).

**Conclusion:** Based on our observations, glycemic and bone parameters are similar between women with and without prevalent osteoporotic fractures.

**Abstract #547**

**AN ATYPICAL PRESENTATION OF MONOSTOTIC PAGET DISEASE**

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**Case Presentation:** Background: Paget’s disease of bone (PDB) is the second most common bone disease affecting the elderly in the United States. It is a chronic progressive disease, characterized by focal alteration of bone remodeling, initially presenting with increased bone resorption, followed by disorganized and excessive formation of bone. Detection is often made incidentally following routine chemistry screening or imaging studies obtained for other reasons. Our case is one in which the diagnosis was difficult to make in a patient presenting with focal back pain.

Case study: A 49-year-old man presented with constant, localized, burning left flank pain that radiated laterally and anteriorly, and was not exacerbated by movement.
History did not reveal trauma or fractures. His physical exam was notable for tenderness to palpation on the left thoracic vertebrae without palpable deformity, abnormal curvature, or restriction in range of motion. Biochemical, radiologic, and histopathologic investigations were performed to further explore the cause of this isolated pain. Biochemical tests revealed a serum calcium of 10.0 mg/dL (reference range 8.4-10.4 mg/dL) and serum alkaline phosphatase 96 IU (reference range 24-126 U/L). A CT of the abdomen and pelvis showed a sclerotic lesion at the L3 vertebral body. The differential at this point included atypical hemangioma, osseous metastatic disease, or other disorders of bone. MRI of the lumbar spine showed radiotracer accumulation at the L3 vertebra extending into the right posterior pedicle. A NM bone scan had isolated abnormal increased radiotracer accumulation at L3 level corresponding to the MRI findings. A CT guided bone biopsy of L3 showed irregular cement lines with active osteoblastic and osteoclastic activity and without histologic features of metastatic carcinoma. The findings were most consistent with PDB. After diagnosis was made, he was started on bisphosphonate therapy and remains on it today. He has had symptomatic relief of pain. In this case, the PDB diagnosis was difficult to reach. His imaging findings appeared independent of any abnormal lab findings. Markedly elevated serum alkaline phosphatase is a constant feature in most presentations of PDB, but may be absent in monostotic disease. His age was also younger than what is typically seen in PDB, with the mean age of occurrence at 59 years.

Conclusion: Diagnosis of PDB is usually made based on radiological examination and biochemical markers of bone turnover. Non-specific, isolated presentations of bone pain can be challenging to diagnose. Diagnosis may be achieved earlier if PDB remains high on the index of suspicion.

Abstract #548

AN INTERESTING CASE OF REBOUND ASSOCIATED VERTEBRAL FRACTURE AFTER DISCONTINUATION OF DENOSUMAB

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Objective: Denosumab is a commonly prescribed therapy in postmenopausal osteoporosis. Although it results in significant increase in bone density and reduces fracture risk, there are few reports of rebound associated vertebral fracture after discontinuation of denosumab. The exact mechanism of these fractures is unknown.

Methods: 64-year-old woman with history of osteoporosis was started on denosumab a year before presentation to us. Denosumab was continued for 3 years with improvement in bone density. 10 months after discontinuation of denosumab, she developed sudden onset back pain and presented with multiple compression fractures of the thoracic and lumbar spine. Case Presentation: 64-year-old woman with history of osteoporosis and premature surgical menopause at 38 years of age presented to establish care for osteoporosis. She had been on HRT since 38 years of age on slow taper at her presentation. She had also received teriparatide for 2 years for declining BMD. A year before presentation to us, she was started on denosumab which was continued and bone mineral density expectantly improved. After completing 3 years of denosumab, she requested a drug holiday for dental implantation. Last Denosumab injection was given in January 2016 and bone mineral density in October 2016 demonstrated T scores of -2.5 at L1-L2; -2.7 at femoral neck; total hip T-score of -2.6. Bone resorption marker urine N-telopeptide (NTX) was 21 units and bone formation marker bone specific alkaline phosphatase (BSAP) was 8.5 mcg/L.

One month later, she complained of sudden, severe lower back pain. MRI of spine revealed endplate irregularities of thoracic 11th, 12th and L1 vertebral with edema. Follow-up MRI showed subacut 50% compression fracture of the T9 vertebral body and subacute compression fractures of the superior endplates of T11 and L1 vertebral bodies with minimal associated vertebral body height loss. Urine NTX was 82 units and BSAP was 44 mcg/L. She was evaluated for hematological and other causes of fragility fractures and restarted on Denosumab.

Discussion: Denosumab is a widely used monoclonal antibody to receptor activator of nuclear factor K-B ligand and is a very effective treatment for osteoporosis. There are rare reports of increased vertebral fragility and fractures which has been attributed to excessive bone remodeling after stopping denosumab.

Conclusion: Discontinuation of denosumab may rarely result in increased bone turnover and rebound associated vertebral fractures. Factors that may increase risk for this complication remain unknown and validated risk assessment tools for this unpredictable complication remain an unmet need. Consolidating denosumab with bisphosphonates could be a potential strategy to mitigate this risk.
Abstract #549

CHRONIC AUTOIMMUNE URTICARIA AND COGNITIVE IMPAIRMENT AS UNUSUAL PRESENTING SYMPTOMS OF PRIMARY HYPERPARATHYROIDISM

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Objective: To describe an unusual case of primary hyperparathyroidism (PHPT) presenting with chronic urticaria and cognitive impairment. An unusual feature of this case is that the patient himself undertook the scientific in-depth research, literature search and writing of the case, thus, the patient’s name was added to this case report as a co-author (the second co-author).

Methods: Case Presentation: We present the clinical, biochemical and radiological findings in a patient with an unusual presentation and course of PHPT as well as a review of relevant literature.

Case Presentation: An 81-year-old man of Japanese ethnicity, with past medical history of T2DM and follicular thyroid carcinoma, has been regularly followed in our endocrine clinic for over 10 years. In 2007, he was diagnosed with thyroid cancer, which was believed to be related to ionized radiation exposure from the Hiroshima Atomic Bomb. Serum calcium was noted to be elevated in May of 2015 (10.7 mg/dL) as well as intact parathyroid hormone (iPTH) level (75.8 pg/mL). PHPTH was diagnosed, and it was opted to monitor this mild hypercalcemia with adequate hydration, with the reversible understanding that the case was asymptomatic and with no strong indications for surgical treatment. Serum calcium remains in the normal to high normal range. In parallel, the patient developed a refractory case of chronic urticaria, that was difficult to manage. It was ultimately decided to consider surgery 1 year later when osteoporosis was diagnosed. A large parathyroid adenoma was located and removed. Calcium and iPTH normalized. Urticaria also resolved postoperatively. Mysteriously, the patient noticed significantly improved cognitive function following surgery.

Discussion: Incidence of chronic urticaria among patients with PHPTH is not documented but relatively small. Four case reports have been published, describing urticaria in association with hyperparathyroidism. Our case would be the 5th reported case. To date, there is no systematic study on the relationship between serum iPTH level and the incidence of urticaria. Elevated levels of iPTH was shown to induce mast cell secretion of serotonin and histamine in vivo and in vitro via exocytosis (degranulation). Similarly, this case supports the recently emerging literature about cognitive symptoms of PHPTH.

Conclusion: This case underscores the unusual presentation of PHPT that presented with the unusual symptoms of refractory chronic autoimmune urticaria and significant cognitive decline, which both resolved following parathyroidectomy. This suggests the presence of additional mechanisms other than those involved with calcium homeostasis (that is, additional PTH receptors), in which the PTH affects the skin and brain.

Abstract #550

USE OF C-TERMINAL TELOPEPTIDE OF TYPE-I COLLAGEN (CTX) IN CLINICAL DECISION-MAKING

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Objective: Osteoporosis is a disease of bone that silently progresses until complicated by fractures. Medical therapy is often indicated to prevent fragility fractures. Side effects such as pill esophagitis, exacerbation of reflux disease, osteonecrosis of the jaw and atypical fractures add to the challenge of therapy initiation or continuation. Serum C-terminal telopeptide of type-I collagen (CTX) is a marker of bone resorption that is often used to monitor the progression of disease as well as anti-resorptive effects of medications. While this marker has been available on the market for more than a decade, it has been underutilized in clinical setting, as its efficacy in guiding therapeutic decisions has been limited. The objective of this study is to gauge current ordering practices of the bone turnover marker, CTX in NYU Winthrop Endocrinology Group and establish its role in clinical decision-making.

Methods: We conducted a retrospective chart review of 165 patients with osteoporosis who visited the practice from January 2014 to September 2016. Patient charts were randomly selected from a panel of 5 physicians using ICD code 733.0 for osteoporosis. Binomial data were collected on each patient looking at variables associated with CTX order such as medication changes, patient refusal of medication changes, adverse events, and previous experience of fractures. Subgroup analysis was performed for adverse events categorized as GI intolerance and non-GI side effects. Patients were divided into 2 groups based on CTX ordering status, and Fisher’s Exact Test was used to analyze the association between ordering of CTX and variables.

Results: Out of 5 physicians, 2 physicians utilized the marker most of the time. CTX was ordered on 81/165
(49.09%) patients in the reviewed time period. Of these, 27.16% had medication changes by physicians as compared to 21.43% in the non-CTX group (p=0.4682). Only 7.41% patients with CTX refused medication changes vs. 5.95% in non-CTX group (p=0.0382). Only 7.41% patients with CTX refused medication changes vs. 5.95% in non-CTX group (p=0.0382). In a subgroup analysis, non-GI side effects were noted in 5/81 patients in the CTX group vs 2/84 in the non-CTX group. 6/81 patients with GI intolerance in the CTX group and none in non-CTX group (p=0.0127).

Conclusion: In our small retrospective chart review, CTX appears to be ordered more in patients with GI side effects and may influence patient's readiness to accept treatment changes. Hence, CTX could be used as a tool in patients treated for osteoporosis. The result suggests initiating osteoporosis protocol for all patients on treatment may be warranted with further studies.

Abstract #551

INITIAL CLINICAL PRESENTATION OF PRIMARY HYPERPARATHYROIDISM PATIENTS FROM CHINA AND THE UNITED STATES

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Objective: To compare the initial clinical features, laboratory values and bone mineral density among patients with primary hyperparathyroidism (PHPT) in Changsha (China) and New Brunswick (USA).

Methods: In this retrospective study, we reviewed 190 (21 Asian patients) PHPT patients who presented at Robert Wood Johnson University Hospital, New Brunswick (USA) and 131 PHPT patients who presented in Changsha (China) in the same time period. The following characteristics were compared between the groups: age, gender, BMI, serum calcium, alkaline phosphatase (AKP), Albumin, intact PTH (iPTH), 25 hydroxyvitamin D (25OHD), fasting blood glucose levels and bone mineral density (BMD). All these parameters were also compared according to gender. Associations of iPTH and risk of kidney stone were also assessed along with several other parameters.

Results: PHPT patients from Changsha were younger, less female dominated, with higher serum calcium, iPTH and AKP levels, but lower 25OHD levels compared to the patients from New Brunswick (p<0.05). Patients in Changsha had lower T-score and Z-score in both the lumbar spine and hip regions than those in New Brunswick (p<0.05). Patients in New Brunswick had lower incidence of kidney stones. To check possible race effect, we compared only Asian PHPT patients between New Brunswick and Changsha. There were no significant differences in age and sex ratio (Female to Male) (P>0.05). However, Asian patients from New Brunswick had lower serum calcium, iPTH and AKP levels and higher 25OHD levels. Asian patients from New Brunswick had significant higher z-score in hip region and higher BMD and T-score in both lumbar spine and hip region.

Discussion: PHPT patients from China seem to have more severe PHPT profiles and lower bone mineral density. Asian patients from the United States have less severe clinical profile than those Asian from China with pretty same time of onset of disease. The mechanisms of these differences between the two countries remain unknown. The possible mechanisms include delayed health care in China, nutritional and environmental factors. Genetic factor or race might not as important as we though before since there are still sharp biochemical and clinical differences between Asian patients with PHPT in China and the United States

Conclusion: There are sharp biochemical and clinical differences between patients with PHPT in China and United States. Further study in a larger cohort is warranted to confirm our findings and to explore the underlying mechanisms.

Abstract #552

2 CASES OF AVASCULAR NECROSIS OF BILATERAL FEMORAL HEAD WITH VERY LOW DOSES OF ORAL STEROIDS

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PGIMER & DR Ram Manohar Lohia Hospital, NEW DELHI

Objective: This small case series is to present data of 2 patient who developed AVN while on low dose replacement steroid for endocrinological conditions.

Methods: 2 patients presenting to our tertiary care endocrine clinic with complaints of hip pain and history of glucocorticoid use at low maintainance doses were included to a part of this case series. Only those patients with radiologically (MRI) proven avascular necrosis (AVN) of femoral head were included. Case records of these patients were reviewed, detailed history and physical examination was obtained for each patient. Other causes of AVN were excluded based on history, physical examination findings and lab test results.

Case Presentation: 1st case is of 38 years old man who complained of bilateral hip pain for 2-3 months before presentation. He was diagnosed with non-secretory pituitary macroadenoma 2 years back, for which he was operated
and developed panhypopituitarism. He was managed with replacement of thyroxine, oral steroid (prednisolone) and injectable testosterone. He received oral prednisolone 5mg once daily for next 2 years, when he experienced bilateral hip pain. He was evaluated and MRI pelvis was obtained which showed AVN of bilateral femoral head.

2nd case is of a 60 years old lady who presented with complaint of pain bilateral hip joint for 6 months. She was diagnosed with sheehan’s syndrome at age of 45 years. She received replacement thyroxine and oral prednisolone. She had been taking oral prednisolone at doses of 5 to 7.5 mg once daily for past 14years. She was otherwise active but for past 6 months she developed hip pain. X-Ray Pelvis was obtained which showed AVN of bilateral femoral head which was confirmed on MRI.

Discussion: Steroid induced AVN is understood to be due to interplay and imbalance of bone resorption and formation, impairment of vasculature within bone and apoptosis. There is 4.6 fold increase in incidence of AVN with every 10 mg/day increase in prednisolone dose during first 6 months of therapy. Most of the cases described in literature on steroid incuded AVN are with higher doses of prednisolone(10 to 200mg per day). Only 2 cases have been described with use of replacement doses of prednisolone. Possible reason why some patients develop AVN at even replacement doses of prednisolone could be traced to a study on white rabbits. It was demonstrated that level of steroid metabolizing hepatic activity may increase responsiveness to steroids and thus risk of steroid induced AVN with low steroid dose.

Conclusion: Our cases highlight occurrence of AVN of femur at very small dose of prednisolone used for treatment of panhypopituitarism. Glucocorticoids should be continued at lowest possible doses when stoppage is not possible.

Abstract #553

OSTEOPOIKILOSIS: A RARE AND POTENTIALLY PAINFUL AUTOSOMAL DOMINANT DISORDER

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Objective: Osteopoikilosis is a rare AD genetic disorder, characterized by multiple hyperostotic lesions in different skeletal areas, seen on radiograph in the proximal humerus and femur. These findings may easily be confused with bone metastasis. It is usually asymptomatic, but rarely patients can have mild bone pain.

Case Presentation: A 32-year-old man presented to Endocrine clinic with bilateral humeri, hip, and leg pain which was present for years. On presentation, he was taking hydrocodone. He had previous fractures in his fingers, toes, and ribs. Two years ago he suffered a traumatic fracture of his right 2nd finger. Hearing difficulties and weak teeth were also reported. He had prior radiographs of his pelvis and shoulders. These revealed scattered hyperdensities throughout his pelvis and bilateral humeri. Evidence of osteopoikilosis was demonstrated. His maternal aunt, uncle, and brother were affected by osteopoikilosis. Prior labs revealed normal calcium, alkaline phosphatase, TSH, FT4, TT3, and normal renal & hepatic function. 25-hydroxyvitamin D was found to be insufficient at 21 ng/mL. His primary care physician started ergocalciferol 50,000 units weekly. We obtained a CMP, phosphorous, C-telopeptide, 1,25-dihydroxy vitamin D, intact PTH, and 25-Hydroxy Vitamin D, which were all normal. Technitium 99 Bone scintigraphy and DEXA were obtained to rule out metastatic bone disease. DEXA showed normal Z scores at the total hip and lumbar spine. Whole body bone scan was normal with no areas of increased uptake. He was offered genetic testing and was found to have a LEM domain containing 3 (LEMD3) knockdown mutation, consistent with osteopoikilosis. He was informed that given the AD inheritance pattern of this disease he should inform his sons and their physicians as they may be affected by the disease.

Conclusion: Osteopoikilosis is usually asymptomatic, but rarely can present with pain. It can be an isolated finding or associated with other pathologies, e.g. skin manifestations, rheumatic disorder, or skeletal disorders. The main differential is osteoblastic metastasis. Our patient had multiple, small bony islands scattered throughout the skeleton on radiographs. Subsequent Tc-99m methylene diphosphonate (MDP) bone scan showed multiple enostoses without abnormal focal MDP uptake. Clinical diagnosis was compatible with osteopoikilosis. Osteopoikilosis is usually an incidental finding on radiograph or CT, and a normal MDP can confirm the diagnosis. It is important for clinicians to recognize the specific imaging features to prevent further unnecessary interventions. A known cause of osteopoikilosis is a Loss-of-function mutation in the LEMD3 gene, and was elucidated in our patient’s case.
Abstract #554

DIAGNOSTIC DILEMA TO TREAT OR NOT? ELEVATED 25(OH) VITAMIN D SECONDARY TO WALDENSTROM MACROGLOBULINEMIA

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Objective: To investigate the cause of excess 25(OH) Vitamin D (Vit D) in a patient with actually low 25(OH) Vitamin D.

Methods: We present a patient with fictitious elevation of Vit D due to Waldenstrom’s macroglobulinemia.

Case Presentation: A 65 year-old African American man with Waldenstrom’s macroglobulinemia was referred for evaluation of an elevated Vit D level of >155.9 ng/dL [15-90 ng/mL]. Identical results were obtained on a separate specimen using the same assay. Additionally: parathyroid hormone 79.90 pg/ml [12-65], calcium 9.5 mg/dL [8.4-10.2], phosphorus 2.7 mg/dL [2.5-4.6], albumin 3.8 g/dL [3.8-5.1], total protein 9.2 g/dL [6.4-8.2]. DXA showed osteoporosis. He denied use of OTC or prescription supplements, had limited sun exposure, drank < 1 glass of milk daily and was not taking biotin. Given normal calcium and phosphorus levels, with elevated PTH, we suspected the Vit D elevation to be spurious. A third specimen was analyzed both in-house and by a commercial lab (Labcorp). The in-house assay (Abbott -ARCHITECT platform) again gave a level of >155.9 ng/dL; Labcorp (DiaSorin Liason platform) gave a Vit D level of 11.5 ng/dl.

Discussion: ARCHITECT is a quantitative competitive chemiluminescent microparticle immunoassay (CMIA). Serum is mixed with paramagnetic anti-Vit D coated microparticles. Acridinium-labeled Vit D is added and binds to unoccupied sites on the anti-Vit D coated microparticles. The resulting chemiluminescence is inversely related to the concentration of Vit D. DiaSorin is a direct competitive chemiluminescence immunoassay (CLIA). Here too during incubation Vit D dissociates from its binding protein, but now binding to antibodies (Abs) on a solid phase. A tracer (Vit D linked to an isoluminol) is added, followed by starter reagents which causes chemiluminescence, which is inversely proportional to the concentration of Vit D.

Why the assays gave such varied results is not quite apparent. One possibility is that the assays utilize different Abs; he may have acquired Abs to the reagents utilized in the ARCHITECT assay. Alternatively, the IgM macroglobulins could have bound to unoccupied sites on the paramagnetic anti-Vit D coated microparticles. This would have resulted in less uptake of the Acridinium labeled Vit D, a lower chemiluminescent signal, that would translated into a falsely elevated Vit D.

Conclusion: This case illustrates how Waldenstrom’s macroglobulinemia can lead to falsely elevated Vit D levels. Cases of Vit D elevation may need confirmation with a different assay especially when the clinical picture is not consistent with hypervitaminosis D.

Abstract #555

PARATHYROID CRISIS IN A YOUNG MALE

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Objective: Parathyroid storm is an uncommon endocrine emergency and can be a potentially life-threatening manifestation of primary hyperparathyroidism. It presents as severe hypercalcemia with markedly elevated Parathyroid hormone (PTH) level associated with rapidly deteriorating organ dysfunction.

Case Presentation: A 21-year-old man presented with acute onset of severe epigastric abdominal pain with nausea and vomiting. On further questioning, he reported a few weeks of anorexia, nausea, polyuria, polydipsia, fatigue, and generalized pain. Laboratory data revealed a calcium of 15.9 mg/dL (8-10.5), phosphorus 1.0 mg/dL (2.5-4.7), albumin 3.8 g/dL [3.8-5.1], total protein 9.2 g/dL [6.4-8.2]. DXA showed osteoporosis. He denied use of OTC or prescription supplements, had limited sun exposure, drank < 1 glass of milk daily and was not taking biotin. Given normal calcium and phosphorus levels, with elevated PTH, we suspected the Vit D elevation to be spurious. A third specimen was analyzed both in-house and by a commercial lab (Labcorp). The in-house assay (Abbott -ARCHITECT platform) again gave a level of >155.9 ng/dL; Labcorp (DiaSorin Liason platform) gave a Vit D level of 11.5 ng/dl.

Discussion: ARCHITECT is a quantitative competitive chemiluminescent microparticle immunoassay (CMIA). Serum is mixed with paramagnetic anti-Vit D coated microparticles. Acridinium-labeled Vit D is added and binds to unoccupied sites on the anti-Vit D coated microparticles. The resulting chemiluminescence is inversely related to the concentration of Vit D. DiaSorin is a direct competitive chemiluminescence immunoassay (CLIA). Here too during incubation Vit D dissociates from its binding protein, but now binding to antibodies (Abs) on a solid phase. A tracer (Vit D linked to an isoluminol) is added, followed by starter reagents which causes chemiluminescence, which is inversely proportional to the concentration of Vit D.

Why the assays gave such varied results is not quite apparent. One possibility is that the assays utilize different Abs; he may have acquired Abs to the reagents utilized in the ARCHITECT assay. Alternatively, the IgM macroglobulins could have bound to unoccupied sites on the paramagnetic anti-Vit D coated microparticles. This would have resulted in less uptake of the Acridinium labeled Vit D, a lower chemiluminescent signal, that would translated into a falsely elevated Vit D.

Conclusion: This case illustrates how Waldenstrom’s macroglobulinemia can lead to falsely elevated Vit D levels. Cases of Vit D elevation may need confirmation with a different assay especially when the clinical picture is not consistent with hypervitaminosis D.
Conclusion: We describe an unusual case of primary hyperparathyroidism manifesting as Hypercalcemic Parathyroid crisis with gastrointestinal manifestations. It is important to recognize Parathyroid crisis in the setting of hypercalcemia to avoid a fatal outcome. It is not clear what precipitates a crisis in some individuals. It can be associated with varied manifestations including rapid deterioration of neurologic, cardiac, gastrointestinal, or renal function due to markedly elevated serum calcium and PTH levels. Mortality is 100% if expeditious parathyroidectomy is not performed. Failure of response to medical treatment is an indication for immediate surgical intervention. Prognosis may be poor with 20% mortality even after parathyroidectomy is performed.

Abstract #556

CARBOPLATIN CHEMOTHERAPY AND PTH RESISTANCE: PERILOUS DUO

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Objective: Carboplatin is an alkylating agent often used in chemotherapy. This agent can cause hypomagnesemia which in turn causes often severe hypocalcemia. This phenomenon has been described but is often under treated and under reported. We report a case involving life threatening hypocalcemia after a course of carboplatin.

Case Presentation: A 60 year old African American female with Stage IV adenocarcinoma of the lung presented with severe body ache and shortness of breath after a course of chemotherapy including carboplatin. Labs revealed pancytopenia, corrected calcium 4.9 mg/dL, phosphorous 3.4 mg/dL, magnesium 0.8 mg/dL, BUN 45 mg/dL, creatinine 2.3 mg/dL, 25-hydroxy Vitamin D 9.2 mg/dL, PTH intact 961.1 pg/ml. Corrected QT interval was 495 ms.

Over the course of first four days she received 16 grams IV calcium gluconate, 12 grams IV magnesium sulfate, as well as oral calcitriol 0.5 mcg daily, oral calcium carbonate and magnesium oxide. Low potassium was also replaced. Even though calcium and magnesium were corrected, on day 6 repeat PTH was 986.4. QT interval corrected.

Discussion: Carboplatin can cause renal toxicity with incidence as high as 20%. Renal tubular damage can cause urinary magnesium wasting and hypomagnesemia. Hypomagnesemia can cause hypocalcemia by inhibiting PTH release and inhibiting the action of PTH in peripheral tissues, kidney, and bone. This PTH resistance leads to innappropriately normal or high PTH as was seen in this case. Reduced action of PTH in the kidney decreases hydroxylation of 25-hydroxy Vitamin D further decreasing the calcium level. Plasma magnesium is the primary regulator of magnesium absorption in renal tubules, so abrupt elevation of plasma magnesium can shut down this renal absorption. Correction of hypomagnesemia must therefore be sustained. Hypomagnesemia from carboplatin may persist for months or even years.

Conclusion: Awareness of carboplatin induced hypomagnesemia and hypocalcemia with PTH resistance or PTH deficiency is very important to clinicians. Magnesium is involved in more than 300 enzyme mediated processes. Early detection of hypomagnesemia and hypocalcemia induced by carboplatin chemotherapy and early replacement can prevent morbidity.

Abstract #557

PROPOSAL OF A NEW DIAGNOSTIC NOMENCLATURE FOR A DISTINCT CLINICAL ENTITY OF “HUNGRY TUMOR SYNDROME”

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NIH

Objective: To propose a new diagnostic nomenclature for distinct clinical entity that has clinical and biochemical features of hungry bone syndrome but occurs in the setting of widely metastatic osteoblastic carcinoma. By recognizing this new “Hungry Tumor Syndrome” as new diagnosis entity, it will raise more awareness of this clinical scenario that possibly requires careful management.

Methods: A 72 years-old lady with history of Lynch Syndrome manifested with uterine carcinoma s/p total abdominal hysterectomy, low grade transitional cell carcinoma in 2010 treated with intravesicular mitomycin. Years later, she presented with shortness of breath and CT scan of lung revealed 4.4 x 3.5 cm mass in anterior left upper lobe. Biopsy was performed with pathology showing metastatic carcinoma, consistent with urothelial primary. Patient was treated with different regimens of chemotherapy, and immunotherapy Atezolizumab, all failed to stop the progression of her disease. She was later started on Doxorubicin but developed toxicity with pancytopenia, fatigue, hypocalcemia, nausea, diarrhea, and overall failure to thrive. Patient was found to have profound hypocalcemia, hypophosphatemia, and hypomagnesemia. These electrolytes derangements were noted to be persistent and refractory to routine replacement. Malabsorption syndrome was ruled out and the patient eventually required large amount of Calcitriol, 25 Vitamin D and phosphate and magnesium to correct the electrolytes. CT scan revealed extensive osteoblastic
metastatic disease in the skeleton

**Case Presentation:** The timeline of biochemical findings and the therapy is depicted in figure 1

**Discussion:** This patient has persistent and refractory hypocalcemia, along with hypophosphatemia, and hypomagnesemia, a triad features of hunger bone syndrome, but this patient does not have the classic presentation of hunger bone syndrome, but extensive osteoblastic metastatic disease to the skeleton that is not responding to oncologic therapy. The continuous progression of her extensive osteoblastic metastatic cancer, among other trigger factors lead to decompensation of the overt development of hypocalcemia with secondary hyperparathyroidism

**Conclusion:** Hungry Tumor Syndrome is a distinct clinical entity that has biochemical features of hungry bone syndrome but occurs in the clinical scenario of extensive osteoblastic metastatic cancer and requires different approach for therapy and management

**Abstract #558**

**THE IMPACT OF LOWER EXTREMITY AMPUTATION ON BONE MINERAL DENSITY**

_Amani Alameer, MD, Eric Nylen, MD, Shruti Gandhi, MD_

_VAMC_

**Objective:** Lower limb amputation can result various complications including bone loss. It has been observed that bone turnover rates become discordant between the amputated and intact limb despite prosthetic use. The current guidelines for screening and prospective DXA programs (Dual-energy X-ray Absorptiometry) do not include amputation as a factor for accelerated bone loss and can lead to a missed diagnosis and delay in treatment. To further understand the degree of bone loss, we performed a retrospective chart review of veteran subjects with a high prevalence of limb amputation.

**Methods:** Veterans with lower extremity amputations based on ICD-9/10 coding were cross-referenced with DXA reports at the Washington DC VAMC. Only 6% (33/571) amputees had received a screening DXA post-amputation. We excluded those patients with bilateral lower extremity amputations, history of CVA with paralysis or an incomplete medical record for analysis. 26 male veterans with unilateral amputations were identified and the bone mineral density (BMD) at the femoral necks (FN) and total hips (TH) of the amputated vs intact limb and duration post-amputation were analyzed.

**Results:** Accelerated bone loss ipsilateral to the site of amputation was found at both BMD of the femoral neck (p<0.001) and total hip (p<0.001). More specifically, osteoporosis was prevalent in 42% of patients on the ipsilateral femoral neck vs 7.7% on the intact side. We also found that the difference in BMD ratio of intact limb vs amputation at FN and TH was significantly lower in those with above knee amputation (AKA, n=15) vs below-knee (BKA, n=11) on the site of amputation (p=0.004 and p=0.001 respectively). Lastly, the duration post amputation (range 1 month to 49 years) positively correlated with ipsilateral BMD loss at the FN (r²=0.83) and TH (r²=0.96).

**Discussion:** We identified several issues for patients with lower extremity amputation. First, there is lack of screening DXA in this subset of patients. Additionally, the data demonstrates that the site ipsilateral to the amputation has significantly worse BMD than the intact limb as well as those with an AKA tend to have a higher degree of bone loss compared to those with a BKA. Lastly, bone loss appears to worsen with time post-amputation. Interestingly 4 patients began to have a decline in BMD within the first year.

**Conclusion:** This study found that there is accelerated bone loss ipsilateral to the amputation that appears to be aggravated by time post amputation. Increased awareness in health care providers regarding the risk to patients with amputations is necessary so that patients can be screened earlier with a goal for fracture prevention.

**Abstract #559**

**HEPATOCELLULAR CARCINOMA PRESENTING AS HYPERCALCEMIA**

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_Henry Ford Hospital_

**Objective:** Humoral hypercalcemia is commonly seen associated with squamous cell cancers and breast cancers, but is also reported in other cancers. This is usually mediated through parathyroid hormone-related peptide (PTH-rP). PTH-rP interacts with the PTH/PTH-rP receptor that activates renal calcium reabsorption and promotes resorption of calcium from the bone. Hepatocellular carcinoma (HCC) may present with paraneoplastic syndromes and hypercalcemia was reported in 4-7% of patients. HCC presenting with hypercalcemia without bone metastasis is uncommon. We present one such case along with the discussion of mechanism of hypercalcemia.

**Case Presentation:** 67 year old woman with a history of intravenous drug abuse and alcohol abuse presented with confusion, epigastric pain and generalized weakness of 2 week duration. Her vital signs were normal. She appeared drowsy and was oriented to person only. A magnetic resonance imaging of the brain ruled out a cerebrovascular
event. Her labs showed ionized calcium 1.50 (1.0 – 1.35 mmol/L), intact parathyroid hormone 14 (15 – 65 pg/mL), PTH-rP 39 (14 – 27 pg/mL), 25 hydroxy vitamin D 10 (> 20 ng/mL), 1, 25 dihydroxy vitamin D 24 (20 – 74 pg/mL), alkaline phosphatase 153 (0 – 140 IU/L), creatinine 0.53 (< 1.16 mg/dL) and GFR 110 (> 60 ml/min/1.73m2). Liver function tests were abnormal and hepatitis C antibody was positive. Computed tomography of the abdomen revealed nodular cirrhotic liver with a 10 x 10 cm right hepatic mass compatible with HCC. She had elevated alpha fetoprotein and cancer antigen 19-9 levels. Due to hepatic cirrhosis, initially she was treated with gentle intravenous hydration with no improvement in calcium levels. Ionized calcium worsened to 1.90 mmol/L. She received intravenous zolendronic acid without significant improvement in her calcium levels and mental status. She is planned for further cancer directed therapy.

**Conclusion:** 80% of hypercalcemia in cancer patients is estimated to be PTH-rP mediated. However, additional mechanisms that cause bone resorption or decreased renal excretion may be responsible. Bisphosphonates inhibit osteoclast bone resorption, and are used for paraneoplastic hypercalcemia associated with malignancy because of their favorable efficacy and lower toxicity. Refractory hypercalcemia has been reported in patients with HCC as noted in our patient. The PTH-rP level in our case was not very high in contrast with the expected direct association between severity of hypercalcemia and degree of PTH-rP elevation suggesting other contributing factors. We believe immobilization and volume contraction were the other driving mechanisms for her refractory hypercalcemia.

**Abstract #560**

**SCREENING FOR OSTEOPOROSIS AT FQHC - GAP IN KNOWLEDGE AND APPLICATION**

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**Objective:** The purpose of this study was to identify the disparity between knowledge of osteoporosis screening and its application in post-menopausal female patients ≥ 65 years by medical residents in a federally qualified health center (FQHC).

**Methods:** We included all female patients ≥ 65 years of age who visited our FQHC. Retrospective chart review of all these visits between 01/01/2015 to 05/30/2017 was done. Medical records of the patients were reviewed to see if they were offered screening DXA scan after turning 65. We also checked how many patients actually had the test done among the ones who were offered with the screening DXA scan. We then assessed the number of patients who were appropriately managed. We also checked the appropriateness of osteoporosis screening and its management.

**Results:** Total female patients age ≥ 65 at the time of study were 321. Number of patients who did not visit FQHC after turning 65 was 51 and they were eliminated from the study. Of the 270 patients who were studied, 82 patients (29.39%) were offered DXA scan whereas majority of patients, 188 patients (69.29%) were not offered DXA scan. Patients who were offered DXA scan, 57 patients (69.29%) underwent DXA scan whereas 24 patients (29.39%) did not go for the DXA scan. One patient out of 82 patients who were offered DXA scan actually refused the test. Among the 57 patients who completed the test, 21 patients (36.86%) were diagnosed with osteoporosis. Of the patients who were diagnosed with Osteoporosis that is out of 21 patients, 20 patients (95.23%) were treated with Bisphosphonates and one patient refused the treatment. Also, among 57 patients who had the DXA scan, 36 patients (63.15%) had BMD more than -2.5 (Osteopenia or normal BMD) and 7 out of these 36 patients (19.44%) were inappropriately overtreated for osteoporosis. There was also lack of residents’ documentation of ordering DXA Scan in 19 patients who underwent the test.

**Conclusion:** As per current USPSTF guideline, every female ≥ 65yrs should be routinely screened for Osteoporosis with DXA scan and if osteoporosis is diagnosed, patients should be appropriately treated and monitored for it. However, many patients still remain unscreened, undiagnosed and untreated in our FQHC. Important reasons are due to lack of knowledge about osteoporosis screening and its application in our health care providers which need to be addressed.

**Abstract #561**

**OSTEOPENIA AND β-THALASSEMIA - A CASE ILLUSTRATING MANAGEMENT OF BONE DISEASE IN A COMMON HEMOGLOBINOPATHY**

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**Objective:** β-Thalassemia (BT) is increasingly seen in the Western hemisphere by way of immigration and refugees. Despite mainstay therapy with intensive transfusion and iron chelation, prevalence of osteopenia/osteoporosis is near 50% in treated patients. Pathogenesis of bone disease is thought to be related to marrow hyperplasia from inadequate erythropoiesis causes widening of marrow
Case Presentation: A 23-year-old refugee woman from Iraq, diagnosed with BT major was seen for osteopenia. She received weekly blood transfusions and iron chelation therapy prior to moving to the US since age 5. She reported normal menstrual cycles since menarche at age 16. She had no history of rheumatoid arthritis, steroid, tobacco or alcohol use, and no family history of osteoporosis. Dietary intake of calcium and vitamin D was poor. Review of systems positive for marked bone pain and extreme fatigue. Current medications included ascorbic acid, aspirin, and deferiprone. She had no allergies. Medical history included secondary hemochromatosis. Family history was negative for hemoglobinopathies, or other endocrinopathies. She had splenectomy at age 5. Physical exam was notable for normal height of 160 cm, weight 57.6 kg, normal vitals. Prominent frontal bossing was apparent, without evidence of other skeletal deformities.

Discussion: Treatment was started with cholecalciferol 5000 IU daily, calcium carbonate-vitamin D3 – 500 g-200 IU twice daily, folic acid 1 mg daily and spine films to evaluate silent fractures. Bisphosphonate therapy was discussed as part of future therapy if bone mineral density (BMD) scan did not show improvement after optimal calcium and vitamin D therapy.

Conclusion: Osteopenia and osteoporosis causes significant morbidity in patients with BT. Early treatment with adequate calcium, zinc and vitamin D intake, bone mineral density scans every 2 years, and assessment of gonadal axis periodically helps prevent progression of bone disease in these. BMD scan using trabecular bone score better predicts osteopathy. Bisphosphonates can be considered for osteoporosis, but long-term efficacy and outcome trials are unavailable to guide therapy.

Abstract #562

PRIMARY HYPERPARATHYROIDISM PRESENTING WITH SEVERE HYPERCALCEMIA REQUIRING URGENT PARATHYROIDECTOMY IN EARLY PREGNANCY

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Objective: Primary hyperparathyroidism (PHPT) is a common endocrine condition often underdiagnosed during pregnancy. Physiological changes of pregnancy can mask biochemical abnormalities and nonspecific symptoms from PHPT are frequently confounded with symptoms of normal pregnancy. PHPT is known to carry high rates of maternal and fetal complications, approximately 67% and 80%, respectively. Common maternal complications include nephrolithiasis and hyperemesis, and in severe cases, pancreatitis and hypercalcemic crisis. Diagnostic and treatment options are restricted during pregnancy increasing management complexity.

Case Presentation: We report a 22-year-old woman G3P1102 at 8 weeks of gestation with medical history of hypertension and nephrolithiasis admitted to the hospital for worsening nausea, vomiting and abdominal pain for 3 days. She also reported constipation and bone pain intermittently. The physical exam showed normal vitals and mental status. Diagnostic evaluation showed calcium level of 15.5 mg/dL; normal albumin; phosphorus of 2.2 mg/dL; intact PTH of 376 pg/mL; 25-hydroxyvitamin D of 11 ng/mL; and 1,25-Dihydroxyvitamin D of 132 pg/mL. Neck ultrasound showed a 2.4 cm oval hypoechoic mass posterior to lower pole of the right thyroid compatible with parathyroid adenoma. Renal ultrasound demonstrated bilateral kidney stones. She was initially treated with aggressive IV hydration resulting in a gradual decrease of calcium level to 13.6 mg/dl with improvement of nausea and vomiting. Surgical consultation was obtained for consideration of parathyroidectomy. She underwent successful surgical parathyroidectomy of right inferior parathyroid adenoma with intraoperative decrease in PTH of > 50%. Pathology confirmed 3.1 cm hypercellular adenoma weighing 2.13 grams. She had no postoperative complications and hypercalcemia resolved after surgery.

Conclusion: PHPT during pregnancy poses many diagnostic and therapeutic challenges. An increased rate of maternal and fetal complications, including pregnancy loss, have been observed in pregnant patients with PHPT and elevated calcium levels. Delays in intervention may significantly jeopardize maternal and fetal well-being. Conservative treatment is recommended for mild hypercalcemia, however surgical intervention may be required in cases of severe symptomatic hypercalcemia, even at early gestational age. A high index of suspicion, effective multidisciplinary approach and prompt treatment are essential to reduce fetal and maternal morbidity and mortality.
MORTALITY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) AND WEIGHT ARE REDUCED IN 400 HYPOGONADAL MEN ON LONG-TERM TESTOSTERONE THERAPY (TTH) COMPARED TO 376 UNTREATED HYPOGONADAL CONTROLS: REAL-LIFE DATA FROM A 10-YEAR REGISTRY

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Objective: To study long-term effectiveness and safety of TTh with 3-monthly injections of testosterone undecanoate (TU) in comparison to a control group (CTRL).

Methods: 776 hypogonadal men with total testosterone (T) ≤350 ng/dL participate in an ongoing registry study in a urological office. Measures are performed 1-4 times per year. Mean changes over time between groups were compared by mixed effects model for repeated measures with random effect for intercept and fixed effects for time, group and their interaction, and adjusted for age, weight, waist circumference, fasting glucose, blood pressure and lipids to account for baseline differences between groups. Mean (median) follow-up was 7.3 (8) years in both groups.

Results: Mean age: 58±7 years (T-group), 64±5 (CTRL). Most patients were obese. Weight decreased from 103.9±16.7 to 86.1±8.4 kg in the T-group (p<0.0001) and increased slightly in CTRL, between-group difference: 20.4 kg (p<0.0001). Waist circumference decreased from 106.2±8.7 to 96.4±6.4 cm in the T-group (p<0.0001) and increased slightly in CTRL, between-group difference: -12.4 cm (p<0.0001). BMI decreased from 33.1±5.4 to 27.8±2.8 kg/m2 in the T-group (p<0.0001) and increased slightly in CTRL, between-group difference: -6.3 kg/m2 (p<0.0001). Per cent weight change at 10 years was -18.7±7.3% in the T-group (p<0.0001) vs +2.7±4% in CTRL (p<0.01), between-group difference: -19.5% (p<0.0001). The waist:height ratio declined from 0.6±0.05 to 0.55±0.04 in the T-group (p<0.0001) and increased slightly in CTRL, between-group difference: -0.07 (p<0.0001).

Major adverse cardiovascular events (MACE): in CTRL, there were 39 deaths (10.4%), 45 myocardial infarctions (12.0%), and 42 strokes (11.2%). There were 6 deaths (1.5%) in the T-group.

In the T-group, 9 men (2.3%) were diagnosed with prostate cancer, in CTRL, 26 men (6.9%).

Medication adherence in the T-group was 100 per cent as all injections were performed in the office and documented.

Discussion: This was neither a randomized study nor was it designed to investigate mortality. This may have in part been compensated by the long-term follow-up. In a previous analysis, propensity matching was used to further validate our observations. This approach had confirmed that, after matching for age, waist circumference and BMI, the proportions of deaths and MACE remained unchanged in comparison to the total group presented here.

Conclusion: Weight and waist circumference decreased sustainably in the T-group and increased slightly in CTRL. These improvements, together with improvements in metabolic parameters, may have contributed to reducing MACE in hypogonadal men receiving adequate TTh.

EFFICACY OF SELF-HYPNOSIS IN TYPE 2 DIABETICS WITH BMI ≥ 25: A RANDOMIZED CLINICAL TRIAL

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Objective: To compare treatment of obese diabetic patients with self-hypnosis, certified diabetes educator, and no special treatment (control) as respects weight loss and changes in A1c levels after one year.

Methods: Protocol was approved by an external IRB and registered with ClinicalTrials.gov. Considered for study in this outpatient Endocrinologist’s practice were diabetic patients with a body mass index above 25 kg/m2 and a desire to lose weight. Out of 189 consecutive subjects, 13 were screen failures and 74 were randomized. 115 subjects declined participation. Follow up data was available for 102 of the latter subjects (control group). The 74 patients who agreed to the study were randomized to receive either certified diabetic educator treatment (38 patients) or self-hypnosis instruction (36 patients). Both groups received two 1.5 hour training sessions at the beginning of the study, and bimonthly emails for encouragement and motivation. Prespecified primary outcome measures were weight and A1c levels. Patients were also compared as respects initial weight, initial A1c levels, birth year, height, and gender.

Results: After 1 year certified dietician subjects lost, on average, 3.7 pounds (95% CI 0.1, 7.2 pounds) more than did controls. After 1 year self-hypnosis subjects lost, on average, 5.2 pounds (95% CI 1.6, 8.8 pounds) more than did controls. There was no reason to think certified dietician patients and self-hypnosis subjects differed as respects weight loss after one year (P = 0.68). Differences among treatment groups as respects declines in A1c levels after one year, initial weight, initial A1c levels, birth year, height, and gender might have been due to chance (P > 0.40 for each analysis).

Discussion: After one year, self-hypnosis training resulted in similar weight loss compared to certified diabetes educator (and both were superior to usual care with no special weight loss treatment) and was effective in reducing A1c levels.
loss weight occurred within the first 3-6 months, and plateaued thereafter. A similar trend (not statistically significant) were also seen with reduction in A1Cs (data not shown). Greater adherence to either treatment resulted in a trend of greater weight loss (data not shown).

**Conclusion:** Self-hypnosis should be considered a viable option for overweight, type 2 diabetic patients who seek to lose weight. The group session model (only two sessions per group) has potential to be very cost effective. Given the plateauing of effect at six months, future application of this model might want to include additional group sessions for reinforcement at 6 and 9 months, and thereafter.

**Abstract #603**

**INCREASED LEVEL OF RETINOL BINDING PROTEIN 4 (RBP4) AND BODY WEIGHT IN RATTUS NOVERGICUS (WISTAR) WITH SUBCHRONIC INHALATION EXPOSURE OF TRANSFLUTHRIN**

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**Objective:** Recent data suggest an increasing number of population with obesity in Indonesia. Genetic, and lifestyle play a role in obesity. Not all obesity can be explained only by those factors. In the last few years, many studies shows influenced of endocrine disrupting chemicals (EDC) causes weight gain despite calorie restriction and increased physical activity. Transfluthrin, is a pyrethroid-based insecticide which is used frequently in Indonesian house hold. In recent years, research on obesity is increasingly linking between weight gain and increasing levels of RBP4. In this study, we wanted to determine the level of Retinol Binding Protein and change of body weight in rattus novergicus (wistar) with subchronical inhalation exposure of transfluthrin.

**Methods:** True experimental in vivo, post-test only, control group in 35 male rats (Rattus norvegicus strain Wistar), divided into five groups, namely negative control (without exposure), positive control (expose with n-hexana solution as solvent of transfluthrin), group 1 (inhalaion with transfluthrin 0.1mg/dl), group 2 (inhalaion with transfluthrin 0.2mg/dl), and group 3 (inhalaion with transfluthrin 0.4mg/dl). On the 60th days, the rats was sacrificed and serum level of Retinol Binding Protein (RBP) was measured with ELISA methods.

**Results:** Means and SD of Retinol Binding Protein level in negative control was 0.683 ± 0.05 mg/mL, positive control was 0.799 ± 0.07 mg/mL, group 1 was 0.722 ± 0.05 mg/mL, group 2 was 0.751 ± 0.06 mg/mL, and group 3 was 1.574 ± 0.25 mg/mL. One way ANOVA test shows there were significance differences in group 3 both with negative control (p=0.000), and positive control (p=0.000). Based on Pearson correlation test, there was a significant positive correlation between transfluthrin level and RBP-4 (r = 0.801 and p = 0.000). This indicates that the higher the serum transfluthrin level, the higher the RBP-4 produced in the serum. This study also showed a correlation between transfluthrin levels and weight changes (r = 0.609 p=0.0039)

**Discussion:** There is a strong correlation between increased of transfluthrin with weight gain. It is possibly due to the increasing number and size of adipocyte cells. Some studies mentions the activation of the nuclear receptor (possibly PPAR-γ) as the cause. We believe an increase in the number and size of these fat cells causes an increase in RBP4 levels

**Conclusion:** Level of RBP 4 and body weight were increased in rats with subchronical inhalation exposure of transfluthrin. Does this increase causes the onset of insulin resistance still require further investigation.

**Abstract #604**

**OBESITY IN A PARAPLEGIC MULTIPLE SCLEROSIS PATIENT TREATED WITH DULAGLUTIDE**

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**Objective:** Multiple Sclerosis (MS) is a common inflammatory demyelinating disease of the CNS and the most common cause of nontraumatic disability and paraplegia in young and middle aged adults. Patients with chronic spinal cord injury and paraplegia suffer from increased weight gain, with studies showing the majority become overweight or obese. GLP -1 analogues have been shown to reduce gastric emptying and appetite contributing to weight loss. We demonstrate a case of an obese and paraplegic MS patient who lost significant weight with GLP-1 agonist treatment

**Case Presentation:** 69 year old female, with history of MS and hypothyroidism, presented at a weight of 244 pounds and BMI of 39.4, with a desire to lose weight. She was paraplegic secondary to MS, limiting her ability to exercise. She had gained about 20 pounds in the prior 6 months. Her remaining vitals were within normal limits. She was taking levothyroxine 175 ug 6 days a week, with labs showing TSH – 1.24, T3 total - 0.92, free T4 1.83, vitamin D – 27.7, LDL – 110, total cholesterol of 187, creatinine of 0.7, and hemoglobin A1c of 5.0. She was started on dulaglutide 0.6 mg SC daily, and was counseled on reducing caloric intake. There was no significant
change in activity level. She lost about 50 pounds over the subsequent nine months. Locaserin 10 mg oral BID was then also prescribed for about 4 months, helping bring her total weight loss to 60 pounds in 12 months. She has been followed subsequently for 3 years, over which she regained 20 pounds. Her weight stabilized at just under 200 pounds for the past 12 months, a decrease of 40 pounds in weight and 7 points in BMI as compared to her weight/BMI before starting dulaglutide.

Discussion: GLP-1 therapy has been shown to delay gastric emptying and gut motility, as well as inhibit food intake by acting on both central and peripheral receptors. In studies, weight loss observed with GLP-1 therapy was associated with reductions in total body fat and was sustained for up to a period of three years. In our paraplegic MS patient, GLP 1 agonist treatment resulted in significant weight loss. Positive energy balance due to the limited mobility from paraplegia was the likely cause of weight gain in our patient. However, with the use of GLP-1 therapy, she was able to significantly decrease caloric intake, thereby achieving a negative energy balance resulting in significant weight loss, most of which she was able to maintain for the follow-up of greater than 4 years.

Conclusion: GLP-1 analogs can be used to assist in weight loss of patients with paraplegia from MS.

Abstract #606

THE EFFECT OF BARIATRIC SURGERY ON NEPRILYSIN AND VASOACTIVE FACTORS

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Objective: Since morbid obesity is associated with congestive cardiac failure and hypertension, and gastric bypass surgery is followed by a reduction in blood pressure and a reduction in the risk of congestive cardiac failure, we hypothesized that weight loss following bariatric surgery in morbidly obese patients is associated with a decrease in plasma concentrations of neprilysin, mediators of renin angiotensin system, catecholamines and endothelin-1 with an increase in the concentrations of vasodilators.

Methods: Fasting blood samples were obtained from fourteen patients with morbid obesity and diabetes prior to and 6 months after Roux-en-Y gastric bypass (RYGB) surgery. Plasma and serum were separated for the measurement of neprilysin; vasoconstrictors, angiotensinogen, renin, angiotensin II, endothelin-1, epinephrine and norepinephrine; and vasodilators, ANP, BNP, cGMP, and cAMP. The mRNA expression of angiotensin converting enzyme (ACE) and adenylate and guanylate cyclases in circulating mononuclear cells (MNC) was also measured.

Results: Six months after RYGB, BMI fell from 52.1 ± 4.8 to 40.4 ± 4.0 kg/m2 and there were significant improvements in the HbA1c. Plasma concentrations of neprilysin, angiotensinogen, angiotensin II, renin and endothelin-1 fell significantly by 27 ± 16%, 22 ± 10%, 22 ± 8%, 35 ± 13% and 17 ± 6% (p<0.05 for all) respectively, while ANP concentrations increased significantly by 24 ± 13% at 6 month following surgery. There was no significant change in aldosterone, BNP, cAMP or cGMP concentrations and ACE mRNA expression.

Conclusion: RYGB suppressed neprilysin concentrations, which may contribute the observed increase in plasma ANP concentrations. In addition, RYGB resulted in a reduction in plasma angiotensinogen, angiotensin II, renin and endothelin-1 concentrations. These changes may contribute to the reduction in the risk of congestive cardiac failure and blood pressure after RYGB.
Abstract #607

IS BODY MASS INDEX THE BEST INDICATOR FOR DIAGNOSING OBESITY IN TYPE 2 DIABETES PATIENTS?

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Objective: Body Mass Index (BMI) has long been the conventional criterion for assessing obesity. Existence of obesity sub-groups like metabolically healthy but obese, or metabolically unhealthy but normal weight has prompted the search of new indicators which correlates better with body fat percentage. Central obesity is more represented by waist circumference than BMI and waist-to-height ratio has been suggested as a better indicator on measuring body fat percent in healthy adults. Indicators calculated form anthropometric data which best correlate with the measurement of body fat percent in Type 2 Diabetes patients (other than BMI) has not been studied in detail. Objective of this study was to compare some of the new indicators proposed for diagnosing obesity with BMI and waist circumference in a group of Type 2 Diabetes patients.

Methods: BMI, waist circumference, waist-to-height ratio and a new formula derived from Body Adiposity Index (Figure 1) were measured and calculated for 1448 consecutive adult patients with Type 2 Diabetes, newly registered in a large tertiary care hospital Diabetic clinic. Total body fat percent was measured with the bioelectrical impedance analysis technique using the OMRON HDBS-362 body fat analyzer in all patients.

Results: Study population comprised of 64% women, 36% men, mean age 51.3 years (SD=10.8). The mean duration of diabetes was 6.7 years (SD= 9.7). According to BMI criteria 20.2% were overweight and 45.1% were obese. When body fat percentage cut off for obesity was taken as 25% in men 35% in women, 50.5% and 59.9% were obese respectively (Figure 2). BMI showed a strong positive correlation with total body fat percent \( r = 0.51 \), \( p <0.001 \) while waist circumference showed a moderate positive relationship \( r =0.31, \ p<0.001 \). Waist-to-height ratio and the new formula (Figure 1) also showed a strong positive correlation with total body fat respectively \( r = 0.55, \ p <0.001, \ r = 0.61, p <0.001 \).

Discussion: BMI remains as a good indicator for total body fat in Type 2 diabetes patients and showed a strong positive correlation with total body fat percent. Waist-to-height ratio which was shown to be a better predictor than BMI previously in healthy adults (Swainson MG, 2017), showed similar results in Type 2 Diabetes patients. The waist circumference alone showed only a moderate correlation with body fat percent but a new formula based on waist circumference and height (derived from the Body Adiposity Index formula) showed the highest correlation with total fat percent and would warrant further study.

Conclusion: New calculated indicators of obesity may give a better idea about obesity in Type 2 Diabetes patients and it is worthwhile exploring further.

Abstract #608

STUDY OF EFFECTIVENESS OF MEDICATIONS IN OBESITY MANAGEMENT IN OUR OBESITY CLINIC

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Objective: To compare the proportion of patients achieving clinically meaningful (at least 5%) weight loss with use of drugs for weight management.

Methods: Design: Retrospective, observational cohort study

Patients: A total of 9 patients aged 18 years or older (mean age 43.6 years, 77.78% female) with a body mass index of 27 kg/m2 or greater (mean BMI 42.56 kg/m2) who are being managed at our obesity/healthy weight management program in the internal medicine and endocrinology outpatient departments were selected. One patient had DM Type 2, four patients had A1C at baseline between 5.7% and 6.4% and the rest had normal A1C at baseline.

Results: Measurements and Results

We measured the percentage change in weight from baseline to at least 12 weeks or later (i.e, closest weight to 6 months) with use of Bupropion, Topiramate, Liraglutide, Phentermine, Naltrexone either alone or in combination. Results

The percentage of patients achieving clinically meaningful (at least 5%) weight loss after at least 12 weeks in the Bupropion, Topiramate, Liraglutide, Phentermine, Naltrexone Combined were 33.33% [3 out of 9]

None of 3 patients on bupropion alone achieved clinically meaningful weight loss goal from baseline to at least 12 weeks or later.

In the Topiramate group , all patients (2) had clinically meaningful weight loss . One of them achieved 9.5% at 12 weeks and further weight loss of 11.8% at 6 months.

One patient on combination therapy (Bupropion, Victoza and Topiramate) and had weight loss 7% after one year.

Three patients on combination therapy (Bupropion plus Liraglutide, Bupropion plus naltrexone/phentermine, Bupropion plus topiramate) failed to achieve clinically meaningful weight loss.
meaningful weight loss at 12 weeks.

**Conclusion:** Obesity is currently a worldwide public health problem and it is increasing at alarming rate. The use of medications for obesity has been suboptimal despite the availability. Topiramate achieved meaningful weight loss in our study (2 out of 3 patients). Medications like Bupropion and Topiramate which are FDA approved for other indications like depression and migraine prophylaxis respectively can be tried alone or in combination with other drugs for obesity management.

Abstract #609

**EFFECT OF RESTRICTED CALORIC INTAKE AND BARIATRIC SURGERY ON PCSK9 CONCENTRATIONS IN PLASMA**

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**Objective:** PCSK9 is a major modulator of LDLc through internalization and endosomal degradation of LDL receptor. It has been shown that PCSK9 plasma levels predict CVD risk. The fact that it gets into plasma and maintains high concentrations raises the issue of whether it has specific functions as a plasma protein. Bariatric surgery is known to reduce both LDLc and CVD. However, its exact effect of PCSK9 has not been fully investigated. One recent study has demonstrated that biliopancreatic diversion with duodenal switch surgery with weight loss results in approximately 10% reduction in plasma concentration of PCSK9 over a period of 12 months.

**Methods:** We have now investigated the effect of strict caloric restriction and Roux-en-Y bariatric surgery (RYGB) in 15 morbidly obese patients. Subjects were instructed to follow a regimen of four liquid shakes, each containing up to 16g carbohydrate, 0g fat, and 33g of protein (total daily intake was 550-785 calories) during diet intervention and the usual dietary regime after surgery. Blood samples were obtained at 2 weeks before, at the time of surgery and 6 months after RYGB.

**Results:** There was a significant weight loss of 7.8±2.4 Kg during the 2 weeks prior to surgery and of additional 26.6±5.3 Kg 6 months after surgery. At completion of the high protein diet intervention subjects had a significant reductions in glucose, insulin and HOMA-IR (7.1±1.1 to 4.5±1.0) which continued following surgery (HOMA-IR (4.5±1.0 to 2.1±0.3). LDL(c) fell significantly by 11±7% (from 120±6 to 109±7mg/dl) following the dietary intervention and by 15±8% (from 109±7 to 95±6mg/dl) following surgery. There was a reduction of 38±11% (from 227±25 to 139±15 ng/ml) in plasma PCSK9 concentration in the two weeks of caloric restriction. Thereafter, PCSK9 levels increased to 166±22ng/ml over the next 6 months.

**Discussion:** Our data show that there is an impressive and concurrent fall in PCSK9, LDL(c) concentrations and insulin resistance following caloric restriction with a high protein diet. The marked weight loss over 6 months has only a marginal effect on PCSK9 concentrations while metabolic improvements persisted.

**Conclusion:** This reduction in PCSK9 may contribute to the known benefit in cardiovascular outcomes following bariatric surgery.

Abstract #610

**BMD/BMI RATIO AND TRABECULAR BONE SCORE: NEW POTENTIAL TOOLS TO ASSESS THE RISK OF FRACTURE IN OBESE PATIENTS**

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**Objective:** Obesity and osteoporosis represent two major public health problems in Western countries. The traditional belief that obesity plays a protective role against osteoporosis has recently been questioned. Indeed, some epidemiological and clinical studies have shown that excess fat mass, especially visceral adipose tissue, can be a risk factor for low bone mineral density, and for fragility fractures. Bone Mineral Density (BMD) is the most used parameter to assess bone fragility, and Trabecular Bone Score (TBS) is a recently introduced assessment tool for lumbar spine (LS) bone microarchitecture. We herein present a new index (BMD/BMI) that could be helpful in investigating the bone health of obese patients.

The aim of the study was to assess the correlation of BMD/BMI with TBS and that of LS BMD, TBS, BMD/BMI with anthropometric parameters and cardiovascular risk factors in overweight-obese patients.

**Methods:** We enrolled 2225 overweight-obese Caucasian patients (82% female, BMI 36.5±6.2 kg/m2) aged 45±12, assessing anthropometric parameters and cardiovascular risk factors in overweight-obese patients.

**Results:** Consistent with previously reported data, with increasing BMI, BMD increased, while TBS decreased significantly. We identified BMD/BMI, the ratio between LS BMD and TBS, as a promising index that showed a positive and very significant correlation with TBS, stronger
than that of BMD with TBS. Patients with Metabolic Syndrome (45.7%), a condition that has been suggested to pose at risk of fracture, had LS BMD comparable to that of metabolically healthy patients, whilst TBS and BMD/ BMI were significantly lower (p < 0.001).

**Discussion:** According to recent evidence, obesity does not seem to be protective against fractures as it was previously believed. However, BMI has a well known direct correlation with BMI, suggesting reduced reliability as a marker of fracture risk in case of weight excess. Conversely, TBS appears to better reflect bone fragility in this category of patients and it is inversely related to body mass, but its calculation may not be readily available to all.

**Conclusion:** Given its strong correlation with TBS, a simple ratio such as BMD/BMI is an interesting potential tool to easily assess the risk of fracture in obese subjects, where impaired metabolic health may play a detrimental role on bone strength.

**Abstract #611**

**REAL WORLD TREATMENT OF OBESITY WITH LIRAGLUTIDE IN MEXICAN PATIENTS OF A MEDICAL CARE NETWORK**

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**Objective:** Obesity is considered the 21st century epidemic. It is associated with development of diabetes, cardiovascular disease and various types of cancer. By 2020 two thirds of the world population will be overweight or obese. To date, Mexico is the second leading country in obesity. Treatment includes diet and exercise. Drug use is recommended in patients with a BMI ≥ 30 kg/m² or ≥ 27 kg/m² with associated comorbidities. Liraglutide is FDA approved for obesity treatment. At a dose of 3.0 mg/day it has demonstrated a 9.2 % loss of initial weight with improvements in metabolic parameters. The objective of this study is to evaluate real life treatment of obesity with liraglutide in primary care.

**Methods:** Liraglutide was offered to patients in a primary care clinic of a medical care network who had a BMI ≥ 30 kg/m² or ≥ 27 kg/m² with associated comorbidities. Initial somatometry with laboratory tests that included glucose, insulin, HbA1c, amylase, and liver tests was performed. Abdominal ultrasound was performed to rule out gallbladder stones. Liraglutide was initiated at a dose of 0.6 mg/day with weekly elevations until a final dose of 3.0 mg/day was achieved. Monthly follow up was given with measurements and laboratory tests described above.

**Results:** A total of 10 patients accepted treatment (17 patients declined), with mean age of 47 years, 70% were female, 70% had prediabetes, 33% hypertension, 20% sleep apnea, 40% dyslipidemia, and 20% polycystic ovary syndrome. After 3 months 4 patients stopped liraglutide because of side effects. In patients that continued, a mean weight reduction of 8.08 kg was observed (8.9%), with a mean loss of 10 cm in waist circumference. Improvement in mean glucose (12 mg/dL), HbA1c (0.2 %), insulin (3 µU/mL), liver enzymes, lipid profile (triglycerides 39 mg/dL, LDL-C 25 mg/dL). A mean elevation of amylase was observed (10 UI/L), with no cases of acute pancreatitis. At 3 months 83 % continued with early satiety. One patient presented acute cholecystitis.

**Discussion:** These results are in line with previous clinical studies, attaining at 3 months the desired percentage of weight reduction, with improvements in clinical and biochemical markers of metabolic disease. Almost half of patients stopped treatment; all of them attributed to side effects of the drug. This is a relevant finding that demonstrates that liraglutide could be an option in primary care to treat obesity.

**Conclusion:** The use of liraglutide in a real-world environment provided clinical and biochemical benefits, nonetheless almost half of initially treated patients stopped treatment because of side effects. This drug can be a tool in treatment of obesity in primary care.

**Abstract #612**

**SAFETY AND EFFICACY USING ANTI-OBESITY MEDICATIONS IN ELDERLY PATIENTS**

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**Objective:** Current published data using anti-obesity medications in elderly patients is limited. Managing obesity in elderly patients is important. Therefore, evaluating these interventions in this population is valuable.

**Methods:** A retrospective chart review was performed in 57 patients from a specialty obesity metabolic clinic in Venice, Florida. Patients over 65 years of age who were treated with anti-obesity medications (phentermine/topiramate ER [PTER], naltrexone/bupropion SR [NB], lorcaserin [L], phentermine [P], phentermine/topiramate [PT]), and liraglutide [LG]) for at least 3 months were analyzed. Patients were classified as responders (greater than 5% weight reduction), non-responders (less than 5% weight reduction) or intolerant to therapy.

**Results:** The mean age was 71.1 +/- 4.2 years; all subjects
were Caucasian and 80.7% were female. Mean weight was 96.6 +/- 17.7 kg; mean body mass index was 36.1 +/- 5.3 kg/m². Most patients (96%) had multiple obesity-related comorbidities. The mean weight reduction (from baseline) in all responders was 11.4 +/- 1.4%. A total of 50.9% (29/57) were responders, 28.1% (16/57) were non-responders and 21% (12/57) were intolerant to therapy. Specific response rates to therapy included: PTER: 53.9% (n=26), NB: 30.7% (n=15), B: 100% (n=5), P: 50% (n=4), PT: 66.7% (n=3), and LG: 25% (n=4). Intolerance to therapy occurred in 15.4% PTER, 40% NB (gastrointestinal), 33% PT, 25% LG, and none in B and P groups.

**Discussion:** The amount of weight reduction using anti-obesity medications in this small cohort of elderly patients appeared similar to published data in younger populations. However, almost half of the cohort were either non-responders or intolerant to therapy. PTER appeared the most efficacious. There was a high degree of intolerance to NB, B, P and PT samples were too small to make conclusions. The small sample size limits generalizability.

**Conclusion:** Current anti-obesity medications can be used successfully for clinically meaningful weight reduction in elderly patients. Additional studies are warranted using such interventions in this group.

Abstract #613

**EMPAGILFLOZIN EFFECT ON WEIGHT REDUCTION AND GLYCEMIC CONTROL IN A PATIENT WITH PRADER-WILLI SYNDROME**

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**Objective:** To report a case describing the effects of empagliflozin in a patient with Prader-Willi Syndrome (PWS).

**Case Presentation:** A 26-year-old man with a history of obesity, hypertension, hyperlipidemia, obstructive sleep apnea, intrauterine growth restriction, low birth weight, developmental delay, and intermittent stress-induced hyperphagia presented for management of type 2 diabetes. He was diagnosed with type 2 diabetes at age 20, initially started on insulin and then transitioned to metformin only. Over subsequent years he was treated with various combinations of diabetes medications with fluctuation in weight and glycemic control. In June 2017, it was suspected that he had PWS and this was confirmed with a genetic test. In 4/2017 empagliflozin was added to his medication regimen: first with metformin, glimepiride and liraglutide for 3 months (4/2017 to 7/2017) and then in combination with metformin, liraglutide and insulin glargine for an additional 3 months (7/2017 to 10/2017).

After initiating empagliflozin, HbA1c decreased from 7.9% in 4/2017 to 6.6% in 7/2017. His weight decreased progressively from 167 pounds in 4/2017 to 158 pounds in 8/2017, and 151 pounds in 10/2017. His hyperphagic behavior significantly improved with fewer episodes of stress-related eating.

**Discussion:** A rare genetic disorder, PWS has a prevalence of 1/25000. It is caused by a deletion in the paternal copy of the long arm of chromosome 15. It is associated with hyperphagia, obesity and type 2 diabetes leading to significant morbidity and mortality. Management of hyperglycemia and obesity is a challenge in these patients. Empagliflozin was used in our patient as part of combination therapy. It was effective in lowering HbA1c, reducing weight and was well-tolerated. The mechanism of obesity in PWS is not well understood. Increased levels of ghrelin have been found in obese PWS patients compared to obese controls. While the use of empagliflozin has been associated with weight loss in type 2 diabetes patients, this case indicates that it can have similar effects in patients with PWS who have been shown in the literature to be resistant to other weight loss medications. To the best of our knowledge this is the first report of its use in PWS patients.

**Conclusion:** Empagliflozin is effective in improving glycemic control in patients with PWS and type 2 diabetes and may also be effective in weight loss in these patients in combination with other medications.
CUSHING SYNDROME DUE TO ACTH-PRODUCING BRONCHIAL CARCINOID: A RARE ENCOUNTER

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Objective: Bronchial carcinoids leading to Cushing Syndrome are an uncommon group of lung neoplasms. Worldwide, only a few patients have been reported till now. Here we report the first case of Cushing Syndrome due to ACTH-producing Bronchial Carcinoid from Pakistan.

Methods: Case Study

Case Presentation: A 70 years old Pakistani female consulted AKU neurology clinic with the complaint of weight gain and inability to stand (from sitting posture) & walk properly from 7 months. She was diabetic and hypertensive for 3 years. There was also history of on & off bone aches, mild cough and shortness of breath on exertion for 1 year. Examination showed body mass index of 30.2, rounded plethoric face, central obesity, proximal myopathy, purplish striae over abdomen with normal respiratory examination. So she was referred to Endocrine clinic for evaluation of Cushing Syndrome. Her serum Cortisol failed to suppress after overnight dexamethasone suppression test (15μg/dl) and 24-hr urinary cortisol turned out to be high (852μg/dl). It was followed by the finding of high ACTH level (111pg/ml). High dose dexamethasone suppression test was then carried out to differentiate between pituitary or ectopic source of ACTH which failed to suppress less than 50% of basal level, suggesting an ectopic source. CT chest revealed a 2.5 x 1.6cm mass lesion in left lower bronchus, the bronchoscopic biopsy of which proved it to be bronchial carcinoid. Consequently her 24-hr urinary 5-hydroxyindole acetic acid level was found to be high (20mg/24h). Pulmonary function tests established severe obstructive impairment. So after a systematic evaluation course, she was diagnosed as a case of Cushing Syndrome due to rare ectopic ACTH-producing bronchial carcinoid. She was referred to thoracic surgeon for lobectomy but keeping in view her old age along with several comorbidities and severe pulmonary dysfunction, surgeon and the patient declined the option of surgery. She was then placed on Sandostatin analogue treatment which resulted in moderate amelioration of her symptoms.

Discussion: About 1-5% of Bronchial Carcinoids are associated with ectopic ACTH secretion, which represents 1-10% of Cushing syndrome cases. They systematically present as Cushing syndrome. Bronchial symptoms are present in only 8% pts. So 27% of such patients undergo unnecessary hypophysectomy due to improper evaluation and diagnosis. Surgery is the treatment of choice in the form of lobectomy while sandostatin analogues are used for metastatic or unresectable tumors.

Conclusion: Ectopic ACTH production by bronchial carcinoid is a rare presentation of Cushing Syndrome. Therefore, it requires the adoption of systematic evaluation pathway to avoid unnecessary hypophysectomies.
to continued vascular compromise resulting in testicular infarction. As scrotal rings are frequently recommended by urologists, warnings associated with prolonged use should be discussed with patient’s including testicular failure.

**Abstract #702**

**A CLINICAL DIAGNOSIS OF MEN1 WITH P.GLU45ASP HETEROZYGOUS VARIANT**

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**Objective:** Multiple endocrine neoplasia type I (MEN1) is a rare autosomal dominant disorder that is characterized by the combined occurrence of multi-gland parathyroid disease, anterior pituitary adenomas, and neuroendocrine tumors. While clinical diagnosis of MEN1 has been well established, confirmation via genetic testing remains a challenge. Although sporadic presentation of hyperparathyroidism and pituitary adenoma clinically meets criteria for diagnosis of MEN1, the yield of current genetic testing is approximately 7% in these individuals. This low sensitivity highlights the need for further investigation to better understand the impact of variants that currently have unknown clinical significance. We describe a case of a patient with clinical diagnosis of sporadic MEN1 with p.Glu45Asp heterozygous variant.

**Case Presentation:** 35-year-old Caucasian male with past medical history of recurrent nephrolithiasis presented to endocrinology for evaluation of hypercalcemia and history of elevated prolactin. He was diagnosed with primary hyperparathyroidism with iPTH 95 pg/mL (14-64), Calcium 10.5 mg/dL (8.6-10.3), and Vitamin D25 16 ng/dL (30-100). CT neck was significant for bilateral superior parathyroid adenomas. Prolactin was found to be elevated at 21 ng/mL (2-18). FSH and LH were inappropriately low in the setting of a relatively low testosterone level. MRI was inconclusive for pituitary tumor. Family history was negative for neuroendocrine/pituitary tumors, hyperparathyroidism, consanguinity, or Ashkenazi heritage. MEN1 gene sequencing with duplication/deletion analysis was pursued with Invitae labs and was significant for Exon 2, c.135G>C (p.Glu45Asp) heterozygous, which is deemed a variant of uncertain significance.

**Discussion:** To the best of our knowledge p.Glu45Asp heterozygous variant has only been reported in one other individual who had primary hyperparathyroidism with multiple lesions in the absence of family history suggestive of MEN1. Another missense substitution at this codon p.Glu45Gly has been shown to be pathogenic, which suggests that this residue is important in the overall function of the menin protein. Because a similar phenotype has been seen with this variant in addition to known pathological missense mutations at this residue, we feel that this variant correlates with the clinical diagnosis of MEN1 in this patient and plan to move forward with MEN1 surveillance.

**Conclusion:** The described case in conjunction with prior reports of disease with mutations at this residue, suggests that p.Glu45Asp could represent a pathological MEN1 missense mutation.

**Abstract #703**

**PRIMARY HYPERPARATHYROIDISM IN PRESUMED PREGNANCY**

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**Case Presentation:** A 23-year-old woman with recurrent staghorn nephrolithiasis presented with abdominal pain, nausea, and vomiting. Her mentation was normal with no seizures. Physical exam revealed neck mass with no jaw tumor. Her corrected serum calcium was 15.28 mg/dL on admission with an iPTH of 532 pg/mL. Her serum pregnancy test was positive. She was initially treated with aggressive intravenous fluid (IVF) and corrected serum calcium (cCa) moderately decreased to 11.72 with normalization of renal function on Day 2. On Day 3, cCa was 13.9. Therefore, intravenous furosemide and calcitonin were started with continued aggressive IVF. On Day 4, cCa was 12.3 and prednisone 10 mg daily was added. On Day 5, cCa was 13.9 and prednisone was switched to hydrocortisone 40 mg IV BID with continued aggressive IVF. Furosemide was switched from subcutaneous to intravenous drip. Neck ultrasound showed a 4.2 cm vascular lesion posterior to the right thyroid lobe and a 1.5 cm isoechoic and vascular lesion in the region of the inferior thyroid lobe. MRI neck showed a 4.6 cm multi-lobed single parathyroid adenoma or a conglomerate of parathyroid adenomas and a 6.3 cm left thyroid nodule. TSH was normal. Her cCa remained elevated, 12.5-13.0 mg/dL, despite medical treatment. A fine needle aspiration of the left thyroid nodule was benign. The patient underwent parathyroidectomy on hospital day 10 and the surgical pathology report was consistent with a parathyroid adenoma. Her calcium normalized to 10.0 one day after surgery. The obstetrician team eventually determined that the patient was not pregnant and that the positive serum pregnancy test is due to a positive heterophile Ab.
iPTH 532, cCa 13.2
25OHD: 10.4 (ref 30.1-100.0 ng/mL)
1,25OHD: 36 (ref 18-72 pg/mL)
24 hour urinary calcium: 324 mg
24 hour urinary creatinine 69 (ref 80-120 mL/min)
Prolactin 9.7 (ref 5.2-26.5 ng/mL)
Plasma free fractionated metanephrine: normal
PTHrP: 12 (ref 14-27 pg/mL)
Prolactin 9.7 (ref 5.2-26.5 ng/mL)

Conclusion: There is no evidence-based treatment for gestational primary hyperparathyroidism. Therapeutic management may be challenging because some pharmacologic agents are contraindicated in pregnancy. Serum calcium above 11.4 mg/dL is associated with high risk of fetal loss. Therefore, parathyroidectomy is recommended in pregnant women with calcium level above 11 mg/dL especially those with prior pregnancy loss. Given the young age of our patient, MEN 1, MEN 2A, familial parathyroid hyperplasia syndrome, jaw tumor syndrome and benign familial hypocalciuric hypercalcemia needed to be excluded. Our presumed pregnant patient underwent parathyroidectomy since her calcium levels remained above 11 mg/dL despite medical management.

Abstract #704

AN UNUSUAL CASE OF HUMORAL HYPERCALCEMIA OF MALIGNANCY CAUSED BY A DYSGERMINOMA

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Objective: Humoral hypercalcemia of malignancy is a common paraneoplastic syndrome occurring often secondary to elevated levels of parathyroid hormone related protein or bone destruction from metastatic disease. We present a rare case of hypercalcemia secondary to autonomous production of 1 alpha-hydroxylase in a dysgerminoma.

Case Presentation: A 42 year old Caucasian woman presented to the emergency department with fatigue, generalized malaise, and an unintentional 15 lb weight loss. She denied the use of any dietary supplements. Initial laboratory revealed Calcium of 14.1 mg/dL, Albumin 4.6 mg/dL, and intact PTH 11 pg/mL. CT scan of the abdomen revealed a 16 cm heterogeneous pelvic mass without ascites. She was referred to our institution for further evaluation by Gynecologic Oncology. Physical exam showed a thin patient with distended abdomen and palpable mass of the lower abdomen. Significant labs at our institution following fluid resuscitation included Calcium 11.9 mg/dL, Albumin 3.5 mg/dL, Cr 1.68 mg/dL, Alk Phos 205 IU/L, Phosphorous 2.9 mg/dL, PTH 6 pg/mL, Vitamin D 25-Hydroxy 30 ng/mL, HCG 148 mIU/mL, and Cancer Antigen 125 109.96 U/mL. Initial differential diagnosis included PTH-rp mediated humoral hypercalcemia of malignancy, granulomatous disease, sarcoidosis, and both Hodgkin’s and non-Hodgkin’s lymphomas that can develop 1 alpha-hydroxylase mediated hypercalcemia. She was managed with intravenous fluid and received one dose of IV Pamidronate 60 mg. Subsequent laboratory data revealed PTH-rp 19 pg/mL (Reference Range 14-27) and an elevated Vitamin D 1,25 of 135 pg/mL. Our patient underwent extensive gynecologic surgery. Pathology was diagnostic for a left ovarian dysgerminoma with ovarian capsule intact, pelvic washings positive for neoplastic cells, and other tissues negative for malignancy. She was diagnosed with Stage IIC left ovarian dysgerminoma. After surgical intervention and subsequent chemotherapy with bleomycin, etoposide, and cisplatin, calcium levels have remained normal in long term follow up.

Discussion: In recent years there have been 12 case reports of young female patients with dysgerminoma and hypercalcemia secondary to elevated Vitamin D 1,25. An additional study of 12 dysgerminomas were found to demonstrate a significant increase in 1 alpha-hydroxylase expressed by both neoplastic cells and in the tumor-associated macrophages.

Conclusion: Autonomous production of extra-renal 1-alpha hydroxylase is a rare etiology of humoral hypercalcemia of malignancy, but can be seen in patients with a dysgerminoma. Surgical excision of the tumor followed by chemotherapy is typically curative for treatment of this form of hypercalcemia.

Abstract #705

EVALUATION OF GDM SUBJECTS WITH POST PARTUM PERSISTANCE OF GLUCOSE INTOLERANCE

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BIRDEM

Objective: This study is conducted to identify the clinical, biochemical and other relevant factors for the candidates, who were diagnosed as GDM and not resolved their glucose intolerance after delivery.

Methods: From records of Jan 2014- Dec2016, Retrospective data were collected for analysis. 176 diagnosed GDM subjects were followed up 6-8 weeks after delivery. All the subjects were treated with Insulin ± Metformin. Two sample OGTT with 75 Gm Glucose was done at post delivery follow up. Cut off value of all glucose intolerance according to ADA diagnostic criteria
(IFG, IGT or DM). Abnormal Glucose Tolerance from FPG ≥6.1 and 2PG ≥7.8 mmol/L. HbA1c was not taken for analysis. DM cut off value also according to ADA.

**Results:** Among 176 GDM subjects, 88 (50.00%) were diagnosed in 25-36th weeks of gestation according to LMP, 71 (40.34%) were diagnosed as GDM in 13-24th week and 17 (9.60%) subjects in 4-12th weeks of pregnancy. ADA one step diagnostic criteria for GDM is used (anyone of the three: fasting, 1 hour & 2 hour cut off value). FPG ≥5.1 mmol/L was 64 (36%) cases, 2 hours post 75 Gm Glucose ≥8.5 mmol/L among 176 (100%) cases. 1-hour value ≥10 mmol/L was 154 (88%) case. Mean FPG 8.8±3.4 mmol/L and 2PG 15.7±4.6 mmol/L. BMI 29.3±3.9. Seventy eight cases (44.32%) are primi, 88 (50.00%) cases are at 2nd gravida and rest (13.15%) are with >2 pregnancy before. One hundred sixty seven (94.88%) cases having F/H of diabetes among first degree relative. Seventy three (41.48%) cases were diagnosed as PCOS. Insulin dose was Short Acting Human/ RA Analogue (Aspart) 64±26 units and NPH/ Detemir 26±14 units per day. Metformin were in 15 (8.5%) cases with insulin. 170 (96.60) cases were delivered by LUCS. Maternal age 29.8±3.6 years.

**Discussion:** The glucose intolerance seen in most patients with GDM resolves following delivery. To find out the high risk subjects for the persistence of GDM after delivery, this retrospective analysis was done.

**Conclusion:** Predictors for persistence of GDM may be early GDM detectors, F/H of diabetes, PCOS and higher BMI and positive family history. Higher both FPG and 2h PG value at diagnosis of GDM also correlates strongly as future persistence of glucose intolerance.

**Abstract #706**

PARATHYROMATOSIS: A RARE BUT IMPORTANT CAUSE OF RECURRENT HYPERPARATHYROIDISM

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**Objective:** To present a rare case of parathyromatosis and recognize the challenges of preoperative diagnosis and treatment.

**Case Presentation:** A 33-year-old man with history of right parathyroidectomy for parathyroid adenoma five years ago was admitted for severe hypercalcemia 15.6 mg/dL with elevated plasma parathyroid hormone (PTH) 1289 pg/mL. Ultrasound, CT, sestamibi, and PET scan were unremarkable; however, a four-dimensional CT (4D-CT) of the neck showed an area of increased signal enhancement and hypervascularity without discrete nodule in the posterior right thyroid region. The patient then underwent parathyroid surgical exploration with right hemithyroidectomy. Right inferior, left superior, and left inferior parathyroids appeared normal and were not hyperplastic. Intraoperative frozen section analysis revealed presence of parathyroid tissue intimately involved and in the right thyroid lobe. The patient also underwent central compartment neck dissection due to persistently high intraoperative parathyroid hormone levels. PTH levels dropped to 208 pg/mL postoperatively; calcium decreased but remained elevated at 12.7 mg/dL. Pathology revealed the presence of several small nodular foci of atypical hyperplastic parathyroid tissue in right thyroid and soft tissue in the left central neck compartment consistent with parathyromatosis.

**Discussion:** Parathyromatosis is a rare condition of multiple nests of hyperfunctioning parathyroid tissue. It is likely either the result of spillage and seeding of parathyroid tissue around operative area during parathyroid surgery or the change in embryologic foci of parathyroid tissue that become hyperplastic with physiologic stimuli. Preoperative diagnosis is difficult as there are few radiologic findings associated with this condition. Ultrasound can sometimes detect multiple small nodules in thyroid tissue suggesting the diagnosis. CT, sestamibi, and PET scans are often negative. 4D-CT may reveal hypervascular findings, like in our patient and may be useful pre-operatively. Patients with parathyromatosis are at high risk for incomplete surgical resection and need for revision surgery due to small nests of ectopic hyperplastic parathyroid tissue within the surgical bed.

**Conclusion:** Parathyromatosis is a rare but problematic cause of recurrent hyperparathyroidism. It is difficult to diagnose preoperatively, but ultrasound and 4D-CT may represent the best imaging modalities for possible identification and perioperative management to remove all affected tissue without reseeding.

**Abstract #707**

GLUCAGONOMA: A RARE CASE REPORT

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Walter Reed National Medical Center

**Objective:** Glucagonoma is a rare pancreatic neuroendocrine tumor (PNET) with an estimated global incidence of 1:20 million people. Major clinical manifestations of glucagonoma syndrome include necrolytic migratory erythema (NME), diabetes mellitus and glucagon-secreting tumors. Several reports emphasized the importance of recognizing the NME for early diagnosis of glucagonoma; however, not all
patients will develop the typical rash, which will delay the diagnosis even further. We present a case of glucagonoma that was diagnosed biochemically incidentally one day prior to surgery for metastatic PNET.

**Case Presentation:** A 53 year-old Caucasian male presented with several months of intermittent abdominal pain, constipation and 20-lbs weight loss. Abdominal MRI revealed bilateral liver lesions and a 4.2x3.3cm pancreatic tail mass. EUS-guided biopsy revealed PNET in the pancreas while the liver biopsy was nondiagnostic. An octreotide scan confirmed activity in the pancreatic tail mass and bilateral liver metastases. One day prior to debulking surgery, patient was found to have asymptomatic nonketotic hyperglycemia (>500 mg/dL). He had a pre-diabetic A1C level one year prior, no presence of skin rash or other associated symptoms. Fasting serum glucagon level was greater than 5000 pg/ml (diagnostic of glucagonoma). Patient underwent distal pancreatectomy, splenectomy and partial liver excision. Postoperative pathology revealed positive staining of chromogranin A, synaptophysin and glucagon. He subsequently completed 2 cycles of CAPTEM chemotherapy. His insulin requirement dropped significantly and glucagon level normalized at 6 months post-treatment.

**Discussion:** Glucagonoma is a slow-growing tumor though the delay in its diagnosis remains the most challenging issue for both clinicians and patients. Patients without metastatic disease could achieve up to 100% for 10-year survival rate compared to 51.6% in patients with metastasis (1). Due to the rarity of this disease, few clinicians would suspect glucagonoma in patients who present with new onset diabetes mellitus and NME. Our patient had no NME. His blood glucose was not checked during the initial visit for abdominal pain and the elevated blood glucose was not discovered until the day of surgery, which delayed his surgery by one week to control blood glucose.

**Conclusion:** Glucagonoma usually presents with NME, new-onset diabetes mellitus, and glucagon-secreting tumor. However, atypical presentation can delay the diagnosis. In clinical practice, physicians need to consider glucagonoma diagnosis in a patient with a new-onset diabetes mellitus and NME. In addition, biochemical screening for all PNET prior to surgery is a must to avoid delay in treatment.

**Abstract #709**

**AN UNUSUAL CASE OF DIGEORGE SYNDROME PRESENTING AS SEIZURES IN ADULTHOOD**

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**Objective:** DiGeorge syndrome (DGS) is associated with a defective development of the pharyngeal pouch system due to a chromosomal deletion at 22q11.2. The classic presentation includes conotruncal cardiac anomalies, hypoplastic thymus, and hypocalcemia. It typically manifests in the neonatal period with symptomatic hypocalcemia or found during workup for cardiac malformations. We describe an unusual case of DGS diagnosed in adulthood after presenting with seizures from late onset hypocalcemia.

**Case Presentation:** This is a 29-year-old female with a past medical history of anxiety, gastroesophageal reflux, and recurrent respiratory tract infections, referred for an endocrinology workup after experiencing seizures due to hypocalcemia. Further testing revealed primary hypoparathyroidism (PTH 11, corrected calcium 6.8, vitamin D 26.2, phosphorous 4.1). She was started on calcium carbonate and cholecalciferol with improvement of her levels and resolution of her seizures. The patient reported a history of developmental delay and learning difficulties during childhood. Physical exam was notable for epicanthal folds, squared nose, and hypertelorism. Among DGS, autoimmune polyglandular syndrome type 1 was also considered due to her history of esophagitis and hypoparathyroidism. Esophagogastroduodenoscopy showed no Candidal infection and anti-adrenal antibodies were negative. Genetic testing revealed two pathogenic changes including a deletion on chromosome 22q11.21 confirming diagnosis of DGS. Electrocardiogram and echocardiogram revealed no cardiac anomalies. Immunological workup showed a low IgG subclass 3 with no leukopenia. Imaging of the neck revealed hypoplasia of the right submandibular gland with no evidence of parathyroid adenoma or thyroid abnormalities.

**Discussion:** The 22q11.2 microdeletion has an estimated prevalence of 1 in 4,000 live births. Diagnosis is suspected based on clinical findings and confirmed with genetic testing. The triad of cardiac anomalies, hypoplastic thymus, and hypocalcemia is seen in majority of patients with DGS. Approximately 80 percent will have cardiac defects, commonly upon initial presentation. Our patient surprisingly had no cardiac abnormalities detected. She had a history of recurrent upper respiratory and sinus infections which is a common finding in DGS due to
immunodeficiency from thymic hypoplasia. Parathyroid hypoplasia resulting in hypocalcemia develops in the neonatal period in up to 60 percent of patients. Symptoms of hypocalcemia occur early in life; prompting workup and diagnosis in the initial stages.

**Conclusion:** It is very rare for a patient with DGS to remain asymptomatic from hypocalcemia until adulthood, as seen in our case.

**Abstract #710**

**A SURVEY ON THE NUTRITION RISK LEVEL OF PATIENTS SUBJECTED TO STANDARD PRACTICE OF ENTERAL NUTRITION PROVISION ADMITTED AT THE INTENSIVE CARE UNIT OF CEBU DOCTORS’ UNIVERSITY: A ONE-YEAR RETROSPECTIVE CHART REVIEW**

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**Objective:** We assessed the nutrition risk levels as measured by NUTRIC score among admitted patients who were given enteral nutrition (EN) at the Intensive Care Unit of Cebu Doctors’ University Hospital from June 2016 to June 2017.

**Methods:** This is a one-year single-center cross-sectional retrospective chart review study on admitted ICU patients from June 2016 to June 2017. Categorical profiles were expressed in frequency and percentage while those continuous variables were described in mean and standard deviations. Moreover, incidence rate of nutrition risk levels of patients was computed. By comparing the required and actual feeding amount of patients was compared using the Paired t-test wherein a p-values lesser than 0.05 alpha were considered significant. IBMSPSS ver 21 was used as software.

**Results:** This study has shown that 86% of the patients admitted in this institution’s ICU were started on early EN within 24 to 48 hours of ICU admission. From the subjects given EN, only 6% were able to achieve the energy requirement. In those subjects who did not achieve the required energy requirement, there is an associated increased length of stay in the ICU (p-value of 0.045). Out of 52 patients with NUTRIC scores included in this study, 75% of the subjects were identified to be at low risk while 25% were at high risk for a 28-day mortality.

**Discussion:** Only 6% of subjects provided with EN achieved the required 25kcal/kg/day energy requirement. There was also a high proportion of underfed patients although initiated on EN within 24 hours who had longer duration of ICU stay. Our study also showed that most of the patients who were not given the required kcal had a higher rate of improved condition thus revealing that feeding requirement adherence does not guarantee favorable outcome. It was also revealed that majority of the ICU patients admitted had been receiving early EN. A total of 86% of patients were initiated with early EN within 24 to 48 hours from ICU admission and 61% were discharged improved. The study revealed that patients with high NUTRIC score, there was a strong positive association between nutritional adequacy and 28-day survival. This association diminished with lesser NUTRIC score.

**Conclusion:** Early initiation of EN was being practiced among patients admitted to ICU in our institution. However, majority of patients given EN were not given the required energy requirement. The ICU patients who were given early nutrition feeding were associated with decreased length of ICU stay.

**Abstract #711**

**A CASE OF LATE ONSET POLYGLANDULAR AUTOIMMUNE SYNDROME**

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Henry Ford Macomb

**Objective:** Polyglandular Autoimmune syndrome (PAS) is a deficiency in the function of several endocrine glands due to an autoimmune cause. Type 3 PAS is characterized by a combination of autoimmune thyroiditis, type 1 diabetes and other autoimmune processes. This case is a rare late onset of type 3 PAS.

**Case Presentation:** A 93-year old male with a medical history of CAD, stage 4 CKD, hypertension presented with dizziness leading to a fall. Patient was found to be in severe DKA with blood glucose of 805 and beta-hydroxybutyrate of 6.04. Patient has no known history of endocrinopathy. His blood sugar was normal during a previous hospitalization three weeks prior when he had an upper respiratory infection. Diagnosis of latent autoimmune diabetes of adults (LADA) was supported with elevated GAD antibodies and low C-peptide of 0.8. Further work-up revealed TSH of 15.71, free T4 of 0.6 and a positive Thyroperoxidase antibodies suggesting autoimmune thyroiditis. Patient did have episode of hypotension. However, morning cortisol level was not suggesting of adrenal insufficiency. Patient was diagnosed with type 3 PAS.

**Discussion:** Environmental exposure or intrinsic changes in the gene were hypothesized as the triggers for PAS in the genetically susceptible population. Patient did have a respiratory infection before the diagnosis of LADA and autoimmune thyroiditis, which could trigger PAS if he is genetically susceptible. However, type 3 PAS typically
happens in the fourth decade of life. A diagnosis at age 93 was considered a very late onset for LADA and type 3 PAS. It was not clear if the patient has type 2 PAS. Cortisol was collected after possible steroid use for hypotension workup, which can cause falsely elevated cortisol. A 21-hydroxylase antibody was collected for further workup. It is possible that this patient developed adrenal insufficiency, which could classify him as type 2 PAS.

**Conclusion:** When a patient develops one autoimmune endocrinopathy, it is important to screen for others especially in sudden onset endocrinopathy. More comprehensive studies and research about PAS will reveal information and facts that can clarify the epidemiology and etiology which may help preventing foreseeable complications.

**Abstract #712**

**BEYOND TURNER SYNDROME: 45X/46XY RARE GENOTYPE OVOTESTICULAR DISORDER OF SEXUAL DEVELOPMENT PRESENTING WITH TURNER PHENOTYPE**

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Nil Ratan Sircar Medical College

**Objective:** The incidence of ovotesticular disorder of sexual development (DSD) in individuals with 45, X/46, XY mosaicism is low, and the reports are rare. In addition, distinction between ovotesticular DSD and MGD may be difficult. We report this case of ovotesticular DSD with rare genotype presented with Turner phenotype.

**Case Presentation:** 16 Year old girl presented with short stature and primary amenorrhoea. On examination height was 126.8 cm (<3rd p), (-4.93 SD), height age 8 years, target height was 151.8 cm (-1.4SD), arm span 135 cm, upper segment lower segment ratio 0.95, weight 29 kg (<3rd p), BMI 25th percentile, breasts and pubic hair were Tanner 1, axillary hair A0, multiple naevi over face and neck, shield chest, increased carrying angle, bilateral short 5th metacarpal and short left 4th metatarsal. External genitalia was unambiguously female. On investigation bone age was 13 years, FSH 142.28 micro IU/ml. Ultrasound of pelvic organs shows uterus (3×0.6×1.2) cm, volume 1.1 cm³, endometrial thickness 1 mm, ovaries non visualised. MRI of pelvic organs couldn’t localise ovaries. Karyotype revealed 45 X (82%)/46XY (18%).

So a diagnosis of mixed gonadal dysgenesis was made. Laparoscopic visualisation of gonads and gonadectomy done. Both gonads showed ovarian and testicular tissue. A histopathological diagnosis of ovotestis was made. So a final diagnosis of bilateral ovotestis with mos 45 X/46 XY karyotype with Turner phenotype was made.

**Discussion:** 45X/XY is a very rare genotype as reported in the present case to be associated with ovotestis. The clinical phenotype associated with 45X/46,XY mosaicism is broad, ranging from women, with or without Turner syndrome stigmata, to apparently normal males, with intervening variable ambiguous phenotypes. Gonad histology associated with 45X/46,XY mosaicism is also variable with partial, complete, mixed, or asymmetric gonadal dysgenesis showing streak gonads. The majority of patients with a diagnosis of ovotesticular DSD (59.5%) have a 46,XX chromosome constitution and 12.3% a 46,XY karyotype. About 28% have sex chromosome abnormalities, the most frequent being 46,XX/46,XY chimerism (12.8%). Mosaicism – as 46,XX/47,XXY (5.6%) and 45X/46,XY (3.5%) – and rarer chromosome abnormalities account for the remainder.

**Conclusion:** The incidence of ovotesticular DSD in individuals with 45X/46,XY mosaicism is low, and the reports are rare. In addition, distinction between ovotesticular DSD and MGD may be difficult. This rare variety of ovotesticular DSD can present with Turner stigmata.

**Abstract #713**

**PROTON PUMP INHIBITORS AND HYPOCALCEMIA: DOES IT REALLY HAPPEN?**

Franco Vallejo Garcia, MD, Melissa Sum, MD

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**Objective:** Long-term Proton pump inhibitors (PPIs) used has been associated with hypocalcaemia, but few cases have been reported in literature. The risk only appears to exist with PPI use of over 1 year. We report a case of severe hypocalcemia after 4 days of PPI use.

**Case Presentation:** A 58 year-old female with prior history of thyroidectomy due to papillary thyroid carcinoma, with post-surgical hypoparathyroidism presented to the hospital. She was on vitamin D treatment. Due to history of calcium kidney stones she was not on calcium supplement. Patient started PPI due to reflux symptoms. After 4 days of treatment with PPI, she experienced numbness and tingling of all extremities, leading to presentation in the emergency department. She was on vitamin D treatment. Due to history of calcium kidney stones she was not on calcium supplement. Patient started PPI due to reflux symptoms. After 4 days of treatment with PPI, she experienced numbness and tingling of all extremities, leading to presentation in the emergency department. She was on vitamin D treatment. Due to history of calcium kidney stones she was not on calcium supplement.
trousseau’s sign, also magnesium levels normalized to 2.0 mg/dL and serum calcium increased to 7.0 mg/dL. She was discharged on calcitrol, calcium citrate, and PPI stopped.

**Discussion:** Bioavailability of the calcium source (digestibility and solubilization) plays an important role in patients with increased risk of hypocalcemia, as hypoparathyroidism. Solubility is mainly determined by the pH of the gastrointestinal tract. When pH increases, calcium solubility decreases. The low pH of the stomach dissolves calcium salts into Ca^{2+} ions. The pH is acidic in the duodenum, being the site with the maximum solubility. The pH rises to alkaline levels in the lower half of the small intestine. As a result of this change in pH, less calcium is solubilized.

PPIs cause an increase in the pH. O’Connell et al. (2005) using a radiolabeled calcium isotope, reported that 7 days of omeprazole 20 mg daily reduced calcium absorption in elderly women under fasting conditions compared with the placebo group. Although conflicting evidence exists.


Calcium carbonate is the most widely used calcium salt, but it is the least water-soluble salt at a neutral pH. For this reason, less-soluble calcium salts, or almost insoluble as calcium carbonate, is a relatively poor source of calcium, and in patients using PPIs, is absorbed poorly.

**Conclusion:** We recommend in patients with increased risk of hypocalcemia using a more soluble calcium salts, instead of calcium carbonate, when the use of PPIs is needed.

**Abstract #714**

**LITHIUM ASSOCIATED HYPERPARATHYROIDISM: SYMPTOM RELIEF AND IMPROVED QUALITY OF LIFE AFTER PARATHYROIDECTOMY**

Deva Boone, MD, Emily Heuker, BA, James Norman, MD

**Objective:** Long-term lithium use is an established but uncommon cause of primary hyperparathyroidism (pHPT). We sought to evaluate the symptomatic presentation of patients with lithium associated hyperparathyroidism (LAH) and assess for symptomatic improvement postoperatively.

**Methods:** Patients undergoing parathyroidectomy for pHPT between January 2013 and July 2016 were evaluated for lithium usage and duration, preoperative subjective symptoms, and objective measures of disease severity. Patients with LAH were compared to those with sporadic pHPT, and a standardized postoperative survey on symptom complex and quality of life measures was used to evaluate the benefit of parathyroidectomy.

**Results:** During the study period, 9607 patients underwent surgery for pHPT, with 122 of these (1.3%) on concurrent or prior lithium therapy. Lithium treatment duration varied from 3 months to 41 years (mean 17.7±13.9 years); 44 patients were still on lithium at the time of operation. The biochemical presentation of LAH was similar to sporadic pHPT with regard to average highest calcium level (11.0±0.6 vs 11.0±1.7 mg/dl, respectively, p=NS), and average PTH (98±50 vs 96±70 pg/ml, p=NS). In comparing symptoms in patients with LAH to sporadic pHPT, there were similar rates of preoperative fatigue (80% vs. 73%, respectively, p NS), bone pain (50% vs 48%, p NS), headaches (33% vs. 34%), heartburn (41% vs. 38%, p NS), and insomnia (70% vs. 66%, p NS). Patients with LAH reported higher rates of difficulty concentrating (76% vs. 59%, p = 0.005) and memory loss (73% vs. 59%, p = 0.02). Patients with LAH had similar rates of hypertension (50% vs. 52%, p NS), osteoporosis (33% vs. 40%, p NS), and chronic kidney disease stage 3 or greater (34% vs. 30%, p NS) but lower rates of kidney stones (9% vs. 22%, p = 0.01). Postoperatively, 70% of LAH patients reported a reduction in number of number of symptoms and 18% reported a complete dissolution of symptoms. Collectively, LAH patients reported a significant reduction in each of the measured symptoms 3 months after surgery. Most patients (67%) reported that they felt their health had improved significantly postoperatively.

**Conclusion:** LAH presents similarly to sporadic pHPT, with several notable differences. Those with LAH report a greater incidence of neurocognitive symptoms (decreased concentration and memory loss) and develop kidney stones less frequently. Postoperatively, most LAH patients experience symptom improvement and report overall improvement in their health.

**Abstract #715**

**ENDOCRINOPATHIES IN CHILDREN WITH THALASSEMA: AN INDIAN PERSPECTIVE**

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**Objective:** Undiagnosed endocrinopathies is associated with increased morbidity and impaired quality of life. Data is scant from India on the burden of endocrinopathies in children with thalassemia. This study aimed to determine the burden and predictors of short stature, delayed puberty, thyroid and adrenal disorders

**Methods:** We analysed 96 consecutive patients thalassemia major or intermedia, attending the out patient services of a tertiary care hospital and screened them for
endocrinopathies between January 2016 till October 2017. We analysed the burden of endocrinopathies with regards to serum ferritin levels.

**Results:** Most common endocrinopathy was short stature, followed by hypogonadism, hypothyroidism and hypocortisolism (Table-1). Occurrence of endocrinopathies was significantly higher in patients in highest quartiles of serum ferritin as compared to the lower quartiles. Hypergonadotropic hypogonadism was more common than hypogonadotropic hypogonadism (Table-1). Thalassemia intermedia or major per se was not an independent predictor of endocrinopathies. Serum ferritin (iron overload status) was the primary predictor of occurrence of endocrinopathies.

**Conclusion:** Endocrinopathies are common in children with thalassemia, and frequent go unrecognized, contributing to significant morbidity. Serum ferritin is a good predictor of endocrinopathies in thalassemia. Maintaining a good chelation viz. maintaining a low serum ferritin has an important role in reducing the burden of endocrinopathies in children with thalassemia.

**Abstract #717**

**TRANSIENT HYPERPARATHYROIDISM IN A PREVIOUSLY HYPOPARATHYROID PATIENT**

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**Objective:** To describe a case with elevated plasma parathyroid hormone (PTH) level in a patient who was previously hypoparathyroid secondary to parathyroid surgery for primary hyperparathyroidism.

**Methods:** We present a case of a hypoparathyroid patient who became transiently hyperparathyroid with severe hypercalcemia due to an unknown etiology.

**Case Presentation:** The patient is a 71-year-old man with past medical history of hypertension, hyperlipidemia, gout, osteoporosis, and primary hyperparathyroidism status post parathyroidectomy. He had a left superior and inferior parathyroidectomy in 2012, followed by a right parathyroidectomy in 2015 due to persistently elevated plasma PTH. He became hypoparathyroid following the second parathyroid surgery requiring calcium and vitamin D supplements. During clinic visit in May 2017, he was taking calcium 500mg TID and calcitriol 0.25mcg TID. He reported occasional leg cramps and foot tingling, especially when he missed his calcium dose. Repeat labs showed plasma calcium (Ca) 8.8mg/dL, low serum ionized calcium (iCa) 1.09mmol/L, and low plasma 25-hydroxy vitamin D at 18ng/ml. Calcitriol was increased to TID and cholecalciferol 2000 IU daily was started. He was asked to repeat labs in 2 weeks but he did not return for labs. In July 2017, he was admitted for severe hypercalcemia with plasma Ca 15.3mg/dL, albumin 3.6g/dL, and elevated plasma creatinine (Cr) 3.3mg/dL. He was taking his medications as prescribed. On subsequent labs, he was noted to have elevated plasma PTH was 89.2pg/mL, PTH-related peptide <1.1pmol/L, 25-OH vitamin D 44ng/mL, and low plasma 1,25-dihydroxy vitamin D 12.4pg/mL. Aggressive hydration and withholding of calcium and calcitriol improved plasma Ca to 9.6mg/dL and Cr to 1.9mg/dL over the next few days. Repeat plasma PTH level again decreased to <2.5pg/mL and he again became hypocalcemic requiring calcium and vitamin D supplementation.

**Discussion:** It is unclear why a hypoparathyroid patient became hyperparathyroid with hypercalcemia. This case is unique as the hypercalcemia was transient and likely due to hyperparathyroidism.

**Conclusion:** We present a case where a hypoparathyroid man who became hyperparathyroid with hypercalcemia and subsequently returned to a hypoparathyroid state.

**Abstract #718**

**A RARE CASE OF PERSISTENT HYPERCALCEMIA DUE TO PARATHYROMATOSIS**

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**Case Presentation:** A 62 year-old woman presented to the ED with somnolence, constipation and abdominal pain. Examination was positive for well-healed surgical scars but no neck mass/adenopathy. Her serum-calcium was 21mg/dL(8.4-10.2), ionized-calcium >2.08mmol/L(1.05-1.30), creatinine 1.57mg/dL(0.38-1.02) and intact-PTH 815pg/mL(12-88).

There was no family history of hypercalcemia. Eighteen years before presentation, she underwent resection of a mediastinal mass deemed to be an ectopic parathyroid gland. Six years after, she had recurrent PTH-mediated hypercalcemia and had 2 parathyroid glands removed. She did well until a year before presentation when again developed severe PTH-mediated hypercalcemia. Imaging studies were unremarkable and she was treated medically with Cinacalcet and Denosumab with reasonable calcium control. However, due to insurance issues she was not able to continue therapy, which led to multiple ED visits with symptomatic PTH-mediated hypercalcemia. Additional evaluation showed 25(OH)-vitamin D 17ng/mL, PTH-rp <2.0pmol/L(0.0-3.4), normal albumin,
phosphorous, TSH and FT4. SPECT parathyroid scan, neck US, CT neck/parathyroid and PET-CT were unremarkable. Her hypercalcemic crisis was treated aggressively with IV fluids and calcitonin with improvement in calcium and renal function. Further treatment with Cinacalcet and Pamidronate was also initiated. She underwent central neck exploration, revealing multiple areas of masses/lymph nodes that were removed, and total thyroidectomy. Pathology was consistent with parathyromatosis. Postoperatively calcium normalized and intact-PTH decreased to 133pg/mL. As of last follow-up patient was doing well and was being treated for dysphonia.

**Conclusion:** Parathyromatosis is a rare condition in which hyperfunctioning parathyroid tissue is distributed throughout the neck and superior mediastinum leading to PTH-mediated hypercalcemia. It can occur as overgrowth of embryologically derived parathyroid rests or after intraoperative seeding during parathyroid tumor resection. Most commonly, it presents as recurrent persistent hypercalcemia. Imaging studies are usually negative and the majority of cases are diagnosed during intraoperative exploration or postoperative histology. Clinical management is difficult due to the high recurrence rate, usually severe hypercalcemia and the risks associated with multiple reoperations. Given its diagnostic and therapeutic challenges, clinicians should consider this condition as part of the differential diagnosis of recurrent PTH-mediated hypercalcemia.

**Abstract #719**

**INTRATHYROIDAL HEMORRHAGIC PARATHYROID CYST DIAGNOSED BY THYROSEQ V3 MOLECULAR TESTING**

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**Case Presentation:** A 36-year-old female presented to her primary doctor for neck swelling. Thyroid ultrasound revealed a 4.7 cm anechoic cyst. Forty milliliters of fluid was aspirated from the cyst at an outside facility with benign cytology. Several weeks later she presented to the ED with progressive left neck swelling, pain, fever, and dysphagia. CT scan demonstrated a low-density indeterminate lesion within the left thyroid. Repeat FNA was performed by otolaryngology in the ED and pathology interpretation showed blood, inflammatory cells, and debris; surgical intervention was advised. She presented to the Endocrinology clinic seeking a non-operative alternative, specifically percutaneous ethanol injection (PEI). Repeat thyroid US showed a 3x4x6 cm left thyroid lesion with hemorrhage and clot. A third FNA sample was obtained and interpreted as atypia of undetermined significance. Thyroseq v3 molecular testing was sent to ensure benignity prior to ethanol ablation. Results of the molecular testing revealed strong expression of PTH and Chromogranin A genes, suggesting intrathyroidal parathyroid cyst. On follow up, the cyst had spontaneously decreased in volume by 92%, and patient was symptom free. Calcium and serum PTH remained normal throughout her course.

**Discussion:** Parathyroid cysts are uncommon, accounting for 0.08-3.41% of all parathyroid lesions. Intrathyroidal parathyroid cysts are even more rare. Parathyroid cysts have variable presentations, and can be either non-functioning (majority) or functioning (minority). These cysts are also at risk for hemorrhage, which can result in hypercalcemic crisis or bleeding complications (e.g., hemothorax, cervical hematoma with airway compromise). PTH washout on FNA samples can be diagnostic if there is clinical suspicion (e.g. clear cyst fluid on initial drainage). Thyroid molecular tests now include genes for parathyroid and non-thyroid tissue, which can aid in diagnosis. While surgery has been the mainstay of treatment for functional or recurrent symptomatic cysts, ethanol ablation is a new treatment modality. In one case series, ethanol ablation was effective at reducing both size and symptoms, with no complications reported.

**Conclusion:** The diagnosis of intrathyroidal parathyroid cyst requires a high index of suspicion. Parathyroid hemorrhage can occur after parathyroid cyst drainage, with potentially serious complications. Ethanol ablation is an emerging non-surgical therapeutic option.

**Abstract #720**

**PREDICTORS OF PERMANENT HYPOPARATHYROIDISM AFTER TOTAL THYROIDECTOMY IN A SINGLE TERTIARY INSTITUTION**

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**Objective:** Postoperative hypocalcemia is the most common complication following total thyroidectomy (TT). Predicting patients at risk for permanent hypoparathyroidism (PHypoP) may allow for early discharge and appropriate management after TT. Risk factors for developing hypoparathyroidism have been studied, but not clearly defined. We conducted a retrospective study to evaluate if postoperative PTH and calcium levels in TT patients are predictive of permanent hypoparathyroidism.
Methods: We reviewed charts of 250 post-thyroidectomy patients (215F/35M, 52±13 yrs, 101C/11AA/115H/21other race) with thyroid cancer from 1999 to 2013. We analyzed data of 176 patients after excluding for missing follow up (n=72) or outlying data (n=2). PHypoP was defined as patients with persistently low PTH level (iPTH <12 pg/mL), low calcium level (serum calcium <8.0 mg/dL), and/or requiring calcitriol to maintain a normal calcium level for more than six months after TT. For further stratification, patients were divided into four groups based on immediate post-op values: 1. Low PTH, Low Calcium; 2. Low PTH, Normal Calcium; 3. Normal PTH, Low Calcium; 4. Normal PTH, Normal Calcium.

Results: 30/176 (17.0%) patients developed PHypoP. This group did not differ from the non-PHypoP group in terms of age, sex, or race. There was a significant percentage drop in PTH (69.7% vs 29.7%, p=0.016) and in calcium (17.8 % vs 14.3%, p=0.042) after surgery in the PHypoP vs non-PHypoP groups. Further, a significantly higher percentage of Group 1 (Low PTH, Low Ca) developed PHypoP (30.3%, p=0.0007) compared to 19.4% in Group 3, 10.0% in Group 2, and 2.0% in Group 4. The odds ratio of Group 1 developing permanent hypoparathyroidism was 4.3 (95% CI=1.9, 9.9) compared to the other groups. Preoperative calcium, PTH, and Vitamin D levels did not predict PHypoP.

Discussion: Having both low iPTH and Ca in the immediate post-op period after TT increased the risk of developing PHypoP. The percentage drop in the pre vs postoperative levels of serum PTH and calcium was also predictive of PHypoP.

Conclusion: This study highlights the importance of obtaining both preoperative and postoperative PTH and calcium levels in total thyroidectomy patients to assist in predicting patients at risk for developing permanent hypoparathyroidism and managing the postoperative course appropriately.

Abstract #721

ENDOCRINOLOGY FELLOW IN THE ERA OF TELEMEDICINE: AN ACADEMIC CENTER QUALITY INITIATIVE

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University of Massachusetts Medical School

Objective: Endocrinology Fellows at our institution, like many across the country, are frequently on call. Yet, few specialties prepare trainees on how to take telephone call. Calls that are answered are usually patient generated concerns or urgent inpatient consultations. For patients, a phone conversation with a covering provider who is not familiar with their care is often dissatisfying. Additionally, excessive non-urgent calls to Fellows after-hours could lead to increased workload, sleep deprivation & decreased well-being; which is a high priority for the ACGME. Our aim with this quality initiative was to analyze the frequency & nature of after-hours calls to Endocrinology Fellows at our institution; & to streamline patient care to their primary Endocrinologists, whenever appropriate.

Methods: IRB determination of 'Not Human Research' was obtained. The On-Call Endocrinology Fellows logged calls that came to them 5p-8a on workdays & through the weekends. They logged the date & time of call, the reason for call & then marked the call as to whether they deemed it to be urgent or non-urgent. Between July & August 2017, 100 calls were logged. We then sought to implement interventions to help direct appropriate patient care to the clinic during work hours.

Results: Average calls per 24 hours was 1.6. Of all calls-47% were marked non-urgent by the Fellows. 24% of all calls came in between 8p–3a. In terms of reasons for calls: 17=insulin refills, 13=test strip refills, 9=insulin pump failure, 14=hyperglycemia, 9=hypoglycemia, 9=insulin regimen concerns, 9=non-insulin medication refills, 5=thyroid related medication concern, 4=test result requests, 6=reports of fever/rashes & 5=inpatient consults.

Discussion: Fellows didn’t log some calls that came during busy inpatient service days, reflecting that average call per 24 hours is likely higher. Majority of the calls (~40%) were for refills; that could have been directed to the clinic previously. Our ongoing interventions include patient education to request refills 3 business days ahead of need & to call during work hours for test results. We are also reminding providers to ask for script refills during clinic visit & to discuss appropriate blood glucose thresholds with their patients that warrant an after-hours call. Another thought was to implement triage services such as nurses, who have been shown to help with after-hour calls.

Conclusion: Our after-hours call logs reflected that many calls to the Endocrinology Fellows were not urgent & could have been directed to the clinic. Our ongoing interventions would allow patients to continue to receive care from their primary Endocrinologists & to decrease the work burden on Fellows. Results from these are pending.
Abstract #722

CORRELATES AND ASSOCIATION OF VITAMIN D LEVELS IN PATIENTS DIAGNOSED WITH H1NI – SWINE FLU VIRUS

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Objective: It has been well documented that a Hypovitaminosis D has been linked to poor immunity and susceptibility to infections. Tuberculosis has seen a cause and effect relationship. In the recent outbreak of influenza A and in particular H1N1 variant, we tried to look for this correlation in viral infections. In fact, vitamin D deficiency can precipitate the influenza virus. Influenza A incidence has been documented to be less in Vitamin D3 supplemented group with the benefits being lost over a period resulting in enhanced risk despite adequate supplementation.

Methods: We measured the Vitamin D levels in patients diagnosed positive with H1N1 virus (Swine flu) in 16 patients admitted to a tertiary care centre over a time span of 3 months. Also, other comorbidities were looked for and noted. In particular diabetes and other endocrine dysfunctions were enlisted.

Case Presentation: There were 10 females and 6 males. The mean age of the patients were 49 years (min 19 yrs-max 76 years, 95% CI 39-58). The mean Vitamin D levels were 23ng/ml (min 3 – max 79; 95% CI 9.5-37). The levels of Vitamin were typically low in comorbidity of type 2 diabetes mellitus and hypothyroidism.

Discussion: We observed a peculiar deficiency of Vitamin D in our series of patients diagnosed and admitted for H1N1 positive swine flu. All patients with co morbid endocrine issues like diabetes and hypothyroidism had more marked deficiency. We recommend that the patients be tested and treated with bolus dose for vitamin D deficiency to prevent exacerbation of a respiratory infection. This is useful from the preventive angle for the predisposed population in a susceptible season.

Conclusion: We postulate that the Vitamin D supplementation could act as an immunotherapy and help alleviate the immunomodulation providing a progressive early recovery in H1N1 positive - swine flu patients. Routine testing and supplementation should be the aim especially in those patients who are having diabetes and other comorbidities.

Abstract #723

ADMINISTRATION OF EXOGENOUS TESTOSTERONE AS A NEW KIND OF SEXUAL ABUSE: BROADENING THE DIFFERENTIAL FOR CLITOROMEGALY

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Objective: In the treatment of clitoromegaly, surgical correction alone may be inadequate and may also lead to future problems regarding psychological development and gender identity. Here we present a case of clitoromegaly that resulted from administration of exogenous testosterone in an effort to change the child’s gender. This case highlights the effects of androgens on psychological play behavior, and the ethical dilemmas of gender assignment.

Case Presentation: A 21-month-old female presented for evaluation of clitoromegaly. Her grandmother brought her to the clinic and reported that she showed substantial weight gain, increased appetite, and voice deepening. The patient’s growth curves for height, weight, and BMI had increased from below the 15th percentile to above the 85th percentile in one year. Physical examination revealed significant clitoromegaly of 60 mm with protuberant labia majora but no labia minora (Prader classification of III–IV). Laboratory tests revealed a total testosterone level of >2000 ng/dL, DHEA-S of <15 µg/dL, and 17-OHP of <10 ng/dL. Chromosomal analysis was positive for 46 X,X. It was then discovered that the patient had been administered Androgel for a total of 14 months by the patient’s grandmother’s boyfriend, who wanted to change the child’s gender, and who was eventually convicted. The grandmother desired the patient be treated by surgical correction. However, further questioning revealed that the patient was already identifying herself as a boy. Therefore, it was decided to closely monitor the patient’s psychological and physical progression to prevent future social isolation, relationship difficulties, and further address problems with sexual identity.

Discussion: Androgen exposure in female children at a young age can influence psychological play behavior to resemble that of male children. They are observed to play with toys that are generally preferred by males, such as trucks and cars, and tend to prefer males as playmates. Even after surgical correction, these children tend to continue playing with toys that are preferred by males, and have higher risks of gender dysphoria, and an increased incidence of future gender identity conflicts.

Conclusion: This case illicitates that prescribing androgens to family members with young children has to be done with caution. Endocrinologists must also be
familiar with the complexity of gender assignment at a young age in order to prevent future problems related to sexual and emotional maturity. Further analysis of psychological development in these patients may lead to better assessment of gender identity disorder and methods for improving quality of life in this patient population.

Abstract #724
TRIPHASIC RESPONSE FOLLOWING RESECTION OF CRANIOPHARYNGIOMA- A CLASSICAL CASE
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Objective: Patients undergoing pituitary surgery can develop disorder of sodium and fluid balance. Insufficiency of antidiuretic hormone (ADH) levels leads to Central Diabetes Insipidus(CDI) whereas excess leads to SIADH. Water balance disorders can also develop in a Biphasic or even Triphasic fashion with reported incidences of 3.4 and 1.1%, respectively. Triphasic Response is interesting but often challenging to manage. We present a case of severe hypernatremia and hyponatremia after resection of a craniopharyngioma.

Case Presentation: A 70-year-old male underwent resection of craniopharyngioma. Postoperatively, he developed CDI with sodium levels of 155 mEq/L. He was treated with single dose of desmopressin with the resolution of CDI. On Day 7, he developed hyponatremia (124mEq/L) without any behavioral or neurological symptoms. He was then admitted to hospital where his work up revealed diagnosis for SIADH with high urine osmolality and low serum osmolality. Fluid restriction and sodium chloride tablets were started with gradual improvement of his sodium levels to 133mEq/L on the postoperative day 10. 3 days later, he was again readmitted due to high sodium level of 161mEq/L. Diagnosis of CDI was made and he was started on nasal desmopressin with improvement in his sodium levels to 145 mEq/L over the course of next 2 days which was maintained.

Discussion: In the 1st phase of the triphasic response, manipulation of the pituitary stalk leads to interruption of ADH release and ADH deficiency manifesting as CDI. It presents with excessive thirst, polydipsia, polyuria and dilute urine. Frequent monitoring of fluid intake, urinary output and serial serum sodium, urine specific gravity, and osmolality should be done for prompt recognition of the condition. When severe, DI should be managed with desmopressin (DDAVP). The 2nd Phase of triphasic response is transient SIADH, developing 4-10 days postoperatively, characterized by hyponatremia. Mild hyponatremia should be managed with fluid restriction whereas severe or symptomatic hyponatremia requires aggressive management with fluid restriction, hypertonic saline and/or vaptans. This is followed by 3rd Phase of Triphasic response, characterized by the return of CDI which can be permanent. Management depends on the phase, and it is important not to overtreat the first phase of DI, which can result in severe hyponatremia during the potential subsequent SIADH phase.

Conclusion: Triphasic response following pituitary surgery is relatively underdiagnosed. Frequent and continued monitoring with a goal to prevent frank dysnatremia and associated mortality followed by appropriate management is of utmost importance.

Abstract #725
PARATHYROIDECTOMY REVERSES IMPAIRED QUALITY OF LIFE ASSOCIATED WITH PRIMARY HYPERPARATHYROIDISM
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Objective: Primary hyperparathyroidism (pHPT) is associated with multiple non-specific symptoms such as fatigue, body aches, and neurocognitive symptoms which can impair health-related quality of life. Unfortunately, investigations examining the impact of parathyroidectomy on these subjective symptoms have been limited in size, standardization, and scope, preventing many clinicians from recommending surgery based upon symptoms alone.

Methods: A well-studied, validated, health-related quality-of-life survey, the 36-item Short Form Survey (SF-36), was employed on patients undergoing parathyroidectomy for primary hyperparathyroidism. Patients completed the survey one week preoperatively and three months postoperatively.

Results: During the 1-year study period ending August 2017, 774 patients (79% female; mean age 61±9 years; mean highest calcium 11.1±0.9; average PTH 104±53) completed both the preoperative and postoperative SF-36. Preoperatively, mean quality of life scores in all eight domains (general health, physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy, emotional well-being, social functioning, and bodily pain) were significantly below known USA national averages. Postoperatively, all eight domains showed statistically significant improvement (p<0.001 for all), increasing to rejoin their expected national norms. The most dramatic improvements occurred in the domains of limitations due to physical health with mean scores of 41±22 preoperatively increasing to 76±36 postoperatively, (p<0.001), limitations due to emotional...
problems (55±43 pre vs. 87±29 post, p<0.001), and energy (34±21 pre vs. 62±23 post, p<0.001).

**Conclusion:** Primary HPT is associated with significant impairments in quality of life across both physical and mental domains. Parathyroidectomy produces significant improvements within three months, allowing patients to recover to national norms. Given these improvements, non-specific symptoms that affect quality of life may be considered a valid indication for parathyroidectomy, even in the absence of more objective disease manifestations.

**Abstract #726**

**PROPOSAL OF A NEW DIAGNOSTIC NOMECLATURE FOR A DISTINCT CLINICAL ENTITY OF QUARTERNARY HYPERPARATHYROIDISM**

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NIH

**Objective:** To propose a new nomenclature for distinct form of hyperparathyroidism that has clinical and biochemical features that does not fully encase either tertiary or secondary hyperparathyroidism.

**Methods:** Our patient is 50 year-old male with Sickle Cell Disease with HbSS genotype, complicated with end-stage kidney disease. He underwent cadaveric kidney transplant in 2008, failed 6 years later due to rejection since been on hemodialysis three times a week. His home medications included Renvela 1600 mg per meal 3 times a day, Sensipar 60 mg once a day, Hydroxyurea 500 mg once a day, Megestrol 800 mg daily, among other medications.

Patient was admitted to our center for bone marrow transplant in September of 2017. Two months later, patient started to develop numbness in his hands, and was found to have persistent hypocalcemia along with hyperphosphatemia. His hypocalcemia symptoms did resolve with supplemental IV calcium. His Magnesium level was normal. Patient was found to have profound elevation of PTH and endocrinology was consulted for ‘Hyperparathyroidism’. We discontinued Sensipar due to the presence of hypocalcemia and assumed underlying secondary physiologic process and the patient was treated with Calcitriol 0.25 mcg daily along with Calcium Carbonate 1250 mg three times a day with full resolution of his symptoms and normalization of calcium levels.

**Case Presentation:** Before therapy: Initial PTH: > 5000 pg/mL, Calcium level ranged 6.6-7.3 mg/dL, Ionized Calcium ranged between 0.71-0.94 mmol/L with normal venous PH. Magnesium ranged within normal limit between 0.9-1 mmol/L, Phosphorus ranged between 3.9 to 6 mg/dL, 25-Vitamin D: 29 ng/mL and 1,25 Vitamin D < 5 pg/mL.

After therapy: PTH level decreased in physiologic pattern but still elevated at 1362 pg/mL, Calcium level normalized to around 8.88 mg/dL, Magnesium ranged within normal limit between 0.9-1 mmol/L and Phosphorus levels remained elevated with range of 3.6 to 5 mg/dL.

**Discussion:** This patient hyperparathyroidism carries some features of tertiary hyperparathyroidism such as the presence of PTH level> 1000, presence of hyperphosphatemia in the setting of ESRD. However, symptomatic hypocalcemia is a mark of secondary hyperparathyroidism. Therefore, we believe this patient has secondary over tertiary hyperparathyroidism, therefore, the treatment should be personalized for this specific case, and to increase awareness and to better identify it in other patients, we propose considering “Quaternary Hyperparathyroidism” as a new nomenclature of this clinical entity.

**Conclusion:** Quaternary Hyperparathyroidism is a new clinical entity that has biochemical features of secondary over tertiary hyperparathyroidism, and requires different management.

**Abstract #727**

**A SYSTEMIC ERROR CAUSES MAJOR PROBLEMS IN USING ELECTRONIC HEALTH RECORDS (GARBAGE IN GARBAGE OUT: GIGO)**

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**Objective:** To evaluate the utility of a commercial Electronic Health Record (EHR) to study the epidemiology of type 2 diabetes mellitus (T2DM)

**Methods:** Michigan State University Centricity Business and Health Team database was evaluated for the period 2003-2016 to identify individuals with new onset T2DM. The search strategy was simple: identify patients seen at least twice, once when there was no diabetes-related code (250.xx) and a subsequent visit when there was.

The search strategy was simple: identify patients seen at least twice, once when there was no diabetes-related code (250.xx) and a subsequent visit when there was. A random selection of individuals from this dataset were reviewed to determine: if patients have newly diagnosed T2DM, how many were diagnosed by lab tests obtained for symptoms c/w diabetes. How many were diagnosed on random blood tests?

**Results:** We identified 5058 visits for 2529 patients. Of these 57 were reviewed showing 25 of 57 (44%) were incorrectly classified. 18/25 (72%) The case was incorrectly coded at a previous visit, patients with diabetes had not been assigned a 250.xx code.

In 5/25 (20%) evolution of the diagnostic process e.g.
inclusion of A1c or changes to fasting plasma glucose led to reclassification.

2 Patients (8%) without history or labs consistent with diabetes were “mysteriously” given a 250 code.

**Discussion:** The MSU EHR is a flawed tool for epidemiological research but is unlikely to be unique. The cause appears to be human error and the process of data entry either by clinicians or ancillary personnel (including EHR company transcribers). Three reasons, likely will intensify this move towards increasingly useless databases. First, we are mandated to upgrade from paper charts to EHR which involves manual review and transfer of codes from paper charts to the computerized records. Second, with the introduction of ICD-10, there are many more diagnostic codes, the increased work involved leads to inadequate compliance. Third, many sites are changing EHR providers and again data is transferred manually from one product to another. This problem is likely to go unnoticed by the clinician. It is, a major problem if an attempt is made to obtain data for epidemiological research or other purpose (performance). Probably the best we can do is prevent new errors being propagated indefinitely (consider our patients identified as having diabetes, a diagnosis with no basis in reality). There is little we can do about inactive diagnoses which have been “lost in translation”.

**Conclusion:** The EHR has a serious systemic flaw, any interface where humans are required to input data. This likely happens on a daily basis but, as we have suggested, is probably most intense when records are being entered in large quantities when an EHR is first introduced or being replaced. We suggest, on an infrequent basis, comprehensive chart audits be performed.

**Abstract #728**

**RECURRENT HYPERCALCEMIA SECONDARY TO SARCOIDOSIS IN THE SETTING OF CHRONIC LITHIUM THERAPY**

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**Objective:** Lithium therapy may lead to mild hypercalcemia by indirectly increasing the secretion of PTH, with hypercalcemia usually resolving after cessation. However, more than one cause may contribute to a lab abnormality. We report a case of recurrent hypercalcemia in the setting of chronic lithium therapy found to have sarcoidosis.

**Case Presentation:** 52 year old female with bipolar disorder (treated with lithium for over 10 years), hypothyroidism and nephrolithiasis was evaluated for hypercalcemia. She developed vomiting along with lethargy and was found to have a serum calcium of 13.8 (8.4-10.5 mg/dl) with creatinine 1.6 (0.5-1.2 mg/dL). Additional labs demonstrated PTH 17 (15-65 pg/ml), PTHrP 1.5 (<2 pmol/L), 25-vitamin D 10.2 (32-100 ng/ml), 1,25-vitamin D 61.6 (19.9-79.3 pg/ml), lithium 0.6 (0.5-1.2 mmol/L) and TSH 0.81 (0.27-4.20 mU/L). No previous personal or family history of hypercalcemia was known. During kidney stone workup in 2006, calcium was 9.4 with PTH 37 and fractional excretion of calcium 0.0099. Lithium and levothyroxine doses were stable. She received IV fluids and pamidronate, resulting in improvement of symptoms and decrease of calcium to 10.6. She was taking 1000 IU cholecalciferol daily, which was discontinued after that admission. She was lost to follow-up. 4 months later, her symptoms recurred with calcium of 12.9 and PTH 8. Pamidronate was administered and divalproex was substituted for lithium. DXA demonstrated no evidence of decreased bone mineral density. She had no exposure to endemic mycoses or tuberculosis. She denied dyspnea on exertion or lymphadenopathy but described intermittently present small cutaneous nodules on her knee and nose. Angiotensin converting enzyme level was elevated at 142 (14-82 U/L) and 24 hour urine calcium was 153 (110-250 mg/24h). Chest X-ray demonstrated bilateral prominent interstitial lung markings. Biopsy revealed sarcoideal granulomatous dermatitis. Two months after cessation of lithium, calcium decreased to 10.2 with PTH 9.

**Discussion:** Sarcoidosis can cause hypercalcemia via upregulated 1a-hydroxylase activity. This results in increased conversion of calcidiol to calcitriol in activated mononuclear cells. Lithium can increase serum calcium by interfering with calcium sensing receptor (CaSR) signaling. This case is unusual as our patient was treated with lithium therapy for over 10 years with normal calcium levels in the past. She developed hypercalcemia in the setting of new onset sarcoidosis, with resolution after discontinuation of lithium.

**Conclusion:** It is important to maintain a broad differential to avoid overlooking potential coexisting etiologies, even with obvious explanations available.
Abstract #729

A RARE CASE OF PSEUDO-PSEUDOHYPOPARATHYROIDISM INVOLVING BILATERAL THIRD AND FOURTH SHORT METACARPAL BONES

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Case Presentation: Pseudo-pseudohypoparathyroidism (pseudo-PHP) is a disease characterized by a constellation of clinical features collectively termed Albright hereditary osteodystrophy (AHO), but no evidence of resistance to parathyroid hormone (PTH). AHO displays various features including short stature, round face, short metacarpal bones, obesity and subcutaneous calcification. Exact epidemiology is unknown. A 55-year-old female came to our clinic secondary to chronic intermittent pain in her hands. Her past medical and family history was unremarkable. On physical examination, her vitals were within normal range. Examination of hands showed bilateral short 3rd and 4th metacarpal bones. There was no localized tenderness, swelling, or limited range of motion. The patient denied any trauma to her hands. The rest of the musculoskeletal examination was normal. The patient had short stature and she didn’t reach the mid parental height. Laboratory tests showed WBC 6900/µL, hemoglobin 13.6 g/dL, platelet count 309,000/µL, erythrocyte sedimentation rate 4 mm/h, creatinine 0.9 mg/dL, calcium 8.9 mg/dL, phosphate 3.5 mg/dL, vitamin D, 25-hydroxy 53 ng/mL and parathyroid intact 37.8 pg/mL. Plain radiographs of the hands and wrist showed bilateral, symmetrical shortening of 3rd and 4th metacarpal bones. Our patient met most of the criteria of Pseudo-PTH including normal calcium, phosphate and parathyroid, intact level along with classic clinical and imaging findings of 3rd and 4th bilateral short metacarpal bones.

Discussion: Pseudo-PHP can be considered as an entity only when it is considered within the context of more common disease of PHP. PHP involves abnormal chemical finding including hypocalcemia and hyperphosphatemia in the presence of elevated parathyroid hormones compared to pseudo-PHP, having normal chemical findings. PHP is secondary to mutation of GNAS1, a gene encoding the alpha subunit of the G protein. Maternal transmission of mutation is involved in PHP as compared to paternal transmission of the mutation in Pseudo-PHP. Clinical features including short stature, obesity, round faces along with musculoskeletal findings could be present in either of the disorder. Inheritance is autosomal-dominant. The diagnosis of Pseudo-PHP depends on the presence of features of AHO along with normal serum calcium, phosphate and PTH levels. No specific treatment available. Conclusion: Pseudo-PHP is not life threatening with overall good prognosis. However, detailed clinical examination and family history can help in diagnosing this rare syndrome, which has an autosomal dominant transmission. Genetic counseling should be offered to affected families as multiple family members can have this syndrome.

Abstract #730

POST-SURGICAL HYPOPARATHYROIDISM WITH NORMOCALCEMIA IN PREGNANCY

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Objective: Serum calcitriol (1,25(OH)D) level can be maintained during a normal pregnancy by non-parathyroid hormone (PTH) mediated mechanisms. We present a case of a pregnant woman with severe primary hyperparathyroidism who developed PTH suppression after parathyroidectomy during the second trimester of pregnancy. Serum calcium remained normal with undetectable PTH level up to 6 weeks after surgery.

Case Presentation: A 27-year-old woman at 22 weeks gestation presented to the hospital with vomiting and decreased intake. She had multiple admissions for hyperemesis gravidum and 2 months of depressed mood with generalized muscle aches. Physical examination was unremarkable. Initial workup showed calcium 14.2 mg/dl (12.4 – 13.1 mg/dl in the last 6 weeks), PTH 188 pg/ml and PTHrP <1 pg/ml. 24-hour urine calcium was 1,008 mg/day. Neck ultrasound revealed 1.2 x 1.8 x 1.1 cm hypoechoic mass along inferior right thyroid. Primary hyperparathyroidism was diagnosed. She underwent partial parathyroidectomy. Pathology confirmed parathyroid adenoma. Post-operatively, PTH was <3 pg/ml. Supplemental calcium and Vitamin D were initiated when serum calcium level normalized. On discharge, calcium was 10.4 mg/dl. Frequent monitoring post-discharge showed suppressed PTH and normal calcium. She was maintained on oral calcium 600 mg daily. 6 weeks post-surgery, laboratory testing showed PTH <3 pg/ml, calcium 10.8 mg/dl, phosphorus 3.6 mg/dl, Vitamin D 28 mg/ml and 1,25(OH)D 112 pg/ml (normal range 20 – 62.5 pg/ml). We plan to continue serial calcium and PTH level monitoring.

Discussion: This case illustrates the role of non-PTH mediated mechanisms in calcium homeostasis during pregnancy. The non-PTH mediated increase in serum 1,25(OH)D may be regulated by pregnancy hormones such as PTH-related protein (PTHrP), prolactin, estrogen and placental growth hormone in addition to the placental
production of 1,25(OH)D. Our patient developed severe suppression of PTH level after surgery, likely related to the severity and chronicity of her primary hyperparathyroidism, however she maintained normal calcium and phosphorus levels. This can be explained by the fact that her 1,25(OH)D was elevated. After birth, calcium level is likely to decrease within 24 – 48 hours unless there is a full recovery of parathyroid function. Monitoring and supplementation with exogenous calcitriol will be required.

**Conclusion:** Post-surgical hypoparathyroidism during pregnancy can be masked as a result of increasing production of calcitriol by non-PTH hormones or directly from placenta. After delivery, calcium level is likely to decrease if PTH level is not restored. Therefore, closed monitoring is important to reduce morbidity.

**Abstract #731**

**AGGRESSIVE PITUITARY MACROADENOMA AND ELEVATED BLOOD SUGARS; AN ATYPICAL PRESENTATION**

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**Objective:** We present an atypical presentation, of a growth hormone producing, aggressive pituitary macroadenoma with severe insulin resistance induced by corticosteroids with lack of the typical features of acromegaly/gigantism.

**Case Presentation:** A 25-year-old male with no previous history of diabetes who presented 8/2017 with 2-month history of vision loss in right eye. Head CT revealed a large mass in the sella/suprasellar anterior cranial fossa with cavernous sinus extension with mass effect and resultant obstructive hydrocephalus. He underwent surgery, and pathology stained for GH, prolactin, and α-subunit. However, prolactin was mildly elevated at 29 ng/mL. He was lost to follow up and presented 11/2017 about 2 months later with blurry vision in left eye, vision loss in right eye, worsening headache, nausea and vomiting. The lesion had increased in size compared to prior CT of 8/12/207. He was also started on high doses of steroid, Decadron 4mg every eight hours, and monitored closely in the ICU. His blood sugars in the ICU ranged from 200-300s while receiving 20 units/hr via insulin drip per the ICU glycemic protocol parameters. Despite receiving 480 units in 24 hours, his blood sugars remained in the 200-300 range. He has no clinical signs of acromegaly or growth hormone excess. He also has no family history of diabetes, or other endocrine disorders.

He had a complete pituitary hormone panel tested. This included ACTH, cortisol, IGF-1, growth hormone, prolactin, and gonadotropins. His IGF one level was 796 ng/mL, and his growth hormone was 44 ng/mL. He had an oral glucose tolerance test, at which baseline GH level was 61ng/mL, suppressed to 46 ng/mL. A1c was 5.9%. He had normal calcium levels.

**Conclusion:** There are several interesting aspects to the presentation of this patient. 1) Although GH producing tumors usually present with skeletal features related to GH excess, this patient presented with severe insulin resistance, brought to surface with the use of steroids. This suggests that people with severe insulin resistance with steroids may have an underlying pathology which could lead to that degree of insulin resistance. 2) In cases of aggressive pituitary macroadenoma producing GH, despite lack of clinical manifestations including bony deformities, increased height, and facial features, suggest that the tumors have relatively short duration compared to more indolent tumors. Although growth hormone producing pituitary tumors may present with typical presentation, a high degree of suspicion should be kept with presence of severe insulin resistance, even if induced by steroids or potentially other medications.

**Abstract #732**

**ALTERED MEASURES OF GONADAL FUNCTION AND GLUCOSE HOMEOSTASIS AFTER EPIDURAL TRIAMCINOLONE INJECTION IN MEN**

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**Objective:** We have previously reported inhibition of the corticotropic function after epidural injection of triamcinolone, and dispersion of triamcinolone to the peripheral circulation. The latter is presumed to have other endocrine/metabolic consequences, which were assessed in the present report.

**Methods:** 12 men (ages 25-63 years) were studied at baseline, as well as 1, 4, and 12 weeks after epidural injection of triamcinolone (80mg). Total testosterone (Te: ng/dL), LH (µIU/mL) and FSH (µIU/mL), SHBG (nmol/L, glucose (mg/dL), insulin (µIU/mL), and hsCRP (mg/L) were measured in the blood samples collected at each visit. Free and bioavailable testosterone (bio-Te) were calculated using an XL-based software. Serum insulin and glucose concentrations were used to calculate insulin resistance (HOMA-IR) and beta cell function (HOMA-β). Measures of gonadal function and hs-CRP were available in only 8 subjects.
**Results:** At week 1 after epidural triamcinolone injection, there were significant decreases in total Te (189 ± 25 v 89 ± 14: p < 0.01), free Te (4.2 ± 0.7 v 2.2 ± 0.4: p < 0.01), bio-Te (96 ± 8.2 v 48 ± 9: p < 0.01), and SHBG (27 ± 2 v 22 ± 1.6: p < 0.01), and associated increases in LH (5.7 ± 0.8 v 3.4 ± 0.3: p < 0.01), and FSH (5.8 ± 0.9 v 4.2 ± 0.6: p < 0.05). Measures of glucose homeostasis were significant for increased insulin (20 ± 3 v 13 ± 2: P < 0.05), HOMA-IR (5.2 ± 0.8 v 3.2 ± 0.5: P< 0.05), and HOMA-β (220 ± 47 v 148 ± 21: P < 0.05), without significant change in serum glucose concentrations (99 ± 5 v 104 ± 6: P = NS). Circulating levels of hs-CRP decreased from 4.2 ± 1.8 to 0.72 ± 0.17 (P < 0.01). All values at week 4 were comparable to the baseline.

**Discussion:** Decreased levels of CRP underscores a systemic effect of the epidurally injected triamcinolone on the liver. Similar peripheral glucocorticoid effect is observed at the level of the pancreas, with augmented β-cell function, offsetting the steroid glucogenic effect and therefore maintaining normoglycemia. Increased insulin release is presumed to cause the decrease in SHBG, resulting in lower total Te concentrations. In addition, association of blunted free and bioavailable Te with increased LH and FSH may imply a direct testicular effect of triamcinolone, as well.

**Conclusion:** The results in this study are highly suggestive of peripheral effects of epidurally injected triamcinolone in the liver, pancreas β-cell, and possibly testes. Such functional consequences are transient and tend to recover at the latest 4 weeks after triamcinolone administration. The findings have significant clinical implication, and warrant awareness among practitioners, in order to avoid premature clinical judgments.

**Abstract #733**

**HYPERCALCEMIA AS THE INITIAL MANIFESTATION OF IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN AN AIDS PATIENT ON HAART THERAPY IN THE SETTING OF MYCOBACTERIUM AVIUM COMPLEX INFECTION**

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**Objective:** Granulomatous diseases are a well-known cause of hypercalcemia from the production of calcitriol by macrophages. We report a case of hypercalcemia in Acquired Immunodeficiency syndrome (AIDS) patient from immune reconstitution inflammatory syndrome (IRIS) after initiation of highly active antiretroviral therapy (HAART) in the setting of Mycobacterium Avium Complex (MAC) infection.

**Case Presentation:** A 36-year old African American man was recently diagnosed with AIDS in 4/2017 after an episode of Pneumocystis jiroveci pneumonia. His CD4 count was undetectable and HIV viral load was 675186 copies/ml. In August, before HAART therapy could be initiated, he had another episode of pneumonia. CT chest, abdomen and pelvis showed ground glass peribronchiolar opacities and periaortic lymphadenopathy. HAART therapy was begun late August. Two weeks of initiation of HAART, CD4 count was up to 19 cells/uL and HIV RNA was down to 666 copies/ml. Cultures from this admission grew MAC seven weeks later and treatment was initiated. On November 6, he was admitted with a newly discovered corrected calcium of 15.9 mg/dl (8.4-10.3) with polyuria and polydipsia. His corrected calcium levels were normal from April through September ranging from 9.4-10.2 mg/dl. On this admission, his creatinine was mildly elevated at 1.4 mg/dl but resolved with hydration. Phosphorous was elevated at 6.2 mg/dl (2.3-4.7), PTH was low at 4.6 pg/ml (9-73), 25(OH) vitamin D low at 20.4 pg/ml, 1,25(OH)2 vitamin D was high normal at 69 pg/ml (18-72). He was treated with hydration and Pamidronate 30mg IV. His calcium remains in the 11.0-11.9 mg/dl range one month later.

**Discussion:** IRIS can cause paradoxical worsening of preexisting infections from the restoration of immune function in patients initiated on HAART. Clinical manifestations could occur anywhere from one to four months after treatment has begun. Our patient became hypercalcemic in two months after starting HAART. The suppressed PTH and elevated calcitriol support pathological 1-alpha hydroxylation of calcidiol to calcitriol by macrophages in the setting of granulomatous infection with MAC. Tests for Cryptococcus, Histoplasma, Mycobacterium tuberculosis were negative. No other clinical data was suggestive of sarcoidosis. Immunofixation electrophoresis showed faint IgG lambda clone and UPEP showed no monoclonal light chains excluding other possible causes of hypercalcemia.

**Conclusion:** Hypercalcemia could be the initial manifestation of IRIS in an AIDS patient started on HAART. Clinicians should be aware of this potential complication when initiating HAART. Bisphosphonates or glucocorticoids are useful in the treatment depending on the severity of hosts immunocompromised status.
Abstract #734
MINERALOCORTICOID RESPONSIVE HYponatREMia OF THE ELDERLY: AN EMERGING ENTITY
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Objective: We describe a case of an under-recognized, underreported and emerging entity, Mineralocorticoid Responsive Hyponatremia of the Elderly (MRHE).

Case Presentation: An 82 year old woman was admitted for elective repair of a thoracic aneurysm and successfully underwent endovascular repair. A history of chronic hyponatremia of unclear etiology, with sodium levels in the range of 128-133 mEq/L, maintained on fludrocortisone 0.1 mg on alternate days, for 2 years, was reported. Post-operatively, she developed acute on chronic hyponatremia with a sodium level of 126 mEq/L from 129 mEq/L on admission. She was euvolesmic on physical examination. Fludrocortisone was held to avoid hypertension in view of recent vascular surgery. Thyroid function tests were normal and adrenal insufficiency was ruled out. Laboratory results, notable for serum osmolality of 267 mmosm/kg, urine osmolality of 348 mmosm/kg and urine sodium of 93 mEq/L/24hours, were initially attributed to syndrome of inappropriate antidiuretic hormone secretion (SIADH). However, with fluid restriction, hyponatremia did not improve and in fact worsened to a sodium level of 124 mEq/L. Demeclocycline was initiated, with an improvement in sodium to 130 mEq/L. Her sodium remains in the range of 130-132 mEq/L on demeclocycline 300mg BID.

Discussion: Fludrocortisone has been previously described in the management of hyponatremia in cases of cerebral salt wasting disorder. However, MRHE is an emerging concept and is not well defined. The cases to date have only been reported by Japanese investigators. Recently, a Japanese systemic review proposed the following diagnostic criteria: age> 60 years, laboratory findings of SIADH with worsening hyponatremia on fluid restriction, clinical hypovolemia and correction of hyponatremia with fludrocortisone. Age related hypo-responsiveness of the renin-angiotensin-aldosterone system, leading to increased urinary sodium loss, mild hypovolemia and elevated antidiuretic hormone (ADH), is thought to be the possible mechanism. Demeclocycline impairs the action of ADH on renal collecting tubules, therefore dilutes the urine and raises serum sodium. Our patient possibly responded to demeclocycline due to the secondary excess of ADH.

Conclusion: It is important to differentiate MRHE from SIADH due to the difference in management. It should be suspected in a case of SIADH which worsens with fluid restriction. In order to better define, understand and treat this entity, more cases should be reported to build stronger evidence based literature.

Abstract #735
A RARE CAUSE OF HYPERCALCEMIA
Natalia Burgos
HMC

Case Presentation: Serum calcium concentration is tightly regulated by bone resorption, parathyroid hormone regulation, calcium absorption by the gut and vitamin D effects. The causes of hypercalcemia can be divided into two common etiologies which are primary hyperparathyroidism and malignancy. Even though these etiologies account for 90% of the causes, the differential diagnosis is much more extensive.1 This case presents a patient who presented with a non PTH mediated hypercalcemia secondary to a predominant inflammatory state.

This is the case of a 57-year-old gentleman with past history of controlled diabetes mellitus type 2 on oral agents with A1c of 6.6, hyperlipidemia, and obesity who had presented to the ED with a 1-month history of weight loss, persistent daily fever and dysphagia. He was noted to have high grade fever, thrombocytosis and a retropharyngeal mass. Extensive evaluation was unrevealing as such he was diagnosed with fever of unknown origin. Patient had a prolonged hospital course with no clear etiology of his pharyngeal mass. He was eventually diagnosed with hemaphagocytic lymphohistiocitosis (HLH) Patient was started on treatment with Etoposide and steroids. Subsequently during his hospitalization, he developed hypercalcemia. Corrected calcium levels started to trend upwards with highest value reported at 12.1. Patient underwent evaluation for hypercalcemia and was found with low PTH levels at 12.6, PTHrp of 0.2 and vitamin D 1,25 levels low at 18.7. Patient was also seen to have elevated alkaline phosphatase at 290.He was thus given one dose of Zolendronic acid 4mg IV and calcium levels were then maintained between 8.0 to 8.9.

Discussion: The rare causes are important to be considered in instances when underlying hypercalcemia can not be attributed to primary hyperparathyroidism or overt malignancy. This patient’s non-PTH mediated hypercalcemia does not seem to be related to PTHrp or 1,25 vitamin D levels activity as is described as the mechanism in patients with hematologic malignancies. Given this patient was diagnosed with HLH and this condition is associated with increased cytokine activity, a possible differential of persistent hypercalcemia could be a cytokine mediated process. The literature does describe
that hematologic conditions could stimulate osteoclast-mediated bone resorption by activation of factors such as IL-1, IL-6 and TNF.

**Conclusion:** The extensive list of differential diagnosis and their association demonstrate that the pathogenesis of some of these conditions is still not well understood. For this reason, it is important to maintain under consideration the rarer causes of hypercalcemia when evaluating for this.
PITUITARY DISORDERS

Abstract #800

UNCONSUMMATED MARRIAGE AS THE PRESENTING FEATURE OF MALE MACROPROLACTINOMA

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Objective: Unconsummated marriage (UM) is a medical and sociocultural problem, encountered mainly in conservative Middle Eastern societies. The objective of this case report and literature review is to emphasize the multifactorial origins of sexual dysfunctions and the importance of assessing both biological factors and psychosocial factors in cases of UM.

Methods: A 36 year-old Caucasian male presented with his wife to a sexual medicine clinic for a 2 months history of UM. The couple came from a conservative sociocultural background. Several psychological factors including but not limited to lack of experience, fear of failure, sexual inhibition, and conjugal conflicts were reported during the initial evaluation. Laboratory findings revealed hormonal disturbances.

Case Presentation: Endocrine investigations revealed low serum T, elevated PRL, and a pituitary macroadenoma with compression of the optic chiasma. Treatment with a dopamine agonist significantly improved Prolactin levels and the adenoma size, but not Testosterone levels. The addition of a temporary Testosterone replacement therapy allowed a matrimonial consumption and vaginal penetrative sex.

Conclusion: Male macroprolactinoma manifesting as an unconsummated marriage is a rare event that responds readily to treatment. Serum PRL should be measured in men presenting with an unconsummated marriage associated with decreased desire or and erections difficulties. A multidisciplinary management is recommended in cases of UM.

Abstract #801

PERSISTENT ERECTILE DYSFUNCTION FROM SECONDARY HYPOGONADISM IN A PATIENT WITH A PROLACTIN-SECRETING MACROADENOMA

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Sovah Health - Danville

Objective: Our objective is to report a case of a 52 year old male presenting with persistent erectile dysfunction (ED) in the setting of testosterone deficiency, who was subsequently found to have a prolactinoma.

Case Presentation: A 52 year old male with a history of testosterone deficiency and ED presented to the medicine clinic with concerns about right breast tenderness, which he said had been a problem for over a year. He has also had low testosterone and ED for 2 years. He did occasionally use sildenafil, but admitted that this did not improve his ED. On examination, he had noticeable bilateral gynecomastia and tenderness on palpation of the right breast with no nipple discharge able to be expressed. Due to his gynecomastia and medication refractory ED, we decided to investigate his hypothalamic-pituitary-adrenal (HPA) axis. His luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH) were all within normal limits. His total testosterone level was low at 158.7 ng/dL (190-780 ng/dL). His serum prolactin level was greater than 1000 ng/mL (2.5-17.4 ng/mL). We proceeded with a brain MRI, which showed a 1.2 cm in diameter right pituitary macroadenoma with no displacement of the optic chiasm. We placed him on cabergoline 0.25 mg twice weekly and referred him to an endocrinologist. He is now on 0.50 mg twice weekly and tolerating the medication well, along with noticed improvements in his ED and gynecomastia. His most recent total testosterone and prolactin levels are 791 ng/dL and 23.2 ng/mL, respectively.

Discussion: A prolactinoma is a benign tumor of the pituitary gland that produces excess prolactin. Hyperprolactinemia can cause hypogonadism, resulting in amenorrhea, galactorrhea, gynecomastia, or ED. Symptoms can also be caused by a mass effect of the tumor, such as headaches or visual field defects. Medical management with dopamine agonists (bromocriptine or cabergoline) is preferred over transsphenoidal tumor resection. Cabergoline was chosen in our patient due to its more tolerable side effects, compared to bromocriptine. Dopamine agonists decrease the tumor size and subsequently decrease the serum prolactin levels. They can also reverse secondary hypogonadism, which improves ED and gynecomastia, as seen in our patient. After two years of normal serum prolactin levels and no evidence of the adenoma on MRI, the medication can be discontinued.

Conclusion: Since prolactinomas can cause secondary
hypogonadism, it is important to consider the HPA axis, including prolactin, TSH, LH, and FSH levels in male patients with ED (especially in the setting of testosterone deficiency). Then, if necessary, a brain MRI should be obtained to investigate for a prolactinoma.

**Abstract #802**

**POSSIBLE ROLE OF PROLACTIN IN DYSFUNCTIONAL UTERINE BLEEDING**

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Alexandria University

**Objective:** Regulation of menstrual cycle depends not only on proper FSH and LH, but also on normal prolactin level. Hyperprolactinemia is a common finding in patients with reproductive disorders from menstrual irregularities to anovulation. The aim of the study was to evaluate the serum prolactin level in patients having dysfunctional uterine bleeding (DUB) in relation to histopathological pattern of endometrium

**Methods:** Fifty patients diagnosed as DUB, all were subjected to full and complete history, examination and routine laboratory investigations. Serum prolactin level were estimated and endometrial biopsy were done under general anaesthesia. the curetage sent for histopathological examination

**Results:** The mean prolactin level was 32.70 ng/ml, 68% of the patients had hyperprolactinemia. Perimenopausal patients had a significantly higher prolactin than younger patients. The acyclic bleeding recorded in 34 cases, it was cyclic in 16. Patients with endometrial hyperplasia were found to have significant higher prolactin (43.14 ng/ml) than patients with proliferative endometrium (26.92 ng/ml) and the other types of endometrium (25.80 ng/ml). Galactorrhea was found only in 22% of patients

**Discussion:** Hyperprolactinemia may be the primary abnormality in DUB, which with hyperplasia might have been estrogen induced by unopposed estrogen stimulation. There was a link between hyperplasia and high prolactin level, while galactorrhea was not an essential feature of DUB. Also ,hyperprolactinaemia may be in a part due to endometrial prolactin synthesis

**Conclusion:** Whether hyperprolactinaemia is the cause or an association to acyclic DUB, it seems that this category of bleeding deserves evaluation of prolactin status before planning for medical therapy. Further investigations are recommended on a larger sample of patients

**Abstract #803**

**PHENOTYPIC AND METABOLIC IMPROVEMENTS IN A PATIENT WITH EQUIVOCAL FINDINGS OF HYPERCORTISOLISM TREATED WITH MIFEPRISTONE: PHOTOGRAPHIC AND RADIOGRAPHIC EVIDENCE**

Michael Thomas, MD, PhD, FACE, ECNU1, James Smith, PhD2

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**Objective:** Hypercortisolism is diagnosed when evidence of elevated cortisol and HPA axis dysregulation are coupled with radiological evidence of a source. However, many patients endure years of damaging metabolic and cardiovascular effects related to hypercortisolism before receiving definitive diagnosis and appropriate treatment. A common challenge faced by clinicians is the discrepancies between biochemical test results and clinical suspicion based on patient presentation. This case describes a patient with equivocal biochemical testing and negative imaging who benefitted from medical therapy with mifepristone (MIFE, Korlym®, Corcept Therapeutics), a competitive glucocorticoid receptor (GR) antagonist.

**Case Presentation:** A 59-year-old female patient was seen in 2012 for evaluation of sub-centimeter thyroid nodules with normal thyroid function tests. Her weight was 63.5 kg, BMI 24.8 kg/m2, and her BP was 162/85 mmHg. She returned 2 years later citing fatigue, hair loss, and weight gain despite diet and exercise. Overnight DST was considered normal at 0.7 µg/dL but a random morning cortisol level was elevated 1 month later (31.3 µg/dL) and UFC had reached the upper limit of normal within 3 months (50 µg/24 hr). Subsequent biochemical testing showed 2 elevations in UFC at the upper range of normal, 2 normal UFCs, 4 elevated random AM cortisol tests along with 2 normal DSTs. Pituitary MRI was normal and adrenal CT showed mild bilateral nodular fullness. Five years after first presenting, she had progressed to prediabetic. Her weight and BMI had increased to 68.6 kg and 26.9 kg/m2 respectively, and she developed facial plethora and an enlarged dorsocervical fat pad shown by serial spinal imaging. With no definitive diagnosis of Cushing Syndrome (CS), but with a deteriorating metabolic and phenotypic etiology along with testing suggestive of biochemically less severe hypercortisolism, the patient was given a therapeutic trial of MIFE (300mg/d for 2 weeks and 600mg/d thereafter). Within 1 month, metabolic parameters improved. Within 3 months, FG improved to 95 mg/dL consistent with improved insulin resistance, weight decreased to 65 kg and the patient reported a significant improvement in cushingoid
appearance and mood. 

**Conclusion:** The diagnosis of hypercortisolism can be challenging. Equivocal biochemical results sometimes do not align with the patient’s clinical presentation and the clinician’s suspicion, which may prevent patients from receiving intervention. The approval of mifepristone, an oral GR antagonist that is used in many patients with CS, presents a potentially effective treatment option for patients with hypercortisolism.

**Abstract #804**

ENDOCAN EXPRESSION CORRELATES WITH POOR PROGRESSION-FREE SURVIVAL IN PATIENTS WITH PANCREATIC NEUROENDOCRINE TUMORS

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**Objective:** Endocan (endothelial cell specific molecule-1; ESM-1) expression has been reported to be associated with aggressive tumor progression and poor outcomes in various tumors derived from the lung, kidney, brain, astrocytes, and liver. However, the prognostic value of endocan in neuroendocrine tumors remains unknown. Thus, the aim of this study was to determine the correlation between endocan expression in pancreatic neuroendocrine tumor (PNET) tissues and progression-free survival.

**Methods:** This study included 73 patients with PNETs who were treated in a tertiary center in Taiwan between 1992 and 2015. Immunohistochemical endocan expression and microvessel density (MVD) were examined, and the relationships between these parameters and other clinicopathological characteristics were analyzed. The aforementioned patients were divided into groups according to their endocan expression levels (≥1% or <1%) and median MVDs.

**Results:** Negative endocan expression (p=0.002) and a high MVD (p<0.001) were significant and favorable prognostic factors for progression-free survival (Figure 1). However, positive endocan expression was significantly associated with a low MVD (p=0.037) and tumor mitosis (Ki-67 index) (p=0.028). Multivariate Cox regression analysis showed that positive endocan expression (hazard ratio: 4.778, p=0.018) and lymph node involvement (hazard ratio: 5.121, p=0.005) were independent prognostic factors for tumor recurrence.

**Discussion:** We demonstrated that endocan may have potential as a new prognostic marker for PNETs and there is a strong correlation between endocan expression in tumor tissues and unfavorable prognoses in PNETs. Endocan has been reported that overexpression of endocan increased HEK 293 cells proliferation and facilitated tumor growth. We found that a high MVD was a favorable prognostic factor for progression-free survival and that endocan expression levels were negatively correlated with MVD. Endocan is expressed normal endocrine tissues characterized by a high vascular density. However, all the normal islets of Langerhans analyzed herein displayed negative endocan expression, suggesting that endocan is involved only in tumor mitosis in PNETs. Finally, we performed Cox regression analysis to identify the risk factors for tumor recurrence and found that endocan expression and tumor lymph node involvement are independent risk factors for recurrence.

**Conclusion:** Endocan expression was correlated with poor clinical outcomes in PNETs. Our data suggested that endocan expression could be a reliable marker for prognosis in patients with PNETs.

**Abstract #805**

ACUTE ON CHRONIC PITUITARY INSUFFICIENCY – A NEAR FATAL MISS

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**Objective:** The time constraint in busy emergencies sometimes prevent physicians from performing detailed examination. Examination of axilla and genitalia gets neglected. Relevance of this thorough clinical examination is highlighted in this case where a female presented as acute febrile illness did not respond to treatment & had cardiac arrest. When revived and reexamined she did not have axillary & pubic hairs. Diagnosis of pituitary insufficiency (PI) made & confirmed. She responded remarkably to steroid and thyroxine replacement.

**Case Presentation:** 45 year female presented to busy medical emergency when Dengue epidemic had gripped the city with fever, weakness & decreased oral intake for 10 days. Except amenorrhea for 5 years no significant past history. Examination drowsy, confused, pulse 68/min, BP 100/70 mmHg, temperature 99.9F, pallor, bilateral pedal edema present. Thyroid normal. CNS: No motor weakness, neck rigidity. Bilateral ankle, knee jerks not elicited. Bilateral plantars extensors. Liver 4 cm, mild ascites. Lab: Hemoglobin: 8.5 g/dL, TLC: 4800, DLC: N 57, L 40, E1, M 2, Platelet 1.5x106, MCV 76fL, Na+ 114
ABSTRACTS – Pituitary Disorders/Neuroendocrinology

meq/L, K+ 2.7 meq/L, Blood glucose 86 mg/dL, calcium 8.2 mg/dL, phosphorous 2.0 mg/dL. Paracetamol and injection ceftriaxone started with presumptive diagnosis of enteric fever/dengue/viral. Patient did not respond over next 2 days and had cardiac arrest. She was revived but her consciousness remained altered. Reexamination revealed absent axillary and pubic hairs. Diagnosis was revised and possibility of panhypopituitarism was kept. Hydrocortisone 100 mg every 8 hrly I/V and thyroxine 200 microgram through Rylestube started. Dengue serology, malarial antigen and serum widal negative. FT3: 0.95 pg/ml, FT4: 0.43 ng/dl, TSH 4.99 mIU/ml, S Cortisol 1.12 ug/dl, FSH: 2.76 mIU/ml, LH: 1.19 mIU/ml, Prolactin: 8.19 ng/mL, Estradiol: 5.0 pg/mL, Vit D 4 ng/mL, MRI head revealed empty sella. Patient became conscious and oriented. Discharged on prednisolone 7.5 mg and thyroxine 100 microgram.

Discussion: PI caused by adenoma, surgery, cranial radiation, trauma, subarachnoid hemorrhage, postpartum pituitary necrosis, infiltrative diseases and lymphocytic hypophysitis. Presentations of PI vary from an asymptomatic to comatose. No history suggestive of any causative disease was available in this patient. Signs of hypogonadism, empty sella and hormonal profile confirmed the diagnosis of PI. Lymphocytic hypophysitis may be probably the underlying etiology in this case. Anti-pituitary antibodies not done.

Conclusion: PI is life threatening emergency. In absence of relevant history diagnosis may be missed. This case reiterates the importance of thorough clinical examination as early institution of replacement can be life saving.

Abstract #806

A CASE OF A DOPAMINE SECRETING PARAGANGLIOMA UNDETECTED ON INITIAL URINE METANEPHRINE AND CATECHOLAMINE TESTING

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Objective: We discuss a case of a dopamine secreting paraganglioma with diagnosis initially undetected on 24 hour urine fractionated catecholamines but subsequently made with plasma fractionated catecholamines.

Case Presentation: A 54-year-old woman with sudden onset severe occipital headache was found on CT angiogram of the head and neck to have two right sided neck masses: a 3.5 cm glomus vagale tumor and a 1.2 cm carotid bifurcation lesion. Twenty-four hour urine fractionated metanephrines were normal and catecholamines showed slightly elevated norepinephrine (73 ug/d, ref 16-71 ug/d) and normal epinephrine and dopamine levels. After alpha and beta blockade, a 1 cm carotid body paraganglioma was successfully resected but there was incomplete resection of the larger glomus vagale mass. Upon follow up, she had persistent tachycardia with orthostatic hypotension off alpha and beta blockers. Fractionated plasma catecholamines showed elevated dopamine 200 pg/mL (reference range <30 pg/mL) that was confirmed on repeat testing. Repeat 24hr urine metanephrines and catecholamines were normal. A second resection was considered but was felt to have unacceptable morbidity so she underwent radiation therapy that resulted in normalization of plasma dopamine levels, heart rate, and blood pressure. She had a paternal half-brother and paternal cousin who had paragangliomas. Genetic testing revealed she was heterozygous for a pathogenic SDHD gene mutation.

Discussion: Dopamine secreting paragangliomas are extremely rare with about 50 reported cases. Patients don’t have the classic triad of palpitations, headache, and sweating frequently leading to delayed diagnosis. However, dopamine secreting paragangliomas are important to recognize because of their increased likelihood for malignancy compared to other paragangliomas and need for close biochemical and imaging follow up. We describe a case of two synchronous paragangliomas secreting excess dopamine on plasma fractionated catecholamines but without elevation in urine catecholamines. Current guidelines recommend plasma free metanephrines or urine fractionated metanephrines as the initial biochemical workup for paragangliomas. These tests do not measure dopamine. This case highlights how using these tests alone for evaluation of paragangliomas could lead to a missed diagnosis. This case also demonstrates successful normalization of dopamine levels with radiation therapy.

Conclusion: Dopamine secreting paragangliomas are rare but have an increased risk for malignancy. Measurement of plasma free metanephrines or urine fractionated metanephrines will miss this diagnosis. Plasma free catecholamines should be considered as an additional test in the evaluation of paragangliomas.
Abstract #807

PITUITARY DYSFUNCTION IN GRANULOMATOSIS WITH POLYANGIITIS

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Objective: Granulomatosis with polyangiitis (GPA) is a necrotizing granulomatous vasculitis of small vessels that can affect the pituitary gland in less than 1% of cases, being exceptionally rare. The study aimed to describe the clinical, biochemical and radiological findings of 3 patients with GPA-related hypophysitis. Treatment and outcomes are also discussed.

Methods: Clinical data of patients diagnosed with granulomatosis with polyangiitis (formerly Wegener’s disease) were revised from 1981 to 2017 at a third level specialty center. A cross-sectional retrospective review of those patients with pituitary dysfunction are described.

Case Presentation: We found 197 patients with GPA. From them, 3 (1.52%) showed pituitary involvement. Two patients started with diabetes insipidus together with the GPA clinical manifestations. One of them, also showed central hypogonadism. The radiology studies showed pituitary stalk thickness with normal gland, and diffuse pituitary enlargement, respectively. Both cases received prednisone (1 mg/kg), cyclophosphamide (10 mg/kg) and azathioprine. Diabetes insipidus persisted in the first case, however, pituitary function was recovered and GPA activity persisted with good control. The third case presented with headache, and central hypocortisolism 6 years after GPA was diagnosed. MRI showed pituitary enlargement and pituitary stalk thickness without adenoma nor diabetes insipidus. Treatment used for GPA was with prednisone and azathioprine. At follow-up, the patient continues with prednisone to treat central hypocortisolism.

Discussion: GPA can cause partial or complete involvement of the pituitary gland and infundibulum. It has been reported that hypogonadism and diabetes insipidus are the main manifestations of this condition, presented in one of our cases. Although there is a consensus on the use of steroids and cyclophosphamide in these patients, it has been seen that pituitary hormonal deficiencies usually persisted as seen in two of our cases. Therefore, pituitary dysfunction is difficult to recover despite systemic remission of GPA. Although rituximab has been used in refractory cases, pituitary hormone replacement therapy is also needed permanently.

Conclusion: Although GPA represents an uncommon cause of pituitary dysfunction, it is of great importance to consider it for early diagnosis and therapy in order to avoid chronic hypopituitarism even after remission of the systemic condition.

Abstract #808

NORMETANEPHRINE SECRETING PARAGANGLIOMA DIAGNOSED IN A HYPOTENSIVE PATIENT

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University of Florida

Objective: To present the case of a patient with paraganglioma (PGL) with an unusual clinical presentation which posed a challenge in terms of diagnosis and optimal preoperative management.

Methods: We reviewed clinical, laboratory, imaging and pathology data.

Case Presentation: A 41 year-old female, with sickle cell disease, presented for further evaluation and management of a retroperitoneal mass. This was diagnosed incidentally few years prior on abdominal CT scan. It was monitored radiographically for growth by her hematologist. Additional work-up was not done due to lack of signs or symptoms suggestive of hormone excess. She was referred to our tertiary care facility for management. Tumor was 3.5x3.7x4.2cm in size and was described as having “irregular borders and heterogeneous with an area of central necrosis”. She had non-specific symptoms of mild weight loss and occasional palpitations. Vital signs were significant for blood pressure 90-104/60-73mmHg and heart rate of 99-110, and low BMI (16kg/m2) which were at baseline.

Hormonal work-up was significant for elevated plasma normetanephrine (1902pg/ml, normal<145). Patient had refused to have urine testing for catecholamines. Based on the combination of severely elevated plasma normetanephrine along with the radiographic characteristics and tumor location, the diagnosis of PGL was made.

Preoperative management proved to be challenging considering baseline hypotension. Patient could not tolerate low dose doxazosin despite increased oral hydration and salt intake. The patient was hospitalized for intravenous hydration with normal saline bolus before each dose of the medication and telemetry monitoring. Doxazosin 0.5mg daily was started and increased to 0.5mg twice daily. Systolic blood pressure was low (SBP 80s-90s) but patient remained asymptomatic. One week later patient underwent...
surgical resection of the tumor successfully. Surgical pathology confirmed PGL that was 5.2 cm in its largest dimension with lymphovascular invasion and spread to 1/7 lymph nodes. Genetic testing is pending.

**Discussion:** The etiology of her hypotension may involve several factors such as dehydration and anemia. Although difficult to confirm in this case, another presumed factor for hypotension may involve the effects of dopamine which can affect aldosterone secretion, natriuresis, and inhibit vasocostriction effects of norepinephrine.

**Conclusion:** Identifying a patient with a catecholamine-secreting tumor that is hypotensive is challenging and not intuitive. Once diagnosis is established, a multidisciplinary approach is often necessary to optimize preoperative status and thus reduce perioperative morbidity and mortality.

**Abstract #809**

**PITUITARY METASTASIS CAUSING POLYURIA – A RARE CASE OF CENTRAL DIABETES INSIPIDUS**

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Marshall University

**Objective:** Central diabetes insipidus (CDI) can be the only symptom of pituitary metastasis. Pituitary metastasis is rare, accounting for 1-2% of cases. Here is a presentation of a man with metastatic small cell lung cancer (SCLC) who presented with polyuria and polydipsia.

**Case Presentation:** A 57-year-old man with recently diagnosed metastatic SCLC to liver and brain presented to the hospital for chemotherapy initiation. He was diagnosed with SCLC few months prior and had just completed 3 weeks of whole body radiation. Recent brain MRI with and without contrast showed multiple cerebral and sellar lesions. He reported 2 months history of constant thirst and micturition >30 episodes daily, which also interfered with his nighttime sleep. He stated that these symptoms had negatively affected his quality of life. Physical examination was unremarkable. Laboratory work-up showed sodium 144 mEq/L, urine osmolality 86 mOsm/kg and serum osmolality 291 mOsm/kg. Urine output was > 6 L in 18 hours. CDI was confirmed and he was given Desmopressin 1 mcg subcutaneous. Within 24 hours of therapy, he reported a significant improvement in his symptoms and urine osmolality increased to 440 mOsm/kg. He was discharged home on Desmopressin while undergoing chemotherapy with serial chemistry monitoring to ensure adequate sodium levels. He reported significant decrease in frequency of micturition and polydipsia at his follow up visits. Unfortunately, he died a few months later due to overwhelming disease burden.

**Discussion:** CDI is a condition characterized by vasopressin deficiency causing hypotonic polyuria and polydipsia. The pathophysiology is due to interruption in axons of the hypothalamic-posterior pituitary pathway. Common etiologies are central nervous system (CNS) tumors, infiltrative disease, neurologic procedures/trauma. Pituitary metastases are rare and commonly arise from breast and lung malignancies. Very few cases of CDI caused by pituitary metastasis from small cell lung cancer have been reported in the literature. CDI can result in morbidity with associated poor quality of life as seen in our patient. Most patients have a good thirst mechanism, which allows them to compensate for the excess micturition. If this is disrupted, hypernatremia can occur and detrimental if not diagnosed early. The primary treatment of CDI due to metastasis is Desmopressin. Patients with pituitary metastasis have a poor prognosis as it reflects severe and high disease burden.

**Conclusion:** An increased awareness of the potential of CDI occurring in patients with pituitary metastasis is needed. Early diagnosis and treatment can significantly reduce morbidity and improve quality of life.

**Abstract #810**

**TRANSITION OF CARE IN ENDOCRINOLOGY: ADULT CLINIC PERSPECTIVE AT UNIVERSITY COLLEGE LONDON**

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1. University of Michigan, 2. University College London Hospital

**Objective:** Multiple challenges of transition, including poor transfer of records from pediatrics to adult clinics, dearth of adolescent psychology and reproductive programs, force adolescents with pituitary dysfunction and hypogonadism to follow with pediatric endocrinologists for many years after reaching adulthood. Combined pediatric/adult endocrine clinics and transferring information to adult clinics before first visit are few methods used to transition care. There is not enough literature to access the effectiveness of each technique. Disjointed care can have negative implications for the health and quality of life of these patients.

**Objectives:** A, Identify social factors affecting compliance in adult endocrine clinics; B, Assess transition issues including referral methods and quality of transfer documentation
**Methods:** Medical records of 100 transitioning patients in a dedicated endocrine clinic for young adults at University College London Hospital were reviewed for referral information, attendance at visits, transition issues and social factors. Independence of variables was measured by Chi Square Test and P < 0.05 was considered significant.

**Results:** Mean age was 21.6+/−4.1 years (58% males, 42% females). In adult clinic, 99% of the patients came for 1st visit once scheduled. Attendance decreased subsequently; 59% at 2nd visit, 29% at 3rd, 10% at 4th and 4% at last visit. Attendance was higher if patients were not living independently (50 vs. 14, p=0.1) or seen with parents (62 vs 24, p=0.1). Fifty percent of the patients have transition issues but only 30% were related to poor documentation. Higher education did not play a role in improving compliance. When presence at 2 visits was compared with presence at > 2 visits, social security benefits entitlement predicted poor compliance (8 vs. 35, p=0.02).

**Discussion:** In majority of cases, either internal or external referral, quality of documentation was good. Compliance dropped significantly during long term follow up. For obvious reasons, poor socioeconomic status was associated with decreased attendance. We observed improved compliance if patients were not living independently and were seen with their parents even though it did not reach statistical significance.

**Conclusion:** We concluded that while previous guidelines have highlighted the impotence of promoting young adult independence during the process of transition from pediatric to adult care, parental involvement in the early stages of this process seems to optimize compliance. On the other hand, we also observed that psychosocial history is affected by this presence thus requiring careful management.

Abstract #811

**MANAGEMENT OF A RECURRENT PARAGANGLIOMA IN PREGNANCY**

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**Objective:** In pregnant patients with a paraganglioma, alpha blockade in preparation for surgery is considered adequate once orthostasis is achieved. We present an unusual case of a recurrent bladder dome paraganglioma in which alpha blockade was undermined, but was resected in the second trimester without complications.

**Case Presentation:** A 30 year old G2P0010 female in her 19th week of pregnancy, who underwent resections of two prior recurrences of infrarenal paragangliomas, presented for evaluation of hypertension. Vital signs showed BP 173/105, HR 121, RR 18, and Temperature 98.8 F. On examination, she was anxious, worried and had a tachycardic heart rate. Laboratory tests completed 3 weeks prior to admission showed plasma normetanephrines of 2.30 nmol/L (0-0.89 nmol/L), 24-hour urine normetanephrines of 1188 ug/d (109-393 ug/d), and 24 hour urine dopamine of 392 ug/d (77-324 ug/d). MRI abdomen without contrast revealed a 2.7 cm bladder dome mass, suspicious for a recurrent paraganglioma. She was then admitted for medical therapy in preparation for surgical resection. She was initiated on doxazosin 2 mg daily with a plan to increase the dose until orthostasis and nasal congestion was achieved. Salt and fluid intake was liberalized in her diet. Labetalol was added 7 days after admission. Patient’s BP slowly decreased in the supine position, however, upon sitting or standing, her BP rose above 140/90. This was attributed to fetal activity against the bladder dome causing internal irritation of the paraganglioma, resulting in catecholamine release. Therefore, after titrating doxazosin to a maximum dose, patient was deemed adequately prepared for surgery. She underwent successful resection in her 21st week of pregnancy without post-operative hypotension or cardiac instability.

**Discussion:** The purpose of alpha blockade prior to surgery is to expand plasma volume and block the effects of released catecholamines to prevent toxic cardiovascular effects. This therapy has been reported to have a lower maternal and fetal mortality when compared to those with no alpha blockade, although this has remained controversial. Conversely, asymptomatic, normotensive patients have been studied to have no benefit to alpha blockade prior to surgery. This patient’s case illustrates that medical therapy can be beneficial and that adequate alpha blockade should be determined in an individual, case-by-case basis.

**Conclusion:** An Endocrinologist’s role in management of paraganglioma includes identifying and optimizing medical therapy prior to surgery. Thus, Endocrinologists must recognize the complexity of this disease and analyze each case without generalization, to improve patient care and mortality.
Abstract #812

**IPILIMUMAB INDUCED LYMPHOCYTIC HYPOPHYSISITIS**

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**Case Presentation:** Background: Hypophysitis is a rare, but known side effect of Ipilimumab, an immune checkpoint inhibitor. Headache is a common but serious manifestation of hypophysitis and patients will need MRI to determine the presence of hypophysitis. Patients will require high dose steroids to treat the hypophysitis, and tapering the dose too quickly can lead to recurrence of symptoms.

Case: We present a case of a 36 year old woman with history of T4N1aMx left thigh melanoma in March 2017, who underwent wide local excision, and was subsequently put on Ipilimumab. She presented with left sided headache, fatigue, and a fever for 3 days, and also reported increased thirst and polyuria. Patient underwent an MRI of the brain on October 8, 2017 which revealed diffuse expansion of the pituitary gland and inferior sella with homogenous signal intensity, which likely represented lymphocytic hypophysitis. It did not reveal any metastatic disease in the brain and no intracranial hemorrhage or infarction. Prior to initiation of Ipilimumab, baseline MRI showed a thickened enhancement along the tentorium on the left side representing a meningioma, but no evidence of lymphocytic hypophysitis. Surprisingly, on admission, the levels of TSH, free T4, FSH, LH, IGF-1, cortisol, and ACTH were all within reference ranges. Patient did not have above labs drawn at baseline prior to commencing treatment with ipilimumab. Patient was discharged with prednisone 100 mg/day, which was tapered to 80 mg/day a week after the discharge. Following the decrease in the prednisone, patient was readmitted with fever and headaches, which was attributed to the decrease in the prednisone dose. The plan was for the patient to be transitioned to Nivolumab, however given her lymphocytic hypophysitis, it was not certain if she would be transitioned. The patient was readmitted with prednisone dose. The plan was for the patient to be transitioned to Nivolumab, however given her lymphocytic hypophysitis, it was not certain if she would be transitioned.

**Conclusion:** The incidence of hypophysitis in the general population is less than 1%. For patients treated with immune checkpoint inhibitors, the incidence of hypophysitis is between 0 to 17%, still a rare side effect. Prompt recognition of hypophysitis for patients on immune checkpoint therapies is necessary to prevent life threatening complications. Patients will require prolonged course of high dose steroids to treat the hypophysitis, and tapering the dose too quickly can lead to recurrence of symptoms. Baseline endocrine labs should be obtained prior to starting patients on ipilimumab. It is uncertain if transitioning to a different checkpoint inhibitor like nivolumab can improve the symptoms for patients presenting with hypophysitis.

Abstract #813

**ADULT ATYPICAL SELLAR TERATOID TUMOR PRESENTING AS DIABETES INSIPIDUS**

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Henry Ford Health System

**Objective:** Atypical teratoid /rhabdoid tumor (ATRT) is a rare and aggressive central nervous system tumor that usually occurs in childhood but has rarely been reported in adults. We were able to identify 50 reported adult cases, 12 of which were sellar. We report a case of adult sellar ATRT who died within 2 months of presentation with headaches, visual deficits, polyuria, and polydipsia. Our case aims to highlight the importance of considering ATRT in the differential of sellar masses especially in adults presenting with rapid progression of symptoms.

**Case Presentation:** A 62-year-old female was transferred to our institution for management of a pituitary mass. Her symptoms developed over 2 months, starting with daily headaches, nausea, followed by polyuria, polydipsia and finally double vision. She had left 6th nerve palsy on admission. She was diagnosed with central hypothyroidism with rapid progression of symptoms.

**Histopathological study revealed malignant epithelioid neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consistent with ATRT infiltrating the pituitary gland and fibrocollagenous stroma. The neoplasm, consisten**
of sellar ATRT are headaches and visual symptoms. DI has not been previously reported and increased the suspicion for a non-adenoma etiology in our patient. Definite diagnosis is based on immunohistochemical features. Treatment modalities in adults include surgery, chemotherapy and radiotherapy. ATRT should be considered in the differential for patients with sellar masses presenting with atypical features or rapid progression. Early recognition and aggressive combination therapy is reported to be associated with improved outcomes.

Abstract #814

HYPOPHYSITIS IN NON-AUTIMMUNE HYPERTHYROIDISM. CASE REPORT AND DIFFERENTIAL DIAGNOSIS.

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Objective: It is estimated that from 7% to 56% of patients with autoimmune thyroid disease may present anti-pituitary antibodies, while its prevalence in those with non-autoimmune thyroid disease ranges between 0 and 6%. There are few case reports of hypophysitis in conjunction with hyperthyroidism, being in these cases lymphocytic hypophysitis the most frequent primary cause and, in male patients of the seventh decade of life, IgG4 hypophysitis the predominant secondary cause.

Methods: A 62-year-old male presented fatigue, asthenia, adynamia, and muscle weakness that impeded ambulation. Three months after the onset of symptoms, he started abruptly with polyuria and polydipsia. His MRI study showed an increase in the volume of the gland; absence of hyperintensity of the neurohypophysis in simple T1 and a thickness of the hypophyseal stem of 8 mm. Upon physical examination the patient was cachectic. There was no ophthalmopathy. Neck and thyroid examination was normal, with no data of goiter or nodules. Hyperthyroidism was corroborated by the laboratory data as follows: FT4 1.77 ng/dl, TT4 17.39 μg/dl, TT3 1.85 ng/ml, TSH 0.02 mIU/l, Tg 9.74 ng/ml, FSH 0.80 mIU/ml, LH 0.94 mIU/ml, testosterone 0.20 ng/ml, prolactin 25.17 ng/ml, GH 0.244 ng/ml, IGF-I 91.62 ng/ml. The results of screening tests for other causes of hypophysitis were negative and are shown below: PPD test negative, β-microglobulin 1.84 mg/l, βhCG 0.26 mIU/ml, α-fetoprotein 2.93 ng/ml, carcinoembryonic antigen 1.69 ng/ml and ACE 28.5 U/L.

Discussion: Lymphocytic hypophysitis has been reported in Graves’ disease, as well as in the other autoimmune thyroid diseases, and it is known that these groups of patients usually have positive titers of anti-pituitary antibodies even in the absence of hypophysitis. Hence, IgG4 disease can manifest with isolated hypophysitis, as well as associated with autoimmune or non-autoimmune thyroid disease.

Conclusion: This case report highlights the infrequent association between hypophysitis and thyroid disease from which autoimmunity could not be verified. The differential diagnosis in these cases can be difficult, however due to the epidemiology, with the age group of the patient we suspected IgG4 disease with a seronegative Graves’ disease.

Abstract #815

THE FACES OF METABOLIC ENCEPHALOPATHY

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Objective: Metabolic derangements in severe cases can present with cardio- respiratory compromise or neurologic symptoms such as confusion, coma, seizures or focal neurologic deficits. Clinical features and laboratory data are often sufficient to confirm a diagnosis. When neurologic symptoms predominate the presentation, imaging studies can be helpful. We report two cases of MRI findings related to hypoglycemia and Wernicke’s encephalopathy.

Case Presentation: CASE 1

57-year-old African American female with diabetes mellitus type 2, managed with insulin therapy, who was found unresponsive at home for an undetermined duration of time and brought to the emergency room by family. She had been in her usual state of health 12 hours prior. Initial serum glucose was 29 mg/dl, and she was treated with intravenous dextrose. Serum glucose rapidly improved, however her mentation slowly improved over the next 72 hours. MRI of the brain showed crescentic restricted diffusion within the posterior aspect of the splenium of the corpus callosum, characteristic of hypoglycemic encephalopathy.
CASE 2
44-year-old Caucasian male with a history of alcohol abuse and diabetes insipidus secondary to traumatic head injury who had presented with hypothermia (27 degrees Celsius) secondary to prolonged environmental exposure, after being found down on the ground. He had associated hypotension, acute respiratory failure, and encephalopathy. Hypotension improved and pressor support was discontinued within 24 hours. Mental status did not improve significantly. He required prolonged mechanical ventilation and experienced recurrent episodes of hypothermia (32-33 degrees Celsius), despite intermittent external warming, stress dose steroids and empiric antibiotics. MRI of the brain showed generalized cerebral atrophy and marked atrophy of the medulla and visualized upper cervical cord, unusual for patient’s age and subtle increased signal intensity on FLAIR imaging within the medial aspect of the thalamus bilaterally concerning for Wernicke’s encephalopathy. High dose intravenous thiamine was started with dramatic clinical improvement as encephalopathy resolved, body temperatures normalized and mechanical ventilation was no longer needed.

Conclusion: Although imaging studies are often not required in making a diagnosis of metabolic encephalopathy, they may be helpful determining severity and in excluding other alternate diagnoses when the clinical course is complicated.

Abstract #816

UNUSUAL CASE OF METASTATIC NEOENDOCRINE CANCER PRESENTING AS PITUITARY MASS

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Objective: Metastasis to the pituitary gland is unusual, seen in approximately 1-2% of pituitary masses. We report a case of high grade metastatic neuroendocrine (NE) cancer of unknown primary presenting as pituitary mass with cranial nerve palsies.

Case Presentation: 74-year-old lady with 15 pack year smoking history presented to ED with rapidly progressive worsening right eye vision over 14 days. She endorsed intermittent headaches, 25-pound unintentional weight loss over 8-month period. Denied polyuria or polydipsia. Examination was significant for right sided ptosis, right cranial nerve III, IV and VI palsies, palpable left thyroid nodule and cervical lymph nodes (LN). MRI brain showed 1.2 x 2.2 x 1.2 cm enhancing lesion in the sella, extending into the right cavernous region and abutment of the optic chiasm. Thyroid Ultrasound showed multiple nodules, with a 4.8 x 3.7 x 2.9 cm large left sided solid nodule with coarse calcifications and necrotic cervical LN. CT chest, abdomen, pelvis showed 2 cm left lung nodule with multiple necrotic LNs in the chest, abdomen and pelvis. Pituitary function test showed prolactin 45.1(5.2-26.5 ng/ml), cortisol 7.9 MCG/DL, ACTH 36.4(<=45.9 pg/ml), GH 1.18(0.01 - 8.00 ng/ml), FSH 2.90 (26.72-133.4 mIU/ml), LH 0.54 (5.16 – 61.99 mIU/mL), TSH <0.01(0.35 - 4.94 mIU/L) and Free T4 2.03(0.70 - 1.48 ng/dL).

Pt underwent trans-sphenoidal resection and decompression of the pituitary mass. Pituitary pathology showed high-grade NE carcinoma with bone invasion. Histopathology suggested GI, renal, and ovaries as primary origins. FNA of the thyroid nodule was benign. Cervical LN biopsy was positive for poorly differentiated NE cancer. 3-week post-op, MRI of the brain showed increase in the size of mass within the sella with extension into bilateral cavernous sinuses. Gamma knife radiation was started for enlarging tumor.

Conclusion: Pituitary metastasis (PM) is rare. NE cancer metastasis to pituitary is even more unusual and on review of literature very few cases have been reported. PM should be suspected in patients over 50 years of age with sellar lesions associated with rapid onset of diabetes insipidus, cranial palsies or visual field deficits. Our patient is unique in that PM was the presenting feature of the unknown primary tumor. There are no treatment guidelines for management of PM. Pituitary surgery for symptomatic palliation or alternatively radiotherapy in poor surgical candidates has been used. Treatment should be directed towards the primary tumor. Clinicians should be aware of the rare NE cancer metastasis, so identification and treatment of primary tumor with multidisciplinary team can be expedited.

Abstract #817

GROWTH HORMONE DEFICIENCY WITH EMPTY SELLA SYNDROME SECONDARY TO UNTREATED PRIMARY HYPOTHYROIDISM

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Case Presentation: It is clinically established that untreated primary hypothyroidism can cause pituitary hyperplasia. The risk specifically increases with TSH levels greater than > 50 mIU/ml. Empty sella syndrome is a radiological diagnosis which is commonly idiopathic in origin. To best of our knowledge, its association with untreated primary hypothyroidism is reported in only 4 case reports. We present a case of 14 yr boy who presented with short stature. He was on less than 3rd percentile on growth chart,
and his bone age was delayed by 4 years. Bone age was 10 years by Grech Pyle method. Initial work up revealed primary hypothyroidism, with TSH values of 850 mIU/ml. He was placed on levothyroxine therapy with expected improvement in thyroid function. Despite the treatment, patient did not show any height gain or progression of bone age. Further evaluation revealed deficient Growth hormone axis and Empty sella on MRI. Child was started on Growth hormone and started showing improvement in height. Other pituitary axis were normal.

The case highlights the fact that chronic untreated primary hypothyroidism may cause pituitary dysfunction in selected group of patients. We postulate that excessive thyrotrhaph hyperplasia (as evident on high TSH levels) could impact the function of other cell lines.

**Conclusion:** If the clinical presentation warrants, the treating physicians should consider testing for pituitary function in cases of untreated primary hypothyroidism especially when the TSH values are very high and the untreated hypothyroidism is long standing.

**Abstract #818**

**WAS ATRIAL FIBRILLATION THE HARBINGER OF A THYROTOPH ADENOMA?**

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**Objective:** TSH-secreting pituitary adenomas (TSHomas) account for about 1% of pituitary adenomas. Patients typically present with thyrotoxicosis and/or goiter. The differential diagnosis includes thyroid hormone resistance and primary thyroid disease. Making the correct diagnosis is essential because management differs immensely based upon the etiology. It is estimated 25% of TSHomas cosecrete additional hormones. We describe a man who presented with thyrotoxicosis and was found to have a plurihormonal pituitary adenoma.

**Methods:** Pertinent clinical, laboratory, imaging, and pathology data were reviewed.

**Case Presentation:** A 44 years old male presented to his primary care physician with sudden onset of chest pain and shortness of breath. He was sent to the emergency room where his complete blood count showed pancytopenia. A peripheral smear revealed auer rods. On admission, a bone marrow biopsy from right posterior iliac crest showed acute myeloid leukemia (AML). Patient was started on induction chemotherapy with Cytarabine/Idarubicin 7 + 3. A repeat bone marrow biopsy revealed residual AML. Patient had a reinduction chemotherapy with high dose Cytarabine (HIDAC) in combination with Idarubicin. Patient developed hypernatremia immediately after.
reinduction chemotherapy. He was initially given D5W infusion but his serum sodium level worsened to 154 (136 - 145 mmol/L). A DDAVP challenge test with IV DDAVP 2 mcg showed:

Serum sodium: 148 (136 - 145 mmol/L) before and after. Urine osmolality: 273 (500 - 800 mOsm/kg) at baseline, 258 (500 - 800 mOsm/kg) one hour after and 323 (500 - 800 mOsm/kg) 2 hours after. Urine specific gravity: 1.006 before and after. IV DDAVP was started as patient showed a partial response on DDAVP challenge. MRI brain did not reveal any anterior or posterior pituitary abnormality. Further increase in DDAVP dose did not show any improvement in serum sodium levels. ADH level was checked and it came back normal 1.3 (0.0 - 4.7 pg/mL). Patient was eventually diagnosed having Nephrogenic DI. Treated initially with Hydrochlorothiazide and then with Amiloride due to hypokalemia. NDI resolved after 3 months.

Discussion: Nephrogenic diabetes insipidus (NDI) is characterized by excessive volumes of dilute urine caused by the insensitivity of the distal nephron to the antidiuretic effect of ADH.

In a systemic review of reversible causes of NDI, 155 studies described 30 risk factors. The most reported risk factors were lithium (84 studies), antibiotics (16 studies), antifungals (11 studies), antineoplastic agents (9 studies), antivirals (8 studies), and metabolic disturbances (8 studies). Medline search did not reveal any case of nephrogenic diabetes insipidus (NDI) associated with these anticancer agents. Hydrochlorothiazide, 25 mg once or twice daily can improve NDI by inducing mild volume depletion. Amiloride can be beneficial by its additive effect with the thiazide diuretic and in patients with reversible lithium nephrotoxicity.

Conclusion: This study reports NDI secondary to chemotherapeutic agents Cytarabine and Idarubicin in a male patient with AML. Medline search did not reveal any case of nephrogenic diabetes insipidus (NDI) associated with these chemotherapeutic agents.

Abstract #820
SUCCESSFUL PREGNANCIES IN GONADOTROPIN SECRETING PITUITARY TUMOUR

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Objective: To present a case of successful pregnancies in Gonadotropin secreting pituitary tumour during course of disease

Case Presentation: 27 year woman presented with gradually increasing diminution of vision in both eyes since last 6 months. There was no preceding H/o trauma, fever, hypertension, headache but complained of irregular menstruation since 2 years. Perimetry showed bitemporal visual field loss. CEMRI head 30×36×34 mm lobulated anterior pituitary mass. Patient underwent TSS and biopsy revealed it immunopositive for beta FSH. She was discharged on prednisolone(5mg) and 100µg thyroxin replacement. Post operatively her vision improved markedly and her menstruation normalised in 6 months’ time. Repeat CEMRI after 6 months showed residual tumor size 8.8×13.7×12.9 mm size. Four years later she conceived (at age of 31 years) and stopped replacement therapy at her own. She had an uneventful spontaneous normal vaginal delivery but there was lactation failure. She was asymptomatic for next three years when she conceived again (at age of 34 years). Pregnancy remained uneventful till 8th month when she again complained of diminution of vision from both eyes but without headache. Perimetry revealed restriction of temporal fields left>right. CEMRI showed increase in size of residual pituitary mass (20.8×18.4×23.8 mm). Baby delivered by caesarian section at 38 weeks. She had lactation failure in this pregnancy also. She underwent endoscopic TNTS & total excision of mass after 3 months of second delivery. Post operative hormone profile showed TSH 0.319 mIU/ml(0.550-4.780), FT3:2.13 pg/ml (2.3-4.2) FT4:1.09 ng/dl (0.89-1.76), ACTH 13.80 pg/ml (<46) S. cortisol 14.44 (2.9-17.3µ/dL), Growth hormone0.1 ng/mL (0.06-5ng/mL), IGF 1: 100 ng/mL (> 206ng/mL), prolactin 5.2 ng/mL (1.9-25 ng/mL), LH: 10 IU/L (1.50-9.30), FSH: 2.3 mIU/L (1.40-18.0), E2: 55 pg/mL (27-123). No hormone replacement given.

Discussion: Gonadotropinomas constitute 15–40% of all pituitary tumors. Our patient had FSH secreting adenoma responsible for irregular menstruation & visual disturbances at time of first pregnancy. FSH secreting adenomas present with menstrual irregularities,
galactorrhoea & infertility apart from signs and symptoms of mass effect. Our patient had menstrual irregularity only but conceived twice despite having residual gonadotropinoma (fertility normal). She had no headache & only symptom of mass effect was diminution of vision. Lactation failure was present in both pregnancies. Conclusion: Our patient had only visual symptoms and headache was conspicuous by its absence. She conceived on two occasions without assistance & possibly increase in size of pituitary mass is related to pregnancy induced increase in size of pituitary.

Abstract #821

IPILIMUMAB ASSOCIATED AUTOIMMUNE HYPOPHYSIS: A CASE REPORT

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Objective: The objectives of this case report are: 1) to recognize the immune related adverse events leading to endocrinopathies associated with the use of Ipilimumab, 2) to quickly diagnose and treat patients presenting with endocrine disorders while being on Ipilimumab, and 3) to follow up patients for resolution of symptoms after initiation of treatment.

Methods: We reviewed the patient’s clinical course along with the relevant literature.

Case Presentation: We present a case of 70-year-old female with history of newly diagnosed malignant melanoma for which she underwent local wide excision with sentinel lymph node biopsy, and was receiving adjuvant therapy with Ipilimumab. After completing three doses of Ipilimumab, she presented with severe headache associated with nausea, dizziness, poor appetite, fatigue, diarrhea, and altered mental status. Her vital signs were stable except for mild tachycardia. Physical exam was remarkable for drowsiness. Initial labs were significant for white blood cell count of 17.9 k/µl (4.3-10 k/µl), creatinine 1.5 mg/dl (0.5-1 mg/dl), TSH 0.31 µIU/ml (0.47-4.68 µIU/ml), Free T4 0.8 µg/dl (4.5-22.7 µg/dl), cortisol level after cosyntropin (250µg) stimulation test was 16.6 µg/dl, FSH level 4.4 mIU/ml (21.5-131 mIU/ml), LH 0.4 mIU/ml (13.1-86.5 mIU/ml), and prolactin level <1 ng/ml (3-18.6 ng/ml). MRI scan of pituitary showed enlargement and heterogeneous enhancement of pituitary gland and pituitary stalk. The diagnosis of Ipilimumab induced autoimmune hypophysitis was made and Ipilimumab therapy was discontinued. Patient was started on hydrocortisone. Her symptoms improved and she was discharged on prednisone taper. Radiographic resolution of pituitary enlargement was observed on follow up MRI after 6 weeks.

Discussion: Ipilimumab is fully humanized monoclonal antibody that blocks cytotoxic T-lymphocyte antigen-4, and thereby enhances T-cell activation. While the activation of T lymphocytes has proven beneficial in the treatment of certain malignancies, they also have the potential to induce an autoimmune flare in susceptible patients. Autoimmune hypophysitis is the most common endocrinopathy associated with Ipilimumab use.

Conclusion: Autoimmune hypophysitis is a rare entity but incidence increases many folds with the use of immunotherapy such as Ipilimumab. A high clinical suspicion for hypopituitarism in patients presenting with signs and symptoms of hypopituitarism while being on Ipilimumab is imperative. Corticosteroids should be promptly initiated after the diagnosis is made. Close monitoring and follow up is necessary in patients to see the resolution of symptoms and improvement in MRI findings.

Abstract #822

BEAT THE GIANT

CASE OF GIANT PROLACTINOMA DURING PREGNANCY ON CABERGOLIN

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Objective: Invasive giant prolactinomas is subset of macroadenoma, and are much less common in women than in men, defined as tumors >4 cm, >1000 ng/mL prolactin levels and with clinical symptoms of hyperprolactinemia or mass effect. During pregnancy, the risk of tumor growth is higher in macroadenomas (15-35%). Recommendations to discontinue dopamine agonist therapy once pregnancy is confirmed, usually 1–2 weeks after a missed period, limiting potential fetal exposure to only 3–4 weeks. Macroadenoma contrary, recommendations to continue dopamine agonists for risk of tumor growth and subsequent morbidity. Most studied drugs are bromocriptine. Patients should be monitored and evaluated every trimester, or more frequently for those with larger tumors for changes in symptoms such as headaches and visual field defects. Till now not enough safety data are available to recommend the routine use of these drugs during pregnancy.

Case Presentation: We report a 29-years-old Saudi female, misdiagnosed as non-functioning pituitary adenoma. Initial investigations revealed hyperprolactinemia (2993mIU/l), hypothyroidism and large invading sellar mass (Fig1). She underwent transsphenoidal surgery (TSS), with the removal of 60 % of para sellar lesion that showed positive immunostaining for prolactin (Fig2). Her prolactin levels
with dilution revealed (71000mIU/l), confirming the
diagnosis of invasive giant prolactinoma, so treated with
cabergoline (CAB) at a dose of 0.25 mg twice a week. In
2016, patient reported a six-week pregnancy. We advised
to continue CAB at same dose, Image was repeated at 26
weeks of gestation showed a slight increase in adenoma
size (Fig3) and remained symptom-free during gestation
with normal perimeter test until she delivered, full-term
healthy baby boy. The post-partum period was uneventful.

Conclusion: Pregnancy in a patient with invasive giant
macroprolactinoma is a rare occurrence, and its treatment
is challenging. This case demonstrates the effectiveness
and safety of therapy with cabergoline during pregnancy.
However, adenoma size increased slightly during
pregnancy; she had a successful pregnancy with a favorable
fetal outcome. Our case further supports the importance
of making the accurate diagnosis and to start proper treatment
before pregnancy. Also, a multidisciplinary team involving
endocrinologists, neurosurgeons and obstetricians required
for the safe outcome of both mother and newborn.

Abstract #823

PITUITARY ACROMEGALY DIAGNOSED IN THE
SETTING OF GROWTH HORMONE ABUSE

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Objective: Acromegaly results from persistent over
secretion of growth hormone (GH). Excess GH stimulates
hepatic secretion of insulin-like growth factor 1 (Igf-1),
which causes most of the clinical manifestations of
acromegaly. Acromegaly is a rare disease with an
estimated prevalence of 30-70 individuals per million.
Our patient was diagnosed with pituitary acromegaly after
incidentally being found to be abusing human growth
hormone (HGH).

Case Presentation: A 65 year old man with hypertension
and osteoarthritis presented to the endocrine clinic with
complaints of change in his facial features and worsened
snoring. His cousin first noticed these changes when she
saw him after several months. Physical exam revealed
frontal temporal bossing, macroglossia, dactylomégalgy,
and prognathia.

His IgF-1 was 408 ng/mL and his prolactin was 16.51 ng/
ml. The rest of his pituitary hormonal panel was normal.
Patient admitted that he had been misusing HGH injections
for about 4 months in order to build more muscle mass.
Work up repeated 6 weeks after cessation of HGH revealed
an IgF-1 of 724ng/mL, fasting insulin of 17mU/L, and fasting
glucose of 110mg/dL. A glucose tolerance test showed a GH
levels of 10.5 to 9.97 ng/mL over 3 hours. MRI of the brain
confirmed a 9.6 x 7.0mm adenoma along the anterior midline
of the pituitary gland extending to the right side.

Patient underwent an uncomplicated transphenoidal
resection of the pituitary adenoma. IgF-1 was 211ng/mL 1
month post-surgery.

Discussion: The most common cause of acromegaly is
a GH secreting pituitary adenoma. Excess GH and IGF-
1 have both somatic and metabolic effects. The somatic
effects include stimulated growth of skin, connective
tissue, cartilage, bone, viscera, and many epithelial tissues.
The average interval from the onset of symptoms until
diagnosis is about 12 years. At diagnosis, about 75 percent
of patients have macroadenomas (10 mm or more). There
is no proof that net protein retention is promoted in adults
by using GH, except possibly in connective tissue. The
over-exaggeration of the effects of GH in muscle building
has promoted its abuse. In our patient, incidental abuse of
GH unmasked pathological pituitary acromegaly.

The mortality rate of patients with acromegaly is higher
than the general population primarily from cardiovascular
disease. This may be reduced by strict biochemical control
of the disease.

Conclusion: HGH drug abuse does not preclude the
possibility of a pituitary adenoma causing acromegaly.
Laboratory testing should be repeated after cessation of
drug abuse.

Abstract #824

GENDER DIFFERENCES AND OUTCOME TRENDS
OVER TWO DECADES IN ACROMEGALY: A
SINGLE CENTER STUDY IN 112 PATIENTS

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Medicine1, Emir Veledar, PhD1, Nelson Oyesiku, MD,
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Objective: To evaluate long-term trends in patients
operated for acromegaly.

Methods: A retrospective analysis of 54 men and 58
women operated from 1994 to 2016 by one neurosurgeon.
Surgical remission was defined as IGF-1 after 3 months,
and recurrence as return of high IGF-1 during follow-up.
Events considered for survival analysis were recurrence,
reoperation, radiation, and death.

Results: Men were younger at surgery (43.6±12.7, peak in
4th decade) than women (48.7±12.3, p=0.04, peak in 6th
decade). Indications for testing were phenotypical changes (46% men, 40% women), headaches, incidentaloma, hypogonadism, visual changes, and galactorrhea. Men had higher mean IGF-1 (874±328 vs 716±296 p<0.01) and more frequent hypopituitarism (55% vs 22% p<0.01). Women had larger tumors (2.3±1.5 vs 1.8±1.3 cm, p=0.04). Prevalence of cavernous sinus invasion and mean growth hormone (GH) levels were similar in both genders. Remission rates were similar (56% women and 51% men) and predicted by cavernous sinus invasion and postoperative GH levels. Surgical remission improved after 2/2011 (67.35% vs 43.55%, p=0.01), when mean GH level was lower (30±9 vs 46±18 ng/mL, p=0.03) than in previous years. Fewer patients presented with phenotypical changes in recent years (30% vs 54%, p<0.01), while the frequency of incidentalomas and hypogonadism increased. Mean follow-up was longer in women (5.2±3.4 vs 3.6±3.6 years, p=0.02). Adjuvant treatment for acromegaly (medical, radiation, reoperation) was required in 57% men and 49% women. At last follow up, more women than men maintained surgical remission or achieved normal IGF-1 after adjuvant treatment (89% vs 72%, p=0.03). Six-year event-free survival was higher in women (p<0.01).

Discussion: Phenotypical changes are the usual reason to suspect acromegaly. Recent reports indicate that new cases of acromegaly are rising, but it is not known whether presentation has changed. We show that reasons other than physical changes predominate in recent years, along with improved surgical remission rates. Acromegaly affects both genders equally, and gender-distinct features were previously described regarding metabolic profile and quality of life. We provide novel information regarding gender effect on age, biochemical and imaging parameters. Moreover, gender influences long-term biochemical control and compliance with follow-up visits.

Conclusion: Understanding trends in clinical presentation may lead to earlier detection and improved outcomes in acromegaly. Testing for acromegaly is necessary in patients with incidentaloma and hypogonadism. Men present at a younger age with higher IGF-1 levels and achieve lower rates of biochemical control during follow-up than women.

Abstract #825

PSYCHOSIS IN CUSHING’S DISEASE TREATED WITH ETOMIDATE

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Case Presentation: We present a case of acute psychosis secondary to Cushing’s disease requiring intravenous etomidate.

A 33 year old female with a history of morbid obesity, type 2 diabetes mellitus, hypertension, a known 2.3 cm pituitary adenoma, and current cellulitis presented with anemia and thrombocytopenia concerning for thrombotic thrombocytopenic purpura (TTP). She had uncontrolled hypertension despite 8 agents, a recent fifty-pound weight gain, and newly diagnosed diabetes. Physical exam was notable for a blood pressure of 192/107 mmHg, BMI of 52, scattered ecchymoses, a buffalo hump, abdominal striae, 3+ pitting lower extremity edema, and waxing and waning mental status with easy distractibility. Labs were notable for persistent hypokalemia at 2.6 mmol/L requiring aggressive intravenous replacement. Morning cortisol was 66 ug/dL (Range: 4.5-22.7 ug/dL) with an ACTH of 184 pg/mL (Range: 10-60 pg/mL). High and low dose dexamethasone suppression tests resulted in cortisols of 66 μg/dL and 95.2 μg/dL, respectively. MRI brain confirmed a 1.9 x 2.8 x 2.6 cm pituitary adenoma increased in size from imaging 5 months prior. During her hospitalization she developed an acute encephalopathy with prominent psychotic features. On day 5, the patient became agitated and combative with the delusion that staff was trying to kill her. Due to concern for her safety, she was started on intravenous etomidate at 0.05 mg/kg/hr for Cushing-precipitated psychosis. After twenty hours her serum cortisol decreased from 96.4 ug/dL to 50.2 ug/dL, her insulin requirement decreased by 50%, and all scheduled antihypertensives were discontinued. The patient’s mental status dramatically improved after 48 hours. Ultimately, her thrombocytopenia was attributed to microangiopathic hemolytic anemia secondary to malignant hypertension. Five days after initiation of etomidate she underwent endonasal resection of the pituitary mass which stained positive for ACTH confirming Cushing’s disease. Postoperative cortisol was 2.1 μg/dL and her mental status returned to baseline.

Conclusion: Psychiatric disorders are common in Cushing’s syndrome, usually manifesting as depression or anxiety. Psychosis is a known but exceedingly rare consequence of Cushing’s syndrome. Here we present a case of
severe psychosis necessitating etomidate, a carboxylated imidazole initially developed as an intravenous hypnotic for anesthetic induction. Etomidate works by inhibiting adrenal enzyme 11β-hydroxylase which catalyzes the production of cortisol from deoxycortisol. Although rarely needed, intravenous etomidate is a therapeutic option for managing life threatening Cushing's disease, as demonstrated in our case.

Abstract #826

SOX 2 EXPRESSION IN HUMAN PITUITARY ADENOMAS

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Objective: Sox2 is a marker of embryonic stem cell pluripotency and plays a role in normal pituitary development but also in the progression of tumors. However, Sox2 expression in pituitary adenomas and its possible correlation with clinicopathologic characteristics have not been investigated so far. Objective. To evaluate by immunohistochemistry the expression of SOX2 protein in pituitary adenomas.

Methods: Pituitary adenoma samples prelevated during neurosurgery from 34 patients diagnosed and treated at the C.I. Parhon National Institute of Endocrinology in Romania were analyzed by immunohistochemistry for SOX2 expression in the primary tumor samples by the avidin-biotin-HRPA method using monoclonal primary anti-SOX2 antibodies. From the 34 tumors 13 were GH-secreting, 10 were prolactinomas and 10 clinically non-functioning adenomas.

Results: Sox2 positive expression was detected in 16 patients (47.05 % of cases): 8 acromegaly cases, 6 prolactinomas and 2 non-functioning adenomas and did not show an association with tumor size or extension at diagnosis. GH-secreting tumors were immunopositive for Sox2 in 57.14% of cases, prolactinomas in 60% and non-functioning pituitary adenomas in only 20% of cases (significantly higher percentage of Sox2 positivity among secreting tumors, p=0.041). At diagnosis, Sox2 positive tumors were significantly more associated with corticotrophin deficiency (p=0.047) and gonadotrophin deficiency (p=0.041).

Discussion: Our data suggest that it is possible that under certain conditions (for example in the case of compression of the normal pituitary and/or pituitary stalk in a patient with pituitary macroadenoma) these cells regain their ability to multiply and differentiate, protecting from pituitary insufficiency. The design of our study only allows us to speculate on the plausibility of such a mechanism and the small number of cases in our study also limits the power of our results but we believe that this observation deserves further investigation.

Conclusion: SOX2 positive expression is frequent in pituitary adenomas, especially in secreting tumors.

Abstract #827

MODERATE FLUID RESTRICTION AFTER TRANSSPHENOIDAL SURGERY MAY DECREASE THE INCIDENCE OF DELAYED POSTOPERATIVE HYponATREMIA

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Objective: Delayed hyponatremia, defined as hyponatremia occurring 3 to 14 days after surgery, occurs in up to 35% of patients following transsphenoidal surgery (TSS) for a pituitary tumor. Previous retrospective studies suggest that initiating fluid restriction postoperatively may alleviate this problem. We conducted a pilot study to prospectively compare two approaches to postoperative fluid management in patients undergoing TSS and hypothesized that early moderate postoperative fluid restriction decreases the incidence of delayed hyponatremia

Methods: Patients scheduled to undergo TSS were randomly assigned to either a control group (n=19) or an experimental group (n=19). Patients were started on weight-based intravenous fluid after surgery until POD 1 and allowed to drink water freely. Patients in the experimental group were started on a 1.8 liter/day fluid restriction (2 liter/ day if weight > 100kg) on POD 3 until POD 14 and control patients were allowed to drink freely. Serum Na levels were checked every 8 hours in the hospital and on POD 7, 10, and 14. Fluid intake and urine output was recorded while patients were hospitalized and patients were asked to keep track of their fluid intake at home. Average serum Na between POD 0 and POD 14 was calculated between groups and incidence of mild (Na 130-134 mEq/L), moderate (Na 125-129 mEq/L) and severe (Na < 125 mEq/L) delayed hyponatremia was captured.

Results: Average serum Na was lower in the control group compared to the experimental group (137.8 ± 2.8 mEq/L vs 139.7 ± 2.2 mEq/L, p= 0.03). There was a trend towards an increased incidence of delayed hyponatremia in the control group compared to the experimental group (53% vs 28%, p= 0.097). Incidence of mild hyponatremia was similar
between groups (control 26% and experimental 21%). Although being in the control group did not increase the likelihood of developing severe hyponatremia (p=0.127), control patients had a higher incidence of moderate (11% vs 5%) and severe hyponatremia (16% vs. 0%).

Discussion: Preliminary results from this study suggest that patients treated with an early moderate postoperative fluid restriction after TSS have higher postoperative Na levels and may be less likely to develop delayed hyponatremia. No patients in the fluid restricted group developed severe hyponatremia as compared to 5% of patients in the non-fluid restricted group.

Conclusion: Our data suggests that moderate fluid restriction in patients undergoing pituitary surgery may decrease the incidence of delayed hyponatremia. Future studies in a larger number of patients are needed to further characterize the clinical significance of our findings.

Abstract #828

ECTOPIC ACTH PRODUCING EXTRA-ADRENAL CATECHOLAMINE-SECRETING PARAGANGLIOMA

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Objective: Catecholamine-secreting tumors are rare. They most commonly arise from adrenal medulla chromaffin cells, but can develop from sympathetic ganglia tissue. Classic symptoms include hypertension, headache, sweating, and tachycardia. These tumors can co-secrete a variety of hormones including ACTH, PTH, ADH, VIP, and GHRH.

Case Presentation: A 56-year-old male with hypertension and recent coronary stent placement was evaluated for hypokalemia and metabolic alkalosis. Initially this was felt secondary to thiazide diuretics, alcohol abuse, and contraction alkalosis. However, his hypokalemia was refractory to correction. Random plasma aldosterone was 5.8 ng/dL and PRA <0.1 ng/mL/hr, despite being on lisinopril. CT abdomen showed adrenal hyperplasia. Undetectable PRA while on lisinopril raised concern for primary aldosteronism although plasma aldosterone was normal.

Four weeks after initial presentation he was readmitted for new-onset diabetes and confusion. His potassium was 3.2 mEq/L, bicarbonate 40 mEq/L, glucose 347 mg/dL, alkaline phosphatase 446 international units/L, AST 47 units/L, and ALT 160 units/L. He had moon facies and edema. A random serum cortisol was >75 mcg/dL and ACTH was 795 (ref: 7-69 pg/mL). A 24-hour urine collection showed elevated metanephrines and free cortisol. Abdominal MRI revealed a 5.6 cm mass anterior to the inferior vena cava. Repeat lab work confirmed elevated catecholamines. The patient’s refractory hyperglycemia was controlled with mifepristone. His abdominal mass was resected. Pathology showed a paraganglioma with focal expression of ACTH.

Discussion: Extra-adrenal sympathetic paraganglionic tissues are prominent in early postnatal life and later degenerate. Abdominal paragangliomas usually result from this tissue and typically do not hypersecrete catecholamines, making this case unusual. Normal ACTH is a derived from POMC gene products predominantly in the anterior pituitary. ACTH is also produced at low levels in adrenal medullary neuroendocrine cells and other tissues. Ketoconazole is first line medical therapy for Cushings’s syndrome. However, it was contraindicated given abnormal liver function. Mifepristone, a glucocorticoid and progestosterone antagonist commonly known for its abortifacient properties, has been shown to help control cortisol-induced hyperglycemia. Concerning side effects include adrenal insufficiency and hypokalemia.

Conclusion: Catecholamine-secreting tumors can co-secrete a variety of hormones. Cushing syndrome induced hyperglycemia can be managed with mifepristone.

Abstract #829

MACROPROLACTINOMA COMPLICATED BY RIGHT HEMISPHERIC SYNDROME

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Objective: Pituitary apoplexy causing internal carotid artery (ICA) occlusion with resultant cerebrovascular accident has been reported. Compression of the cavernous carotid artery by a pituitary adenoma is rare and usually asymptomatic. We report a case of a patient who presents with right hemispheric syndrome due to complete right internal carotid artery occlusion by a macroprolactinoma.

Case Presentation: A 35 year old man presents with bitemporal hemianopia. Brain imaging revealed a 3.5 x 5.8 x 5.2 cm pituitary adenoma encasing both the internal carotid arteries. Prolactin was markedly elevated at 401522 mIU/L (RI: 77-274 mIU/L). He was started on bromocriptine with reduction of prolactin levels to 2316 mIU/L. Unfortunately, he defaulted follow up. He subsequently returned a year later with acute onset of weakness of the left side of the body. Prolactin was elevated at 118259 mIU/L. Imaging of the brain revealed complete occlusion of the right ICA infraclinoid, cavernous and supraclinoid segments from the macroprolactinoma with right middle cerebral artery territorial infarct. In view of mass effect, patient was started on intravenous...
manitot. Dopamine agonist therapy was resumed. He had significant residual neurological deficit and subsequently require walking aids for ambulation. The latest imaging of the pituitary gland revealed a significant interval decrease in size of the tumor.

**Discussion:** Most patients with stroke arising from compression of the cavernous carotid arteries from a pituitary adenoma occur in the setting of pituitary apoplexy. Mechanisms include direct compression of the vessel from rapid expansion of the tumour by haemorrhage or vasospasm due to extravasation of blood into the subarachnoid space from hemorrhagic apoplexy. To date, there are only 4 reported cases of a non-functioning pituitary adenoma causing symptomatic carotid compression without an apoplectic event. To our knowledge, this is the first case of a macroprolactinoma complicated by right hemispheric syndrome secondary to direct compression of the cavernous carotid arteries. He was managed conservatively with dopamine agonist.

**Conclusion:** When evaluating a patient with stroke, pituitary adenomas are generally not considered in the differentials. Pituitary adenomas, especially if already showing compression of the internal carotid artery need to be treated early to prevent the devastating complication of cerebrovascular accident.

**Abstract #830**

**CROOKE’S CELL ADENOMA MASKED BY POLYCYSTIC OVARIAN SYNDROME**

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**Objective:** Crooke’s hyaline change refers to the cytoskeletal changes in non-neoplastic corticotrophs thought to be in response to glucocorticoid excess. Rare, aggressive forms of corticotroph adenomas may also manifest this change and are referred to as Crooke’s cell adenomas (CCA), with 80 cases reported thus far, as of 2015. We report a rare case of Crooke’s cell adenoma manifesting as Cushing’s disease.

**Case Presentation:** A 41 year old female, with a ten year history of Polycystic Ovarian Syndrome (PCOS), one year history of hypertension and prediabetes, presented with progressive weight gain of 40lbs over 6 years. Physical examination was notable for obesity, moon facies, a dorso-cervical hump, supraclavicular fullness and violaceous striae over the abdomen. Laboratory results were notable for cortisol 17.8mcg/dL after 1mg dexamethasone suppression test, cortisol 3.2mcg/dL after 8mg dexamethasone suppression test, elevated adrenocorticotropic hormone 98pg/mL and elevated dehydroepiandrosterone sulfate 643ng/dL. Follicle stimulating hormone and luteinizing hormone were low at 1.7 and 0.3mIU/mL, respectively. Thyroid function tests, prolactin, 17 hydroxy-progesterone, testosterone, and insulin-like growth factor-1 levels were normal. MRI brain showed a 2.3cm pituitary adenoma abutting the optic chiasm. She underwent trans-sphenoidal pituitary resection, and histopathology confirmed CCA. She remains on thyroid hormone replacement and body surface area based dose of hydrocortisone. MRI 6 weeks postoperatively showed 9mm cystic mass. Further treatment with proton beam therapy is being considered given her young age, long-term side effects of radiation, and aggressive/recurrent predisposition of the tumor.

**Discussion:** Cushing’s disease is an important differential of PCOS and should be ruled out in appropriate patients prior to a diagnosis of PCOS. CCA, accounting for less than 1% of pituitary adenomas, is classified as a “high risk pituitary adenomas” in the 2017 World Health Organization classification of pituitary tumors. Radiation therapy in the management of refractory pituitary tumors is associated with long term side effects, as compared to proton beam therapy, which is more tissue sparing. Retrospective studies have described proton beam therapy as an effective treatment modality in functional pituitary tumors, including persistent corticotroph adenomas, with complete biochemical response, local control and less morbidity.

**Conclusion:** CCA is a rare, aggressive recurrent variant of Cushing’s disease warranting close clinical follow up. It is refractory to conventional treatment modalities and remains a management dilemma, making it crucial to report the treatment successes and failures.

**Abstract #831**

**THE INTRIGUING CASE OF DOUBLE PITUITARY ADENOMA IN A PATIENT RECEIVING PREDNISONE**

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**Objective:** We describe a rare case of immunohistochemically-proven double functional pituitary adenomas.

**Case Presentation:** A 37-year-old woman was treated with prednisone for joint pain, rash and edema attributed to systemic lupus erythematosus. Four months later, she was hospitalized with hyperglycemia >1000 mg/dL. Imaging
revealed a right-sided 1.1 cm pituitary adenoma. Prolactin (PRL) was 152.9 ng/ml (nl: 3-27 ng/ml); bromocriptine was started, and prednisone was discontinued. Two month later, she was seen at our pituitary center. Family history was negative for pituitary disease. Review of systems revealed 100-lbs weight gain, amenorrhea and galactorrhea. Examination showed centripetal obesity, supraclavicular and dorsocervical fat pads, violaceous wide striae and bilateral leg edema. Work-up indicated high 24-hour UFC (284, nl: < 45mcg/day), abnormal low dose dexamethasone test (cortisol 22 mcg/dL), and high ACTH (88, nl: 6-58 mg/ml). Inferior Petrosal Sinus Sampling showed a significant central to peripheral ratio bilaterally. She underwent transsphenoidal adenectomy (TSA) and pathology was diffusely positive for prolactin and focally for growth hormone. Postoperatively prolactin normalized, but hypercortisolemia persisted (UFC 320 mcg/day and ACTH 143 pg/ml). MRI showed a left 2 mm pituitary hypoenhancing lesion. The patient underwent a second TSA and an ACTH adenoma was identified. The patient went into biochemical remission and diabetes mellitus resolved. Eighteen months after surgery, she remains on hydrocortisone replacement.

Discussion: Double adenomas are two coexistent histologically and immunohistochemically different tumors. Pathology series report identification of double adenomas in up to 2.6% operated patients. In a series of 660 patients with Cushing’s disease, only one had a second adenoma positive for both PRL and GH. Our patient presented with clinical and biochemical manifestations of both Cushing’s disease and hyperprolactinemia, and pathology revealed two distinct adenomas. The case has several peculiarities. First, the patient’s diagnosis of endogenous hypercortisolemia was hampered by prednisone use. Second, initial MRI showed a pituitary hypoenhancing lesion. The patient underwent a second TSA and an ACTH adenoma was identified. The patient went into biochemical remission and diabetes mellitus resolved. Eighteen months after surgery, she remains on hydrocortisone replacement.

Abstract #832

TUMOR MARKERS IN FUNCTIONAL AND SILENT CORTICOTROPH ADENOMAS

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Objective: To assess a panel of tumor markers in patients with functional corticotroph adenomas (FCA) and silent corticotroph adenomas (SCA).

Methods: We evaluated tumor samples from 33 FCA and 24 SCA patients operated between 5/2013-7/2016. FCA patients had biochemical confirmation of Cushing’s disease. SCA patients presented with clinically nonfunctioning tumors. We performed immunohistochemistry (IHC) for somatostatin receptors (SSTR) type 2 and 5, aryl hydrocarbon receptor interacting protein (AIP), ki67 and p53. For ki67, we defined abnormal proliferation as >3% positive cells. For SSTR and AIP, we defined strong expression if present in ≥80% cells.

Results: Age at surgery was lower in the FCA than SCA (41±12 vs 51±12, p <0.01) with female predominance in both groups (76 vs 67%). Mean tumor diameter was smaller in FCA (0.9±0.5 vs 2.3±0.7 cm, p<0.01). Postoperative glucocorticoid replacement was required in more patients with FCA (76 vs 29%, p<0.01). Biochemical remission was achieved in 85% patients with FCA. Complete resection was achieved in 94% patients with FCA and 79% with SCA. High ki67 was found in more patients with FCA than SCA (42 vs 17%, p 0.05). High Ki67 was associated with younger age (p<0.01), female gender (p 0.06), presence of mitoses (p<0.01) and strong expression of SSRT5 (p <0.001), but not larger tumors, cavernous sinus invasion or positive p53. Mitoses were detected in 18% FCA and no SCA. There was no difference in p53 expression between groups (48% vs 54%). SSTR2 expression was absent to moderate in most FCA and SCA. SSTR5 expression was strong in 63.64% FCA and 8.3% SCA; mean expression was higher in FCA (p <0.0001). AIP expression was strong in most tumors in both groups (88 vs 87%). One FCA patient was treated with pasireotide and responded with eucortisolemia; the tumor expressed SSTR5 in 100% cells, SSTR2 in 30% and high Ki67 in 5%.

Discussion: Immunohistochemical SSTR subtype exp-
resison in somatotroph adenomas predicts therapeutic response to somatostatin receptor ligands (SRLs). Recently, pasireotide (multi-ligand SRL that binds predominantly to SSTR5) has been approved for patients with functional corticotroph adenomas (FCA). It is not known whether SCA respond to pasireotide. Our study indicates strong SSTR5 expression is more frequently encountered in FCA and majority adenomas with strong SSTR5 expression also have high ki67.

Conclusion: FCA and SCA have different patterns of SSTR5 and ki67 expression. Further study is required to determine whether these markers are predictive of response to SRLs.

Abstract #833

METASTATIC BREAST CANCER TO THE PITUITARY CAUSING PAN-HYPOPITUITARISM

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Case Presentation: Metastatic disease to the pituitary gland is an uncommon complication of systemic cancer and is usually seen in elderly patients. Because of the rarity of metastatic disease to the pituitary, its indolent course, and lack of specific clinical features, it is difficult to differentiate from other sellar lesions and makes management complicated. Even though only 7% of pituitary metastatic lesions are reported to be symptomatic, diabetes insipidus, visual field defects, and ophthalmoplegia are the most commonly reported initial symptoms. Breast and lung cancers are the most common primary tumors that metastasize to the pituitary gland. We present a 53 year old woman with history of diabetes mellitus type 2 and ER+, PR-, HER2+ metastatic breast cancer to sternum and cerebellum presented to emergency room with complaints of double vision. Physical exam revealed cranial nerve VI palsy and PET scan showed increase uptake in her clivus. She was treated with radiation therapy without improvement in symptoms. Two months later, she presented to clinic with complaints of polyuria, nocturia, polydipsia, fatigue and cold intolerance. MRI brain revealed new abnormal enhancing tissue along the hypothalamus and pituitary infundibulum consistent with metastatic disease and tumor infiltration into pituitary gland. Laboratory tests at moment of evaluation revealed HgbA1c 9.2%, TSH 2.34, fT4 0.6, plasma ACTH <5, AM cortisol 0.6, FSH 1.4, LH<0.2. She was started on Synthroid 100mcg and hydrocortisone 20mg twice daily. Urine studies with urine osmolality <100 mosm/kg and was started on DDAVP 0.1mg twice a day for diabetes insipidus. At 2 week follow up, she reported improvement in symptoms. Her pituitary lesion was treated with radiation therapy. Trastuzumab, anastrazole, and zoledronic acid were used for her metastatic breast cancer. Unfortunately, follow up brain MRI showed increased prominence in size of abnormal enhancing tissue along the pituitary and patient reported progressive cranial nerve deficits. She is currently undergoing re-irradiation and is enrolled in a clinical trial.

Conclusion: Treatment of metastatic disease to the pituitary is multimodal and tumor invasiveness often makes resection difficulty. Chemotherapy, radiation, and surgery are treatment methods used and can lead to improvement in quality of life but no significant survival has been documented. Even in a multimodal approach, survival among patients is poor, with mean survival rates ranging from 6 to 22 months.

Abstract #834

INFLAMMATORY PSEUDOTUMOR OF THE PITUITARY GLAND

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Objective: Inflammatory pseudotumor is a rare, poorly understood, benign process that has been described in the literature. Histologically, it is composed of lymphocytes, plasma cells, collagen and myofibroblastic spindle cells. Most commonly involving the lungs, cases involving the orbit, skull base, thyroid, liver, spleen, and other organs, have been described as well. Here, we present a case of inflammatory pseudotumor of the pituitary gland.

Methods: We report a rare case of inflammatory pseudotumor of the pituitary gland and performed a literature review

Case Presentation: A 34-year-old woman with no prior past medical history presented with a headache of one month duration and visual changes of one week duration. On a computed tomography (CT) of the head, she was found to have a sellar mass. Magnetic resonance imaging (MRI) of the sella revealed a 0.5 x 0.9 x 1.0 cm right sellar/parasellar mass encasing and narrowing the right cavernous carotid artery. Hormonal work up revealed an elevated prolactin level of 93.4 and a low free thyroxine level of 0.88. She was started on cabergoline (0.5 mg biweekly) and levothyroxine 50 mcg and discharged home. Her prolactin level decreased to 2.2 while on cabergoline. However, a repeat MRI one month later revealed interval enlargement of the right sellar/parasellar mass to 1.6 x 0.9 x 1.2 cm, concerning for a lymphoproliferative or neoplastic process, although an inflammatory process could not be excluded. She underwent an endoscopic
transphenoidal resection of the sellar mass. Pathology of the mass revealed inflammatory pseudotumor of the pituitary gland. Three months later, she developed worsening headaches with a new left cranial nerve (CN) 3 palsy with a partial left cranial nerve 6 palsy. Repeat MRI revealed a new 0.5 x 0.7 x 2.5 cm hypo-enhancing mass centered in the left aspect of the pituitary gland. She was started on high dose Solumedrol followed by a prednisone taper, with resolution of CN 3 and 6 palsy. She will continue with pulse dose Solumedrol.

**Discussion:** Inflammatory pseudotumor is a rare, benign process that can occur in almost any organ. The cause is unknown. Some cases are associated with trauma, inflammation, or autoimmune disease. It is often confused with malignancy. Treatment is controversial and may include surgical resection, use of corticosteroids, or both.

**Conclusion:** This is a rare case of inflammatory pseudotumor of the pituitary gland, which has not yet been described. Inflammatory pseudotumor should be included in the differential diagnosis of pituitary masses.

**Abstract #835**

**AN UNUSUAL CASE OF EMPTY SELLA SYNDROME AFTER MECHANICAL VENTILATION**

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University of Buffalo

**Objective:** Background: Empty sella syndrome occurs when the subarachnoid space extends into the sella turcica, partially filling it with cerebrospinal fluid. Its causes include congenital incompetence of the diaphragma sellae, pituitary surgery or radiation or postpartum pituitary infarction. Prolactin and growth hormone secreting pituitary adenomas may also cause subclinical hemorrhagic infarction of the gland leading to contraction of overlying suprasellar cistern into the sella. Empty sella after mechanical ventilation has never been reported before. We report a case of empty sella presenting after a uterine surgery with general anesthesia.

**Case Presentation:** Case presentation: 43 year old female with history of asthma, anxiety, hypothyroidism and dysfunctional uterine bleeding underwent laparoscopic vaginal hysterectomy with bilateral salpingectomy in July 2017. Patient started having frontal headache associated with nausea, dizziness and tinnitus immediately after the surgery. She also developed difficulty focusing vision and occasional visual floaters. Patient developed spontaneous galactorrhea, fatigue and hair loss. She was not on any medications that could induce galactorrhea and there was no history of breast or nipple stimulation. She was referred to endocrinology for further evaluation.

Exam revealed obese female with bilateral galactorrhea but no breast lump or inflammation. Eye exam was normal. Prolactin level was elevated (27 ng/ml) with serum prolactin at 1:100 dilution of 79.1 ng/mL, and significantly elevated FSH (63.5 mu/ml), LH (54.1 mu/ml), and estradiol (59 pg/ml). TSH was 1.047 and free T4 0.98. MRI brain showed a partial empty sella turcica and no evidence of pituitary micro or macroadenoma. Craniocevical junction and corpus callosum were unremarkable. Satisfactory flow was seen in the intracranial vessels. There was no prior brain MRI to compare but CT head was normal in 2006 and 2010. Repeat laboratory testing showed normal estradiol, FSH and LH. Prolactin also normalized during follow up testing. TSH and free T4 remained normal.

**Discussion:** Primary empty sella can present as mild hyperprolactinaemia and galactorrhoea. Our patient presented with transient hyperprolactinemia and signs of primary ovarian failure with elevated FSH and LH which got resolved in 3 months. There was no other inciting event for empty sella except the general anesthesia with mechanical ventilation. We propose that increase in intracranial pressure may have been the precipitating factor.

**Conclusion:** It remains unclear if general anaesthesia can precipitate empty sella syndrome in patients who are at higher risk of developing such conditions.

**Abstract #836**

**A RARE CASE OF COEXISTENT CUSHING’S DISEASE AND ADRENOCORTICAL CUSHING’S SYNDROME**

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University of Arizona

**Objective:** The most common cause of endogenous Cushing’s syndrome (CS) is pituitary adenoma and is referred to as Cushing’s disease (CD). A functional adrenal adenoma or carcinoma is a less common cause of endogenous hypercortisolism. We are reporting an interesting case of CD who was subsequently also diagnosed with a functional adrenocortical carcinoma(ACC) causing CS.

**Case Presentation:** A 58-year-old female was referred to our clinic for an incidentally discovered 1.7 cm right adrenal nodule on an abdominal CT done for evaluation of kidney stones. She reported a 6-month history of worsening glycemic control and blood pressure, facial redness and easy bruising. Low-dose dexamethasone suppression test (DST) failed to suppress serum cortisol level (17 ug/dL). This was confirmed with an elevated 24-hour urine cortisol level (139.3 ug/d) and 3 elevated midnight salivary
cortisol levels. ACTH levels were noted to be elevated on two separate occasions (146 pg/dL and 155 pg/mL). An MRI of the pituitary revealed a macroadenoma (3.0 x 2.9 x 1.8 cm). The patient subsequently underwent endoscopic trans sphenoidal resection. Post-operative ACTH levels decreased to 26 pg/mL. Histopathology was consistent with ACTH-secreting tumor. A follow-up pituitary MRI revealed no residual disease.

Further follow up for the adrenal nodule revealed a significant growth within a year (from 1.7 to 3.7 cm) on abdominal MRI. Low dose DST failed to suppress serum cortisol level. Patient subsequently underwent right adrenalectomy. Histopathology was concerning for ACC. A week after surgery, she was diagnosed with adrenal insufficiency and was placed on high dose steroids. Patient is currently on taper dose of hydrocortisone.

Discussion: CD defines the clinical picture of an ACTH-secreting pituitary tumor, almost exclusively a benign adenoma, leading to overproduction of glucocorticoid steroids by the adrenal cortex and clinical features of glucocorticoid excess. Bilateral adrenocortical dysplasia in CD is a well-defined phenomenon and can be found in up to 80 percent of patients with CD. Macroscopic adrenal nodules could be found in CD in up to 40 percent of patients (usually bilateral) and these are thought to develop under the influence of long-standing ACTH stimulation. However, a coexistent functional adrenal adenoma/carcinoma is very rare and has been described in only one other patient according to our literature search.

Conclusion: Our case highlights the coexistence of ACTH-dependent and ACTH-independent Cushing’s syndrome and could suggest a long-standing hypothesis that persistent hyperadrenocorticotropism may lead to autonomously functioning adrenal nodule formation.

Abstract #837

MEN TYPE 1 AND SOMATIC MOSAICISM FOR Y323X VARIANT

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Objective: A Multiple Endocrine Neoplasia (MEN) Type 1 patient was found to have somatic mosaicism for Y323X nonsense mutation involving the MEN1 gene.

Case Presentation: A 27-year-old male presenting with severe headaches was found to have a macroprolactinoma on brain imaging. MRI showed a 3.6 cm pituitary macroadenoma with erosion of the sphenoid sinus. Prolactin levels were initially greater than 2200 ng/mL. Following transphenoidal surgery and debulking, he had been treated with cabergoline and prolactin levels decreased significantly to 34.2 ng/mL. Serum calcium levels were elevated at the diagnosis of his macroprolactinoma and he began developing calcium oxalate kidney stones within one year of his pituitary surgery. A sestamibi scan localized a right inferior parathyroid adenoma for which he underwent parathyroidectomy. At age thirty he was hospitalized for severe abdominal pain and diarrhea. CT imaging was notable for a pancreatic body mass measuring 7.2 x 4.5 cm and a serum gastrin level of 758 pg/mL suggesting Zollinger-Ellison syndrome. Later pancreatectomy revealed a well-differentiated Ki-67 positive pancreatic neuroendocrine tumor. Following pancreatectomy he has been treated with lanreotide. Family history included a paternal grandfather and father with pituitary tumors. Two older sisters had no manifestations of MEN type 1, however one sister did receive genetic testing for MEN type 1 which was negative. Genetic testing of our patient demonstrated somatic mosaicism for Y323X nonsense mutation of the MEN1 gene.

Conclusion: Multiple Endocrine Neoplasia (MEN) Type 1 is a rare genetic endocrine disorder associated with tumors of the parathyroid gland, pancreatic islet cells, and the anterior pituitary gland. MEN type 1 is typically inherited as an autosomal dominant mutation with the defective gene being MEN1 on chromosome 11q13. This case highlights a rare genetic variant of MEN type 1 with classically associated tumors including parathyroid adenoma, prolactinoma, and a pancreatic neuroendocrine tumor. Genetic testing revealed somatic mosaicism for Y323X nonsense mutation of the MEN1 gene. Many genetic defects including familial and somatic mutations should be considered when diagnosing MEN type 1.

Abstract #838

CAN WE PREDICT WHO WILL DEVELOP IPILIMUMAB-INDUCED HYPOPHYSITIS? – A LARGE COHORT STUDY IN PATIENTS WITH METASTATIC MELANOMA TREATED AT A SINGLE ACADEMIC CENTER

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Objective: Immune checkpoint inhibitors, single or in combination, have recently become a cornerstone for the treatment of different advanced cancers. Ipilimumab (Ipi), a CTLA-4 inhibitor, was initially FDA approved for treatment of unresectable or metastatic melanoma. Ipi-induced hypophysitis (IH) incidence is controversial, between 0%-17%. Furthermore, little is known on how to
predict which patients (pts) will develop and how to treat this life-threatening complication.

Methods: Retrospective, IRB- approved review of 117 melanoma patients who received Ipi between 2011-2016 was undertaken. Demographic & clinical characteristics, treatment timing and doses, time to progression after therapy, and survival data were reviewed. Descriptive statistics were used to summarize the demographic and clinical characteristics of the study sample. We predefined 2 groups: pts with and without IH after Ipi.

Case Presentation: Of the 117 pts, 15 (12.8%) developed IH. Incidence: no difference between genders (13.51% in males vs. 11.63% in females). No patient who received systemic cancer therapy prior to Ipi developed IH vs. 15 (17.2%) in pts without prior therapy (P = 0.011). Among male pts, those with IH were older than those without (mean 67.7 vs. 56.4, respectively; P = 0.02). Between IH and non IH pts, there was no difference in race, ethnicity, BMI, diabetes or autoimmune disease at baseline, # of Ipi cycles given, presence of primary melanoma lesion, or BRAF results. Median survival time was 45.0 months in IH pts vs. 29.5 months (P = 0.253).

Of the 15 IH pts, 10 (66.7%) were male, mean age 62.1 years (range 55-69.1), males were significantly older than females (mean 67.7 vs. 50.8, respectively; P = 0.009), 2 had autoimmune disease at baseline, median time from first cycle to IH was 9.97 weeks (range 8.4-14.95), 9 (60%) had no other adverse effect (AE) prior to IH, 2 (13.3%) had colitis, other AEs prior to IH were diarrhea, headache, itching and rash, mean # of cycles prior to IH was 3 (range 2-4), 9 (60%) had tumor progression after IH, median time to progression was 5.5 months (range 2.5-8.1). Mean # of cycles given was similar in those with and without progression (3.5 vs. 3.1, respectively, P = 0.055).

Conclusion: We observed a high incidence, 12.7% for IH in melanoma pts. Older age in men and no prior cancer therapy were associated with IH higher risk. Noteworthy, we may observe higher IH incidence with increased use of immune checkpoint inhibitors as first line treatment in the future. Given the lack of reliable identifiable risk factors, close monitoring of signs and symptoms after each therapy cycle is critical for early detection and treatment of hypophysitis.

Abstract #839

CLINICAL IMPROVEMENT OF ACTH-DEPENDENT CUSHING SYNDROME OF UNCERTAIN ORIGIN IN A PATIENT SWITCHING TO MIFEPRISTONE THERAPY AFTER MULTIPLE SURGERIES

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Case Presentation: Localizing an ectopic ACTH-producing tumor can be difficult because of inconclusive or contradictory laboratory and radiology reports, time constraints, or other factors. Meanwhile, the disease can progress, and clinical symptoms may worsen. In such cases where the tumor is not located and surgery cannot be performed, medical therapy may be an option. The use of the glucocorticoid receptor (GR) antagonist mifepristone (Korlym®, Corcept Therapeutics) modulates the effect of glucocorticoids, allowing control of hypercortisolism while localization of the tumor occurs. We report a patient with surgical and somatostatin-analog refractory ACTH-dependent CS of uncertain origin who attained clinical improvement after switching to mifepristone therapy.

A 59-year-old female was diagnosed with ACTH-dependent CS, hyperprolactinemia, and acromegaly in 2013. She underwent pituitary resection and experienced both clinical and biochemical remission with normalization of 24-hour urine free cortisol (UFC) from 172 to 15 (reference <45 mcg/day), prolactin, and growth hormone (GH). Two years later, she experienced progressive fatigue, weight gain, central adiposity, worsening hypertension, dyslipidemia, and a new diagnosis of prediabetes. A repeat UFC was 83 mcg/day, and MRI revealed new pituitary growth. Prolactin and GH remained normal. A second pituitary resection was performed in the following year despite non-centralizing inferior petrosal sinus sampling (IPSS). Surgical pathology revealed only normal pituitary tissue, and the source of the ACTH-secretion had not been identified. Full body imaging failed to reveal an ectopic source of ACTH. The patient elected to pursue a trial of medical therapy before considering a bilateral adrenalectomy. She was started on pasireotide and cabergoline without relief of symptoms or evidence of biochemical remission. Due to worsening symptoms and development of type 2 diabetes (A1c 6.7%) despite metformin and lifestyle interventions, the patient was transitioned to mifepristone 300 mg daily. Within 6 months, she reported improved mood and energy. A1c normalized to 5.5% (reference <5.7%), as did her blood pressure, and fasting lipid panel. Mifepristone was well...
tolerated other than back pain unrelated to treatment. **Conclusion:** Switching to mifepristone in a patient with surgical and somatostatin-analogue refractory ACTH-dependent CS of uncertain origin resulted in improved clinical outcomes. Further evaluation is ongoing to localize the ACTH-secreting tumor.

**Abstract #840**

**ACROMEGALY, PRESENTATION OF 2 CLINICAL CASES.**

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**Objective:** Present the first two clinical cases of acromegaly documented in British Guyana.

**Methods:** Acromegaly is a slowly progressive endocrine condition considered rare caused by chronic hypersecretion of Growth Hormone (GH) and Insulin-like Factor 1 (IGF-1). The diagnosis is usually secondary to the presence of other diseases.


**Discussion:** The symptoms of acromegaly can be due to tumor expansion: headache, loss of peripheral visual fields and panhypopituitarism as well as seizures (P#2). Or by excess GH: as thicker facial features, prominence of ciliary arches, prognathism, macroglossia, acral growth of hands and feet, excessive sweating, osteoarthrosis, carpal tunnel syndrome, obstructive sleep apnea, diabetes mellitus and hypertension present in both patients. The treatment includes transphenoidal surgery and reserves the medications (somatostatin analogues) for whom the surgery has failed as P#2, among others. Another possibility is the radiotherapy used in P#1. Both patients maintain a stable control

**Conclusion:** The characteristics founded at the time of diagnosis of our patients with acromegaly do not differ with the literature. Cases like this are very difficult to manage properly unless the essential diagnostic and therapeutic resources needed are available.

**Abstract #841**

**SPONTANEOUS GRAM NEGATIVE MENINGITIS AS FIRST PRESENTATION OF INVASIVE MACRO-PROLACTINOMA**

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**Objective:** Meningitis is a rare presentation for pituitary macroadenoma and even rarer is with a culprit gram negative organism. Three patterns of meningitis caused by gram-negative bacilli have typically been associated with trauma or neurosurgery, infants and spontaneous likely in the elderly. Generally, in a patient with an invasive pituitary macroadenoma it is due to an infection of CSF leaking often with presenting symptoms of rhinorrhea. It occurs through the disrupted bony skull into the sphenoid sinus, allowing the entry of nasopharyngeal organisms. It typically presents with the common organisms known to infect adults including the most often reported as Streptococcus pneumoniae. We present a case of a spontaneous gram negative bacterial meningitis without rhinorrhea or surgical intervention presenting with newly found pituitary prolactinoma.

**Case Presentation:** A 28-year-old West African female with medical history of malaria and infertility presented to the Emergency Department with complaints of 3-day history of frontal headaches, fever, nausea and vomiting. Patient denied any visual/auditory changes, nasal discharge, memory problems, weakness or trauma. On examination, there was no focal neurological deficit, but mild neck stiffness and galactorrhea was elicited. Clinical examination prompted neuroimaging-MRI which disclosed an invasive pituitary mass likely macro adenoma without any obvious CSF leakage. A subsequent lumbar puncture was done and CSF analysis was consistent with acute bacterial meningitis. CSF cultures and blood cultures positive for Klebsiella Pneumoniae. No distant
source of infection was found. The remainder work up was negative for cryptococcal antigen and mycobacterium tuberculosis. Other immunodeficiency workup including lymphocyte panel, complement levels and HIV status was unremarkable. Blood tests revealed a serum prolactin level of 1800 ng/mL (2.5-11 ng/mL) and panhypopituitarism. Neurosurgical advice was sought with no immediate plans for intervention. Patient made a full recovery with 21 days of intravenous antibiotic treatment. On diagnosis was initiated on cabergoline with hydrocortisone replacement and scheduled for outpatient clinic followup.

**Conclusion:** This is an unusual presentation of spontaneous gram negative bacillary (Klebsiella) meningitis in a young female with absence of CSF leaking as a first presentation of pituitary macroprolactinoma. Along with the rarity of the simultaneous presentation it also illustrates even in the absence of CSF rhinorrhea or associated risk factors it does not exclude the possibility of a gram negative meningitis.

**Abstract #842**

**PARTIAL HYPOPITUITARISM FOLLOWING MIS-CARRIAGE - A RARE PRESENTATION**

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**Objective:** Hypopituitarism is a rare disorder with a prevalence of 45.5 cases per 100,000 individuals. The term “Selective and Partial Hypopituitarism” refers to the loss of at least one but not all pituitary hormones. The following report describes a case of partial hypopituitarism development after a miscarriage.

**Case Presentation:** A 23-year-old Caucasian female with a history of Systemic Lupus Erythematosus presented with complaints of worsening fatigue for the past 2-3 months. Five months prior to presentation, she was diagnosed with a miscarriage and had a dilatation and curettage. At that time, she was found to be hypotensive and anemic with a hemoglobin of 10g/dL (12.0-15.5 g/dL), and subsequently received IV fluids, iron supplementation, and was discharged home post-procedure. Since then, she has been amenorrhoeic but did not seek medical care. Subsequently, she developed progressive fatigue, limiting her daily activities, and had 10 kg unintentional weight loss over 2-3 months. At this point, she presented again to the hospital for further evaluation. On physical examination, she had a cachectic and malnourished appearance. Laboratory workup revealed a hemoglobin of 9.9 g/dL, normal WBC, electrolytes and glucose, TSH 0.097uIU/mL (0.35-3.74uIU/mL), free T4 0.72ng/dL (0.76-1.46ng/dL), and free T3 1.1pg/mL (2.2-4pg/mL). Workup for the central cause of hypothyroidism revealed a hypoplastic pituitary gland (4mm) on MRI Brain with and without contrast (Figure 1). Prolactin was 2.8ng/mL (2.8-29.2ng/mL), FSH 4.36mIU/mL (low normal), LH 2.61 mIU/mL (low normal), Insulin-like growth factor-I 243ng/mL (119-328ng/mL), and ACTH 44pg/mL (8-42pg/mL).

It was concluded that the patient developed hypoplastic hypopituitarism from possible infarction secondary to the episode of blood loss and hypotension during her previous miscarriage. She was started on levothyroxine before discharge and eventually followed up as an outpatient for gonadal hormone replacement therapy.

**Conclusion:** During pregnancy, the pituitary gland volume tends to increase up to 30% of pregestational volume with no concurrent increase in blood supply and is, therefore, more prone to develop vascular insults. Thus, gravid women are at high risk of developing hypopituitarism after any cause of hypotension including labor, miscarriage or major blood loss. Although it is an uncommon condition, early recognition and management play a crucial role in patient care. Maintaining a high degree of suspicion among such patients for development of potential complete or partial hypopituitarism is of paramount importance.

**Abstract #843**

**WHAT TO EXPECT WHEN SHE IS EXPECTING: ACROMEGALY IN PREGNANCY**

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**Objective:** To review the physiology and management of acromegaly in pregnancy.

**Methods:** We present a rare case of acromegaly with subsequent pregnancy, to discuss growth hormone axis patterns in normal pregnancy and acromegaly. We review case reports and current guidelines for management of acromegaly in pregnancy to highlight best practices.

**Case Presentation:** A 30-year-old woman presented for evaluation of a pituitary mass. She endorsed headaches and increasing foot size, without visual deficits. Biochemical workup demonstrated elevated IGF-1 to 810 ng/mL (normal range 55-331 ng/mL). Oral glucose tolerance test did not suppress growth hormone, consistent with acromegaly. Magnetic resonance imaging (MRI) showed a 13 x 11 x 7 mm pituitary macroadenoma and an additional area of enhancement measuring 3 mm, neither with mass effect. Prior to initiating management, the patient had an unexpected pregnancy. Measurement of IGF-1 in the first trimester decreased to 323 ng/mL. The pregnancy
was remarkable for hypertension and pre-diabetes, with improvement in headaches. Delivery was uncomplicated and post-partum MRI unchanged from prior, with the patient currently planned for surgical evaluation.

**Discussion:** In normal pregnancy, placental GH progressively increases to suppress maternal pituitary GH production. This contrasts patients with acromegaly, where pituitary production is not influenced by placental feedback. However, clinical and biochemical improvement in acromegaly symptoms can be observed during pregnancy. While mechanisms remain unclear, there is suggestion of estradiol-mediated hepatic resistance to GH effects, with alternate consideration for a decreased half-life of the produced IGF-1. With limited safety data for medical management, current society guidelines recommend cessation of medical therapy at the identification of pregnancy and advise against routine laboratory monitoring during this period. Notably, those who enter pregnancy with uncontrolled acromegaly are at greater risk for impaired glucose tolerance and hypertension. Post-partum, there is often a resurgence back to elevated IGF-1 levels, without changes in tumor size.

**Conclusion:** We present a rare case of pregnancy in a treatment-naïve patient with uncontrolled IGF-1 levels pre-conception to review the GH axis during pregnancy, and the variable changes that can be seen with acromegaly in pregnancy. We also review current recommendations for management and the dearth of safety information for medical therapy during pregnancy. Ultimately, there is need for further study into the mechanism and natural history of acromegaly in pregnancy, as well as into the long-term implications of withholding therapies during this time period.

**Abstract #844**

**ROHHAD SYNDROME CASE WITH CHALLENGING MANAGEMENT OF SODIUM AND WATER IMBALANCE SECONDARY TO HYPOTHALAMIC DYSFUNCTION WITH THIRST DYSREGULATION**

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**UMKC**

**Objective:** Rapid-onset Obesity Hypothalamic dysfunction Hypoventilation Autonomic Dysregulation “ROHHAD” syndrome is a rare condition, which was first described in 1965. It is characterized by hypothalamic dysfunction causing multiple endocrine and autonomic dysregulations. Sodium dysregulation can result from one or a combination of different abnormalities described in ROHHAD syndrome; including Diabetes Insipidus (DI), adipsia and SIADH. We present a challenging case of ROHHAD syndrome with difficult to manage sodium dysregulation.

**Case Presentation:** A 23-year-old male patient, known to have ROHHAD syndrome since early childhood, presented to the ED with seizure. At time of diagnosis, ROHHAD syndrome manifested as panhypopituitarism and Diabetes Insipidus and patient has been maintained on hormonal replacement therapy including DDAVP. His DDAVP dose was adjusted several times by his pediatric endocrinologist to manage episodes of Hypo and Hypernatremia. Two weeks prior to current presentation the dose was increased from 0.037 mg PO daily to 0.25 PO mg bid by his adult endocrinologist. Serum sodium level in the ED was 120 meq/dL, urine sodium was 161 meq/dL, DDAVP was held upon presentation and he was started on 3% saline in addition to water restriction of 2-3 L per day. Sodium level improved slowly to 136 meq/dL over two days. DDAVP was then resumed at previous dose of 0.037 mg daily but has caused the Sodium level to drop to 121 meq/dL over two days causing three witnessed episodes of seizure. DDAVP was held again, patient was treated with 3% saline and water restriction of 2-3 L per day. Sodium level had normalized. Patient was discharged home after nine days of hospitalization with sodium level of 145-150 meq/dL. DDAVP was stopped and the caregiver was encouraged to maintain good PO fluid intake with frequent sodium monitoring. Follow up on sodium levels over three months showed normalization of sodium levels.

**Conclusion:** Management of sodium and water imbalance in ROHHAD syndrome can be challenging. In our case, very low dose of DDAVP caused significant hyponatremia leading to a conclusion that Adipsic hypernatremia secondary to thirst dysregulation was mostly the main underlying pathology in sodium and water imbalance rather than DI. DI, Adipsic hypernatremia and SIADH has been described in ROHHAD syndrome and should be all considered in approaching sodium and water imbalance. Finding the exact underlying pathology is crucial in the management.

**Abstract #845**

**SEVERE HYPOTHYROIDISM, NON-COMPLIANCE AND AN ENLARGED PITUITARY: BIGGER NOT BETTER**

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**Jamaica Hospital Medical Center**

**Objective:** Rarely, severe hypothyroidism can lead to marked hyperplasia of the anterior pituitary through loss of feedback from thyroid hormones. If hyperplasia of the pituitary is found on imaging, medical treatment should be initiated to reverse such changes.
We present a case in which lack of compliance with oral levothyroxine therapy led to pituitary hyperplasia.

**Methods:** A 26 year old male presented with shortness of breath at rest. BMI was 44.5. Patient felt cold and tired. He underwent total thyroidectomy in 2001 with supposed benign pathology and since then was given oral levothyroxine. For several months he did not take his prescribed dose of levothyroxine 300 mcg daily. On exam, patient was morbidly obese with a large tongue, anterior neck scar, and slow relax of DTR’s. Because of high AA gradient hypoxemia, CTPA was performed and negative for pulmonary embolism. Thyroid functions were sent.

**Case Presentation:** TSH was 100 (0.47-4.7 uIU/ml) and Free T4 0.2 (0.8-2.2 ng/dl). ACTH came back as <5 (6-50 pg/ml) and cortisol 1.5 (ug/dL). MRI with and without contrast showed mildly enlarged pituitary gland measuring 1.3 cm cranial-caudal with a convex superior border. Homogeneous enhancement was seen with contrast. Cosyntropin test showed good response. FSH, LH, prolactin, total and free testosterone, IGF-1 were all normal. Visual fields were normal. Pt was initially given IV levothyroxine and oral prednisone 10 mg bid. Patient’s symptoms rapidly improved and he was switched to oral thyroxine without steroids. After 8 weeks, TSH was 8.87, Free T4 1.51 and dosing adjusted. Patient was scheduled for repeat MRI in few months.

**Discussion:** Patient’s supra-sellar mass was attributed to severe hypothyroidism since all other hormone levels were normal and he improved with medical thyroid therapy. Pituitary enlargement was due to lack of negative feedback from T4/T3 and is due to excessive production by TSH producing cells in the anterior hypophysis. A supra-sellar mass found in a patient with primary hypothyroidism may be attributed to a hypothyroid state. Unwarranted and drastic interventions may be avoided if patients are followed for clinical improvement in thyroid status and decrease in pituitary size. In addition, a short course of steroids is indicated until adrenal status is clarified.

**Conclusion:** Severe hypothyroidism can lead to an enlarged pituitary. Medical thyroid replacement treatment should be started to reverse such changes.

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**Abstract #846**

**ACTH SECRETING MALIGNANT PANCREATIC NEUROENDOCRINE TUMOR PRESENTING AS RAPID ONSET SEVERE CUSHINGS SYNDROME IN A 53 YEARS OLD WOMAN**

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**Objective:** Pancreatic neuroendocrine tumors (PNET) occur <0.1 per one million persons, malignant tumors are less frequent. Approximately 1.2% tumors produce ACTH with rare reports of cases manifesting Cushing’s syndrome. We report such a case in this abstract.

**Methods:** A 53 year old Caucasian female developed type 2 DM (HbA1c 9.8%), resistant hypertension, weight gain, facial plethora, proximal muscle weakness and striae over a 6 month period. 24 hour urine free cortisol was 1,102.3 micrograms per 24 hours. Sellar MRI and IPSS were conducted with results consistent with ectopic source of ACTH. She was hospitalized for dyspnea and uncontrolled diabetes. Admission serum ACTH and cortisol were 153 (5-58 pg/mL) and 74.5 ug/dL respectively. CGA level was 455 (0-95 ng/mL), 24-hr urine HIAA was normal. CRH level was normal at 3.1 pg/mL (up to 10.0 pg/mL). VIP, glucagon, and gastrin levels were normal. Hepatic imaging for abnormal liver function tests (LFTs) revealed a 3.4 cm pancreatic mass. Due to the degree of elevation of urinary free cortisol, she was placed on PCP prophylaxis. Abdominal CT and DOTATATE scans confirmed a pancreatic mass and hepatic lesions. Four-fold LFT elevation precluded the use of pre-surgical ketoconazole.

**Case Presentation:** Core needle biopsy of the pancreatic mass stained positive for ACTH, synaptophysin, and CGA. MIB-1 index revealed >20% positivity, consistent with a grade 2-3 PNET. She underwent laparoscopic distal pancreatectomy. Two liver metastases were also resected. The pancreatic tail mass was 4.5 cm, consistent with a high-grade neuroendocrine carcinoma invading the peri-pancreatic adipose tissue. Surgical margins were negative. Six out of 16 lymph nodes were positive for PNET. Liver mass pathology positive for metastasis. Postoperatively, 8 AM ACTH was 24.2 ug/dL, cortisol of 16 ug/dL and CGA of 625 ng/mL, indicating residual disease.

**Discussion:** Malignant PNET are rare tumors. Those that secrete ACTH are even less frequently reported. Our patient illustrates the importance of careful yet expedited evaluation and the use of PCP prophylaxis. She may also require bilateral adrenalectomy for treatment of residual Cushing’s syndrome if medical therapy is not effective.
**Conclusion:** Here we report the diagnosis and treatment of a rare case of a metastatic pNET with concomitant ectopic ACTH production resulting in Cushing syndrome. The importance of PCP prophylaxis is also stressed.

**Abstract #848**

**KI-67 PROLIFERATION INDEX AS PREDICTOR OF PROLACTINOMA RECURRENT AFTER TRANSPHENOIDAL ENDOSCOPIC ENDONASAL RESECTION**

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**Objective:** Transphenoidal endoscopic endonasal resection (TSS) is a therapeutic option for dopamine agonist-resistant prolactinomas. It has been described a correlation of Ki-67 proliferation Index and recurrence after resection of prolactinoma. We present a case of dopamine agonist-resistant prolactinoma with recurrence after TSS in the setting of high Ki-67.

**Case Presentation:** A 30 year-old female was referred to our endocrinology clinic for treatment of a dopamine agonist-resistant prolactinoma. She was diagnosed six years prior to presentation in our clinic. Her initial symptoms were irregular menses with progression to amenorrhea and galactorrhea. Prolactin levels were >400 mUI/mL. Pituitary MRI showed a 5mm sellar mass. She was started on bromocriptine but due to severe nasal congestion, it was switched to cabergoline. Cabergoline dose was increased up to 3.5mg twice a week, with resolution of her presenting symptoms. Despite this high dose and initial symptom amelioration, prolactin levels remained elevated, ranging between 160-180 mUI/mL, and caused several side effects, including pain in fingers, lack of concentration, and memory impairment. New laboratory values showed prolactin 170 mUI/mL, FSH 1.9 mUI/mL, LH <0.12 IU/L, normal cosyntropin stimulation test, TSH and IGF-1. A repeat pituitary MRI revealed a 1.6 x 1.5 x 1.2 cm adenoma in the right aspect of the pituitary gland, with no compression of the optic chiasm. The patient underwent a TSS. The Ki-67 proliferation index was 5%. Four days following surgery, prolactin levels were 23.3 mUI/mL, and two months after 172.5 mUI/mL.

**Discussion:** The expression of the human Ki-67 protein is strictly associated with cell proliferation. Lu et al (2014) in retrospective study with 199 women with resistant prolactinoma found that tumors with Ki-67 above 3% were associated with higher rate of recurrence compared to <3% (27.27% vs 8.47%), also incidence of diabetes insipidus and prolactin levels after surgery were higher. Gejman et al (2008) studied 24 patients with recurrence and a control group of 31 cases with no recurrence, and found that Ki-67 was higher in patients with recurrence and conclude that an index higher than 1.3% is an independent predictor of adenoma recurrence within 5 years after surgery. Balinisteanu Et al (2017) reported that prolactinoma has higher Ki-67 values compared to other pituitary adenomas and mainly mixed GH/PRL-secreting adenomas suggesting that some hormones affect proliferation rate more than others.

**Conclusion:** Ki-67 proliferation index is an independent variable that gives a higher likelihood of recurrence in prolactinomas but multiple variables should evaluated to determine risk of recurrence.

**Abstract #849**

**FAMILIAL PUERPERAL ALACTOGENESIS CASE STUDY**

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**Objective:** Isolated prolactin deficiency is a rare disorder manifesting as absence of puerperal lactation. Previous studies have demonstrated an autoimmune etiology. Genetic causes are also implicated based on families with multiple affected women. We report a family with prolactin deficiency due to a nonsense mutation causing a truncated prolactin protein.

**Methods:** Three women in one family (proband, proband’s sister and proband’s niece) reported puerperal alactogenesis, i.e. no milk production postpartum. They noted regular menstrual cycles. The proband is 66 years old with 7 pregnancies and 2 live births. Prolactin level was 1.16 ng/mL (2.8-29.2 ng/mL) at the age of 47. The proband’s sister is 73 years old with 3 children. Her prolactin level was 1.4 ng/mL (2.8-29.2 ng/mL) at the age of 64. Both women had menopause before age 45 years. The proband’s niece is 43 years old with prolactin levels of 1.13 ng/mL, and 0.618 ng/mL at the age of 34 and 0.759 ng/mL at the age of 36. She had infertility of unknown cause and conceived 2 children with fertility treatment. DNA and RNA were extracted from blood of all three women. Genomic DNA for the 6 exons in prolactin were sequenced. cDNA was subjected to RT-PCR with primers targeting exon 5 and 6, to span intron 5. RT-PCR was also performed using a second set of primers to the terminal portion of exon 6. Prolactin mRNA expression was compared between the proband and a control subject.

**Case Presentation:** A heterozygous base pair mutation (c.658C>T) changing CGA (arginine) to TGA (stop codon) (p.Arg220T) was identified in exon 6 of the prolactin
gene. This stop-gain mutation is expected to result in a truncated prolactin protein. PRL exon 5-6 (1.1±0.3 vs. 2.1±0.7; p<0.01) and terminal exon 6 expression (1.0±0.3 vs. 1.7±0.3; p<0.01) was approximately halved in the proband compared to the control.

**Discussion:** We have identified a genetic cause of puerperal alactogenesis resulting from a stop gain mutation in the prolactin gene (PRL) causing a truncated protein. The prolactin assays may have used an antibody that binds to the C-terminal portion of the prolactin protein resulting in artificially low levels. Alternatively, the shortened protein may act to prevent release of the normal prolactin from the lactotroph.

The low circulating prolactin resulted in low prolactin levels and inability to breastfeed. It may also be the cause of infertility and early menopause, but further studies are needed.

**Conclusion:** We report a newly described stop-gain mutation in exon 6 of the prolactin gene (PRL) resulting in familial puerperal alactogenesis.

**Abstract #850**

**LYMPHOCYTIC HYPOPHYSITIS: STILL A DIAGNOSTIC CHALLENGE**

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**Objective:** Pituitary masses have a wide differential with micro- and macroadenomas being the most common. Lymphocytic hypophysitis (LYH) is rare, but not always obvious. We report a case of unsuspected LYH.

**Case Presentation:** A 36-year-old Asian female presented for evaluation of a sellar mass incidentally found on Brain MRI performed for a facial abscess. She had no headache, visual disturbance, or change in weight or menses. Initial blood work revealed only mild hyperprolactinemia of 61.4 ng/dL (N: 5-40). The MRI showed a 1.3x2.0x1.7 cm sellar mass consistent with pituitary macroadenoma. The mass extended into the right cavernous sinus, imposed a mild mass effect on the left cavernous sinus, and had suprasellar extension resulting in compression, thinning, and superior displacement of the optic chiasm. Visual field testing found no deficits. Five months later, repeat MRI showed a 1.4x2.2x1.8 cm mass with slight interval increase in size. Due to size of the mass and displacement of the optic chiasm, Transsphenoidal hypophysectomy (TSS) was performed. Unfortunately, the patient had a prolonged, complicated postoperative course including CSF leak, encephalitis, lumbar-peritoneal shunt and ischemic stroke.

The final surgical pathology revealed LYH.

**Discussion:** LYH is rare in the differential diagnosis of sellar masses. Sometimes the diagnosis is clear or highly suspected from history or imaging characteristics, but not always. LYH can present with headaches, Diabetes Insipidus, Hypogonadotropic Hypogonadism, or history of autoimmune conditions for which investigation into anti-pituitary antibodies are ongoing. Several attempts have been made to develop MRI diagnostic criteria for LYH that include homogeneity of enhancement with gadolinium, symmetry, and thickened pituitary stalk. Despite this, some cases break the rules making them a diagnostic challenge without a tissue biopsy. Distinguishing LYH is important in that once diagnosed, treatment can be first attempted with glucocorticoids, thus avoiding surgical intervention and its potential complications.

Our patient had no headaches, polyuria, or history of autoimmunity. Her MRI did show a symmetrically enlarged mass, fairly homogeneous enhancement, but completely obscured pituitary stalk with slight increase in size over a five-month period. She might have required TSS anyway, but a trial of glucocorticoids was never considered.

**Conclusion:** A sellar mass with no clinical or biochemical abnormalities despite concerning findings on imaging studies should be carefully evaluated with continued observation and pituitary biopsy if possible before the decision for surgical resection is made.

**Abstract #851**

**A CASE OF GONADOTROPIN-SECRETING GIANT PITUITARY ADENOMA**

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**Case Presentation:** The patient is a 53-year-old Haitian female with a past medical history of hypertension, hyperlipidemia, uncontrolled diabetes mellitus type 2, and progressive chronic visual loss in the left eye, who presented to our emergency department with altered mental status. The patient was lethargic on presentation and could not provide much history. Per family, the patient had been increasingly altered over 2 months preceding presentation. CT head was negative for stroke, but did reveal a giant pituitary adenoma. An MRI of the brain, pituitary protocol, was then performed for better characterization of the lesion and showed a 5.5 x 3.9 x 5.0 cm multi-lobulated pituitary macroadenoma with suprasellar extension compressing the optic chiasm, and a large extension in the left frontal lobe as well as into the sylvian fissure and above and below the left A1 vessel.
Collateral history obtained from family at this time was significant for mild near daily bifrontal headaches for the past 2 years, as well as history of premature menopause at age 32. Ophthalmologic evaluation was significant for dense temporal field cut on the right side and no light perception in the left eye. Laboratory evaluation was consistent with gonadotropin producing adenoma with partial hypopituitarism. Luteinizing hormone (LH) was elevated to 110 mIU/mL, follicle stimulating hormone (FSH) elevated to 399 mIU/mL, both diluted and non-diluted levels of prolactin were normal, TSH was 0.024 uIU/mL, free thyroxine was normal at 1.2 ng/dL, growth hormone was 0.1 ng/mL, and insulin like growth factor was low at 48 ng/mL. Cortisol levels were not evaluated as patient was given dexamethasone in the emergency department before labs were drawn. Patient underwent left orbitozygomatic extended to partial transbasal resection of macroadenoma. Post operative course was significant for transient diabetes insipidus. Surgical pathology confirmed pituitary adenoma with neoplastic cells staining for follicle stimulating hormone and luteinizing hormone. Both FSH and LH levels decreased to normal postmenopausal levels postoperatively, FSH 45.6 mIU/mL and LH 15.5 mIU/mL. Conclusion: Gonadotropin-secreting pituitary adenomas may have variable clinical presentation and may be difficult to diagnose, especially in postmenopausal women.

Abstract #852

A CASE OF FSH-SECRETING PITUITARY ADENOMA LEADING TO SPONTANEOUS OVARIAN HYPERSTIMULATION SYNDROME

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Objective: To present a rare case of FSH-secreting pituitary adenoma leading to spontaneous ovarian hyperstimulation syndrome.

Case Presentation: A 28-year-old female presented with 5 months of amenorrhea and abdominal pain. Physical exam was normal. Labs revealed elevated prolactin (94 ng/mL), elevated estradiol (608 pg/mL), inappropriately normal FSH (10.2 mIU/mL), and low LH (0.36 mIU/mL). Transvaginal ultrasound showed numerous ovarian cysts 6-8 cm in size. Pituitary MRI showed a 1.2 cm intrasellar pituitary lesion (see image). A trial of gonadotropin-releasing hormone (GnRH) antagonist therapy was unsuccessful. She next received a dopamine agonist (DA) with normalization in prolactin, estradiol and FSH, reduction in ovarian cysts, and resumption of menstruation, but side effects limited continued use. She underwent transphenoidal resection and 6 weeks later hormone levels normalized, 1 small cyst remained, and menstruation resumed. Final pathology stained positive for FSH and negative for LH.

Discussion: Gonadotroph adenomas are difficult to diagnose and usually not associated with a clinical syndrome. They may present with symptoms of mass effect after a period of silent growth. They rarely exhibit gonadotropin hypersecretion, typically by FSH, which in pre-menopausal women can lead to the distinct clinical presentation of spontaneous ovarian hyperstimulation syndrome (OHSS). The most common presenting symptoms are menstrual irregularity, infertility, and abdominal pain. The hallmark biochemical finding is elevated estradiol with normal to mildly elevated FSH; serum LH is typically suppressed. Hyperprolactinemia is common, usually attributed to stalk effect or hyperestrogenemia. Pelvic imaging demonstrates enlarged ovaries with multiple cysts often greater than 5 cm. The favored treatment approach is surgical which has the highest reported success rate. Medical treatment has been trialed with DAs, somatostatin analogs, and GnRH agonists and antagonists but results are inconsistent. Therapy with GnRH agonists has even caused paradoxical responses with rise in FSH and exacerbation of OHSS. While DAs have lowered estrogen, FSH and prolactin and improved OHSS, they rarely show a reduction in tumor size. Recurrence is not uncommon and long-term surveillance is recommended. Recurrent tumors have been treated with repeat surgery, radiation, and medical therapy.

Conclusion: Functioning FSH-secreting pituitary adenomas are rare and difficult to diagnose, though they have a distinct clinical presentation in pre-menopausal women. Given limited data on long-term follow-up, the role of available therapies is not well defined, though currently surgical treatment is favored as the definitive approach.

Abstract #853

ACROMEGALY WITH NOVEL MEN1 GENE MUTATION

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Objective: Acromegaly is a rare and indolent condition caused by excessive GH (growth hormone) production. Median age at diagnosis is the 5th decade of life with a median diagnostic delay of 4.5-5 years. Persistent elevation
of GH and insulin-like growth factor (IGF-1) levels are associated with increase morbidity and mortality. Here, we describe an unusual case of acromegaly in an adolescent male with a pituitary macroadenoma and rare variant of MEN1 gene mutation that presented with a lack of manifestations of excessive GH on visceral tissue and bone.

Case Presentation: A 17-year-old male presented with worsening headaches, left eye blindness and right eye visual field deficit. Increased appetite, 30 lb weight gain, urinary frequency, nausea, lightheadedness, and extreme fatigue over 6 weeks were also present. Family history was notable for his grandfather being 7 feet tall. On examination, height was 6’1”, and reduced right eye peripheral vision with left eye vision loss and central scotoma was noted. Brain MRI revealed an invasive 2.7 cm pituitary macroadenoma with mass effect on the optic chiasm. Laboratory evaluation was notable for IGF-1 level of 1472 ng/mL (151 – 521 ng/ml) and GH level of 11.8 ng/ml (0-10 ng/ml), consistent with acromegaly. Prolactin and other pituitary hormones were normal. Urgent transsphenoidal resection (TSS) with optic nerve decompression was performed. Pathology revealed an atypical pituitary adenoma, diffusely positive staining for synaptophysin, focally positive for prolactin and GH, high Ki67 proliferation index of 6% and p53 of 5%. Post-operatively, there was significant improvement in visual fields and headaches. There was a significant amount of residual tumor, and GH and IGF-1 levels remained elevated. Lanreotide (up titrated to 120mg every 28 days) was started. A second debulking surgery was performed and Cabergoline 0.5 mg twice a week was added to the medical regimen, but IGF-1 levels remained elevated at 1180 ng/ml. Medical therapy was changed to lanreotide and pegvisomant with a plan for additional surgery vs proton beam therapy for residual tumor. Gene testing revealed a variant of MEN 1 gene mutation (c.784-48G>A).

Conclusion: Recent advances in genetics has led to improved understanding of the molecular and genetic etiologies of pituitary acromegaly. A number of genetic defects predispose to acromegaly, including multiple endocrine neoplasia type 1 and 4. We report an atypical case of acromegaly associated with a MEN 1 gene mutation that has not been previously implicated in the disease and warrants further investigation.

Abstract #854

PPI PROPYLAXIS IN AN UNUSUAL CASE OF AN ACTH-PRODUCING ESTHESIONEUROBLASTOMA AND DUODENAL ULCER

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Case Presentation: Introduction: Olfactory neuroblastomas (ONBs) or esthesioneuroblastomas, are rare malignant neoplasms derived from olfactory neuroepithelium. These tumors only represent 3-10% of sino-nasal malignancies. ONBs may be associated with paraneoplastic syndromes including ectopic ACTH syndrome (EAS). Overall 5-year survival is poor ranging from 45-62%. Hypercortisolism associated with EAS leads to multiple comorbidities including cardiovascular disease, metabolic syndrome, osteoporosis, and hypercoagulable state among other conditions. We present a case of ectopic ACTH-producing olfactory neuroblastoma to discuss peptic ulcer disease prophylaxis in patients with hypercortisolism.

Case Description: An 82-year old male with no medical history developed sudden onset of generalized weakness and fatigue. He was admitted for hyponatremia (126 mmol/L). Laboratory evaluation revealed serum cortisol > 119.6 ug/dL which did not suppress with 1-mg dexamethasone suppression test (DST). 24-hour urine free cortisol was 7167.7 mcg/24 hours. Serum ACTH measured after DST was 1071 pg/mL. MRI of brain showed a normal pituitary gland, but revealed a 3.6 x 1.7 x 3.3 cm right nasal sinus cavity mass. Biopsy of the mass showed an ACTH-producing olfactory neuroblastoma. PET scan showed metastatic disease. The patient was treated with ketoconazole with significant improvement in cortisol levels. His hospital course was complicated by a bleeding duodenal ulcer measuring 3.5 cm for which he was placed on proton pump inhibitor therapy. Due to the decline in his functional status, the patient elected to undergo palliative care and was discharged to hospice.

Discussion: Early detection of ACTH-producing esthesioneuroblastomas is essential as these tumors can be rapidly progressive, resulting in poor survival rates. Surgical excision is the treatment of choice and generally results in resolution of symptoms with marked decrease in ACTH and cortisol levels. Medical treatment, which includes options such as ketoconazole, metyrapone, mifepristone, and etomidate, is necessary to normalize cortisol levels to minimize comorbidities associated with hypercortisolism. Due to the low incidence of gastric
Abstract #855

UNCOMMON PRESENTATION OF CUSHING’S DISEASE IN ADOLESCENT

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Objective: To recognize a rare presentation of Cushings disease in adolescent.

Case Presentation: 18 year old male presents with a concern of delayed puberty and rapid weight gain. On physical exam: patient is morbidly obese with BMI of 71, poor development of secondary sexual characteristics -no facial hair, no voice changes- and ambiguous genitalia. Work up: 24 hour urine cortisol of 166.9 mcg/24 h (N 4.0-50.0), low dose dexamethasone suppression test showed elevated cortisol at 5.18 mcg/dl (N < 1.8) and on later date AM cortisol was 22.79 mcg/dl (N 4.30-22.40) and ACTH was 88 pg/ml (N 6.0-50.0). Brain MRI showed 7.8 mm left pituitary adenoma with no optic compression or cavernous sinus invasion.

He underwent endoscopic transsphenoidal adenectomy.

Discussion: Cushing’s syndrome (CS) is a rare disease in children and adolescent. ACTH secreting pituitary adenoma is the most common cause of endogenous overproduction of cortisol in adolescent. Presentation of CS in children and adolescent highly variable with weight gain being the most common presenting complain in this age group. However, diagnosis is often delayed due to generalizability of symptom. When onset of CS develops during puberty, normal pubertal development does not occur because glucocorticoid excess inhibits gonadotropin release and also directly inhibits sex steroid secretion from the gonads. Patient can present with puberty delay and virilization.

Conclusion: The time of onset of CS is important to recognize, as it will determine the presenting picture of the patient. Males who develop CS at puberty can present with signs of virilization.

Abstract #856

A CASE SERIES REVIEW OF CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF PITUITARY ABCESS IN MEXICAN PATIENTS

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Objective: Introduction: Pituitary abscesses represent between the 0.2 to the 1 % of all sellar masses. To date, only 270 cases are reported.

Methods: Here we present a case series of three pituitary abscesses.

Case Presentation: Case 1: A 29-year-old female who was diagnosed with a pituitary macroadenoma during headache workup. MRI showed an 18x19x14 mm mass and hormonal tests showed no hormone deficit. A trans-sphenoidal resection was performed with pathology report of an adenoma with zones of infarction and zones of lymphocytic hypophisitis. In follow-up, the patient persisted with the lesion on MRI. A second surgery was performed encountering a fluid filled lesion that was drained and cultured. Development of Staphylococcus aureus on culture material was observed and the patient received a course of intravenous antibiotics. To date she has recurred with the abscess and is awaiting new drainage.

Case 2: A 45-year-old female presented to the endocrinology clinic with a history of amenorrhea, galactorrhea, polyuria, polydipsia so a hormonal work up was performed. MRI showed an 18x19x14 mm mass and hormonal tests showed no hormone deficit. A trans-sphenoidal resection was performed with pathology report of an adenoma with zones of infarction and zones of lymphocytic hypophisitis. In follow-up, the patient persisted with the lesion on MRI. A second surgery was performed encountering a fluid filled lesion that was drained and cultured. Development of Staphylococcus aureus on culture material was observed and the patient received a course of intravenous antibiotics. To date she has recurred with the abscess and is awaiting new drainage.

Case 3: A 56-year-old man that presented to the emergency department with a throbbing sudden headache with accompanying III cranial nerve paralysis. MRI showed a pituitary lesion of 27x27mm. During surgery, an abscess was diagnosed and drained. Cultures isolated Staphylococcus epidermidis and...
antibiotic therapy was initiated. Actually, the patient is cured with no hormonal deficiencies.

**Discussion:** Clinical presentation of pituitary abscesses is similar to other sellar masses, with compressive symptoms and hormonal deficiencies; however, mortality ranges between 4.5 to 50 % in different case series. The most common etiology is an abscess secondary to a surgical procedure, a primary lesion is quite rare. Agents usually isolated in cultures are Gram positive rods, although some patients a specific agent cannot be isolated. Treatment includes drainage and antibiotics. Recurrences are common and range between 10 to 30 %.

**Conclusion:** Conclusion: Here we present a case series of pituitary abscesses in which the initial clinical presentation was a primary lesion with no surgical background. The most common agents isolated were Gram positive rods and only one patient had recurrence. In none of the cases described above a there was a deceased patient.

**Abstract #857**

**A DEVASTATING COMPLICATION OF CUSHING’S SYNDROME THAT CAN BE PREVENTED**

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**Objective:** To recognize a rare but fatal complication of Cushing’s syndrome (CS).

**Case Presentation:** 18 year old, morbidly obese male with past medical history of Cushing’s disease status post transsphenoidal resection of functioning pituitary microadenoma. Post operative course was complicated by diabetes insipidus and adrenal insufficiency at which he was started on DDAVP and steroid replacement. He presented one month after the surgery with severe bifrontal headache, CT brain showed superior sagittal sinus thrombosis, Heparin drip started and he was dependent on mechanical ventilation, failed weaning attempts for two weeks and subsequently had a tracheostomy placed. Hospital course was complicated by septic shock secondary to hospital acquired pneumonia and inevitable death.

**Discussion:** Cushing’s syndrome is a hypercoagulable state which place the patient at a higher risk for venous and arterial thromboembolism. Lab findings form multiple studies on haemostasis in CS persistently showed shortened aPTT and increased levels of Factor VIII, fibrinogen, vWF and plasminogen activator inhibitor type 1. In addition, obesity and postoperative period also increase the risk of thromboembolic phenomenon. To prevent a devastating outcome from venous thromboembolism, a risk assessment that includes; patient’s BMI, comorbidities, and parameters for coagulation and fibrinolysis is suggested to evaluate the benefits versus risks for thromboprophylaxis.

**Conclusion:** Cushing’s syndrome predispose patient to thromboembolic phenomenon which can be fatal. Thromboprophylaxis is a suggested recognizable way to prevent such a devastating outcome. We are suggesting a risk assessment for thromboembolism in CS patient to evaluate the need for thromboprophylaxis.

**Abstract #858**

**A CASE OF DELAYED REMISSION OF CUSHING’S DISEASE AFTER TRANSSPHENOIDAL ADENOMECTOMY**

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**Objective:** Our objective was to describe the clinical, biochemical and radiological findings of an interesting case of Cushing’s Disease (CD) following transsphenoidal (TSS) resection of a pituitary adenoma.

**Methods:** We present the clinical, biochemical and radiological findings of a 32 Saudi male with CD after TSS. **Case Presentation:** A 32-year-old Saudi male was referred to our hospital with a presentation of multiple vertebral fractures, along with a history of poorly controlled type 2 diabetes requiring insulin and severe Hypertension for 7 years. Physical examination confirmed Cushingoid features. The biochemical diagnosis of Cushing was confirmed after failing 1mg (DST) with serum Cortisol at 1720 nmol/L; ACTH was high at 33.9 pmol/L (1.6-13.9). MRI-Pituitary showed 8X9 mm pituitary microadenoma and patient underwent TS. Despite immediate improvement in DM and BP control, early postoperative assessment suggested treatment failure with day one morning cortisol 397 nmol/L, and failure of DST on day 4 (serum cortisol 484 nmol/L). The tumour stained positive for ACTH. Four months later, clinical improvement continued and follow up pituitary MRI showed no evidence of residual tumour. Interestingly, 24-hour urinary free cortisol normalised at 255μg/24hr (21-292) and ACTH dropped down to the normal range of 11.8 pmol/L (1.6-13.9).

**Discussion:** Early postoperative assessment of serum cortisol concentration may not be sufficient to predict outcomes in CD post TSS and currently there is agreed consensus. Late remission of CD after TSS occurred has been described to occur in around (5.6%) of patients who had early elevation or normal urinary free cortisol levels and developed a delayed and persistent cortisol decrease after an average of 5 weeks.

The mechanism of the late decline in cortisol after TSS is unclear, however, It may be explained by the progressive necrosis of remaining tumor cells after surgery or the possible gradual resolution of adrenal hyperplasia that
occurred due chronic exposure to elevated ACTH levels during the active phase of the disease. Cortisol cyclicity may be one of the hypothesized mechanisms. Monitoring strategy and retesting may spare some patients from unnecessary further treatment.

**Conclusion:** This case highlights the possibility of late remission of hypercortisolemia after TSS, which is well documented in up to 5.6 % of the cases. Clinicians need to be aware of this possibility before considering additional treatment.

**Abstract #859**

**CONGENITAL GROWTH HORMONE DEFICIENCY AND HYPOGONADOTROPIC HYPOGONADISM IN THE SETTING OF HYPOPLASTIC ANTERI OR PITUITARY**

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**Objective:** Idiopathic, isolated growth hormone deficiency (GHD) is the most common sporadic form of hypopituitarism. Pituitary gland morphology, as noted on MRI imaging, may suggest various etiologies and prognoses associated with GHD. We present a patient with congenital growth hormone deficiency and hypogonadotropic hypogonadism (HH) in the setting of a hypoplastic anterior pituitary.

**Case Presentation:** A 22 year old male presented to adult endocrinology to establish care. He was evaluated by pediatric endocrinology at age 12 for delayed puberty. At the time, he was of short stature and weighed 33.4 kg. He had delayed dentition without any 12 year molars, absent axillary hair, and Tanner stage I genitalia with small 2-3 cc testes. He had no goiter or gynecomastia, and had normal digits without any metacarpal shortening. His legs were equal and appropriate in length. He had no abnormal skin pigmentation or oily texture. Bone age was delayed compared to chronologic age. He had bilateral undescended testicles at birth and underwent bilateral orchiopexy at one year. Family history is remarkable for maternal male cousin with Kallmann syndrome and GH deficiency. Labs studies revealed normal thyroid function and low IGF-1 (124 (127 – 320 ng/mL) with poor growth hormone stimulated response was noted. Pituitary imaging revealed hypoplastic anterior pituitary, with normal posterior pituitary. He was started on testosterone and growth hormone replacement therapy, which patient was on inconsistently between the ages of 13 and 22 years. Upon evaluation by adult endocrinology, he had been off testosterone therapy for 2 months and endorsed fatigue, malaise and weight loss. He reported normal libido and denied erectile dysfunction. He had no facial hair, but axillary and pubic hair was noted, along with Tanner Stage 3 genitalia and small testes.

**Conclusion:** Although we did not pursue genetic confirmation, we hypothesize that our patient may have X-linked familial congenital hypopituitarism given family history. Various genes involved in X-linked HH include ANOS1, DAX1 or NROB1; however there have been no reports of associated hypoplastic anterior pituitary. As such, it is also possible that two independent etiologies underlie the similar clinical presentations in our patient and his cousin. Mutations in various genes encoding transcription factors have been implicated in abnormal pituitary gland development and dysfunction. From our literature search, our case represents the first case of isolated hypoplastic anterior pituitary associated with HH and GHD.

**Abstract #860**

**MASSIVE PULMONARY EMBOLISM AS THE FIRST PRESENTATION OF A PATIENT WITH ACROMEGALY**

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Hamad Medical Corporation

**Objective:** To present a patient with acromegaly who presented with bilateral massive pulmonary embolism (PE).

**Case Presentation:** A 21-year-old Asian male presented with chest pain followed by syncope. He had hypotension and tachycardia. Electrocardiogram showed sinus tachycardia, right ventricular strain pattern with ST segments elevation, so PE was suspected. CT pulmonary angiogram showed bilateral massive PE requiring thrombolysis. Thrombophilia workup was unremarkable and echocardiography was normal. The patient was found to have coarse facial features with abnormally large hands and feet, so acromegaly was suspected. Insulin-like growth factor-1 (IGF-1) was 980 μg/L (0-400) and growth hormone (GH) was 28.90 μg/L (0-10). The 75 g oral glucose load GH suppression test confirmed the diagnosis. MRI pituitary revealed a 2.4 cm well-circumscribed sellar/suprasellar mass displacing the optic chiasm. Visual perimetry showed bilateral superior temporal hemianopia more on the left side. Neurosurgeon opinion was sought; however, he advised to postpone the surgery for 6 months as the patient required anticoagulation. Thus, octreotide long-acting release and cabergoline were started with gradual dose escalations because of non-significant response. Repeated MRI showed a trivial size regression...
to 2.2 cm. Later, trans-sphenoidal resection of the mass was performed. Post-operative fasting GH was 1.77 μg/L, and the patient was discharged in a stable condition. The histopathology showed tumor cells positive for synaptophysin and GH.

**Discussion:** Acromegaly is a rare disease secondary to persistent hypersecretion of GH mostly from the pituitary gland. Annual incidence is 6 cases per million. This is the first reported case of massive bilateral pulmonary embolism as the first presentation of acromegaly. A previous report described 3 cases with acromegaly who had high IGF-1 despite treatment with multiple modalities and they had recurrent venous thromboembolism. This indicates that acromegaly is associated with hypercoagulability; however, the exact mechanism is not clear. It has been suggested that elevated IGF-1 is associated with increased fibrinogen, tissue plasminogen activator and plasminogen activator inhibitor levels while decreased protein S and tissue factor plasminogen inhibitor, creating a prothrombotic environment. Improvement in IGF-1 levels is associated with improved plasminogen levels.

**Conclusion:** Acromegaly induces a hypercoagulable state that associated with changes in the fibrinolytic system; however, the exact mechanism needs to be studied further.

**Abstract #861**

**ABNORMAL PITUITARY FUNCTION SECONDARY TO COMPRESSION OF PITUITARY GLAND BY ALLERGIC FUNGAL SINUSITIS EXTENDING INTO INFERIOR SELLA**

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**Objective:** Allergic fungal sinusitis is a rare cause of pituitary hormonal dysfunction. We describe a patient who presented as sphenoidal sinus mass extending into the inferior sella, causing upward displacement of the pituitary and exhibiting mild pituitary dysfunction.

**Case Presentation:** A 51 year old African American male was referred to Endocrinology Clinic for evaluation of pituitary function. One month earlier, he had developed double vision, for which he was seen by an ophthalmologist who diagnosed Cranial Nerve VI palsy and obtained a brain MRI which revealed a sphenoid sinus mass extending into the inferior sella, with an associated upward displacement of the pituitary, prompting the referral. By the time the patient presented to the Endocrine Clinic, his double vision had resolved. At that visit, he denied fatigue, nipple discharge, polyuria, polydipsia, cold and heat intolerance, hair loss, headache, dizziness, skin changes, abdominal pain, nausea, vomiting, and constipation. He also described no problem with sexual drive or erection. He gave no history of previous sinus difficulties. He was hemodynamically stable with no signs of orthostatic hypotension and his general physical exam was unremarkable. Laboratory studies showed mildly elevated prolactin (20.75ng/ml), low total testosterone (139ng/dl), an apparently inappropriately normal LH (2.49 mu/ml) and (FSH 5.58 mu/ml), normal Free T4 (0.83ng/dl), TSH (0.802 mciu/ml), and random late morning cortisol (6.59mcg/dl).

The patient underwent bilateral total ethmoidectomy, bilateral sphenoidotomy, and mucosal coverage of bilateral carotid dehiscences in the sphenoid cavity without complications. Pathology report showed allergic mucin with fungal elements. Cultures grew Bipolaris species. The patient returned for a follow up appointment two weeks after the surgery. Repeat laboratory studies showed normalized prolactin (8.2ng/ml), improved total testosterone 205ng/dl with normal LH (2.92mu/ml), FSH (4.84mu/ml), Free T4 (1.06ng/dl), TSH 0.948 mciu/ml), and random late morning cortisol (8.53mcg/dl).

**Conclusion:** Allergic fungal sinusitis represents 5-10% of all chronic sinusitis cases. It has the ability to extend outside of the sinus to areas such as bone, orbit, skin and brain. In this case it extended into the inferior sella producing pituitary gland displacement. This case highlights importance of considering abnormal pituitary function in differential diagnosis of any extrasellar mass extending into the sella.

**Abstract #862**

**THYROTROPH AND GONADOTROPH CO-SECRETING PITUITARY TUMOR SUCCESSFULLY TREATED WITH SOMATOSTATIN ANALOGUE**

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**Case Presentation:** Thyrotrophin-secreting pituitary adenomas are a rare cause of hyperthyroidism, accounting for < 2% of all pituitary adenomas. Even rarer are adenomas co-secreting thyrotrophins and gonadotrophins. Patients with TSH-secreting adenomas typically present with symptoms of hyperthyroidism. The diagnosis may be delayed due to failure to recognize the inappropriately normal-mildly elevated TSH in association with an elevated free T4 and/or free T3. Somatostatin analogues (SA) are typically used for diagnostic purposes, reducing
TSH secretion in order to control symptoms, and to facilitate tumor shrinkage prior to surgery. A few reports have described using SAs as primary therapy for these tumors. Use of SAs to treat a co-thyrotroph/gonadotroph secreting adenoma is a rarity.

We present a case of a 70 year-old man referred after the incidental finding of thyroid nodules. He denied symptoms of hyperthyroidism and compressive features. Exam was significant for tachycardia (104 BPM) and goiter. Thyroid functions: TSH 1.604uIU/mL [0.350-5.50], FT4 3.08ng/dL [0.8-2.7], FT3 2.09ng/mL [0.6-1.94] and T4 19.7ug/dL [4.8-11.4]. Thyroid antibodies were negative. Thyroid scan showed a multinodular goiter, the uptake was elevated at 44.5% [10-35]. MRI revealed a 0.9cm microadenoma encroaching the left cavernous sinus. This coupled with an elevated FSH 20.6mIU/mL [1.6-18.1], LH 18.4mIU/mL [1.8-12] and normal testosterone 695.57ng/dL [270-1194], lead us to suspect he had a co-secreting pituitary microadenoma. Additionally: α-subunit 1.7ng/mL [0.09-0.76], sex hormone binding globulin (SHBG) 151.6nmol/L [16.5-55.9], TSH 3.358, FT4 3.91 and FT3 11.2. Diagnosis was confirmed via octreotide suppression: TSH 0.017, FT4 0.92, FT3 3.91 and FSH 13.3, LH 8.4, free testosterone 14.40ng/dL [5-21]. Following the test dose and normalization of labs, he admitted in retrospect to having symptoms of hyperthyroidism.

Since he was symptomatic, had atypia of uncertain significance on thyroid biopsy and refused pituitary/thyroid surgery, we elected to manage him with Octreotide 10mg monthly. Hormonal values normalized, he remained asymptomatic.

**Conclusion:** To our knowledge, only one other case of a TSH and gonadotrophin-secreting tumor that was successfully treated with a SA exists in the literature. Considering the success of SA treatment in our patient, we propose that this can be a primary therapeutic option for patients with a similar presentation. Of discrepancy in current literature is the dosage necessary to obtain a therapeutic effect, therefore necessitating further investigation into different dosing schedules and their potential side-effects.

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**Abstract #863**

**ACASE OF THYROTOXICOSIS FOLLOWING THE RESECTION OF A TSH-SECRETING PITUITARY ADENOMA**

Crystal Carter, DO, Khawla Ali, MD

**Objective:** Thyrotropin-secreting pituitary adenomas (TSHomas) are extremely rare, accounting for less than 1% of all pituitary adenomas. Often times when a TSHoma is present, thyrotoxicosis is present prior to resection of the adenoma. Herein, we report a rare case of clinical thyrotoxicosis presenting after complete surgical resection of a TSH-secreting adenoma.

**Case Presentation:** An 18-year-old man, with history of well-controlled asthma, presented in early 2017 with abnormal thyroid function tests. He denied any palpitations, anxiety, vision changes or headaches at the time of presentation. His TSH at diagnosis was 6.750 µU/mL (0.465-4.680 µU/mL), and free T4 was 2.7 ng/dL (0.78-2.19 ng/dL). Additional pituitary hormonal assessment revealed normal FSH, LH, total testosterone, prolactin, IGF-1, cortisol and ACTH levels. His TSH receptor and thyroid peroxidase antibody testing were both negative. MRI of the pituitary was done revealing a 1.4 cm pituitary macroadenoma with no cavernous sinus invasion, but a mild mass effect on the undersurface of the optic chiasm. His visual field testing was normal. Patient subsequently underwent a complete transsphenoidal resection of pituitary adenoma, with MRI demonstrating gross total resection. Immediately post-operatively, patient was noted to have elevated blood pressure of 174/94 mm/Hg, elevated pulse of 101 beats/minute, and had started complaining of new onset palpitations, tremors and anxiety. Hormonal evaluation obtained at that time showed elevated free T4 of 4.7 ng/dL and TSH of 3.120 µU/mL. Patient was started on propranolol for symptomatic treatment. Repeat thyroid testing the following day showed a decrease in TSH to 0.163 µU/mL and free T4 to 3.4 ng/dL. Normalization of patient’s thyroid tests was noted 4 days post-operatively, with complete resolution of his anxiety and palpitations. On the day of discharge, patient’s TSH was noted to be 0.011 µU/mL, and free T4 was 1.4 mg/dL. Final pathology confirmed the diagnosis of TSHoma with positive staining for TSH.

**Conclusion:** We presented a rare case of thyrotoxicosis presenting after a complete resection of a TSHoma. We hypothesize that manual manipulation of the tumor during resection may be playing a role in induction of thyrotoxicosis. Supportive treatment with beta blockers and/or anti-thyroid mediations may be used to aid in the management of these cases.
REPRODUCTIVE ENDOCRINOLOGY

Abstract #900

ENDOMETRIAL CANCER PRESENTING WITH HIGH TESTOSTERONE LEVELS

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Case Presentation: A 75 year old female with history of obesity and type 2 diabetes presented for evaluation of elevated testosterone. Outside labs prior to visit noted a high total testosterone level of 95 ng/dL (ref: 5-32 ng/dL). Her estradiol was 24 pg/mL (ref: 0.7-31.5 pg/mL), and progesterone was 1.21 ng/mL (ref: <0.9 ng/mL). She complained of irregular vaginal spotting over the past 6 months. Further evaluation revealed elevated free testosterone of 15.5 pg/mL (ref: <3.8 pg/mL) and DHEA Sulfate of 161.8 mcg/dL (ref: 10-130 mcg/dL). Abdominal CT showed a 3.9 cm right adnexal nodule, two cystic structures in the left adnexa (2.4 cm and 2 cm); and two nodular structures (2.4 cm and 1.4 cm) in the uterus likely representing fibroids. She was referred to gynecologic oncology for complete hysterectomy. Final pathology revealed Grade 1 endometrioid adenocarcinoma confined to endometrium with background complex hyperplasia with atypia. Pathology also noted benign stromal hyperthecosis of ovaries, which was most likely the cause of her elevated testosterone preoperatively, as her free testosterone level normalized to 2.3 pg/mL after surgical excision.

Discussion: Endometrial adenocarcinoma is the most common gynecologic malignancy and is known to be driven by hyperestrinism. In women with ovarian hyperthecosis, theca cells synthesize excess androgen which can be converted to estrogen in the peripheral adipose tissue. Interestingly, our patient presented with biochemical hyperandrogenism without hyperestrinism, raising the question whether hyperandrogenism could be an additional risk factor for endometrial carcinoma. A Netherlands-based research team found significantly higher local pelvic androgen levels and increased endometrial androgen receptor expression in patients with endometrial cancer, suggesting androgens are at least a co-factor in the development of endometrial cancer (1); another study revealed short-term treatment with testosterone of postmenopausal women does not stimulate endometrial proliferation (2). Further studies are warranted to evaluate the role for hyperandrogenism from ovarian hyperthecosis in endometrial carcinoma in postmenopausal women.

Conclusion: This case demonstrates an unusual presentation of endometrial cancer in a postmenopausal woman with high testosterone levels due to ovarian hyperthecosis. Further studies are warranted to evaluate this pathophysiology and need to screen for endometrial cancer in the setting of hyperandrogenism without hyperestrinism.

References:
(1) http://news.bbc.co.uk/2/hi/health/808792.stm

Abstract #901

REVERSAL OF PREMATURE MENOPAUSE RELATED TO TURNER'S SYNDROME (45X), OOCYTE RETRIEVAL, AND OOCYTE FREEZING, IN A 13 YEAR OLD GIRL WITH PRIMARY AMENORHEA

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Objective: To determine if a technique of inducing follicle maturation despite apparent ovarian failure by sensitizing some antral follicles that are present to endogenous gonadotropins by restoring down-regulated follicle stimulating hormone (FSH) could be successful in a patient with 45X Turner’s syndrome, and allow oocyte retrieval and subsequent cryopreservation.

Methods: A 13 year old patient with 45X Turner’s syndrome and primary amenorrhea with an undetectable serum estradiol (E2) level and serum FSH of 67.2 mIU/mL was given ethinyl estradiol to lower FSH to hopefully restore sensitivity of a few remaining antral follicle to endogenous and/or exogenous FSH, allowing oocyte retrieval and subsequent freezing.

Case Presentation: By day 14 the serum E2 rose to 88 pg/mL (ethinyl estradiol does not contribute to serum E2 when measured by ELISA) but dropped without luteinization. However, another follicle was recruited by day 39 of the cycle with a serum E2 of 251 pg/mL, progesterone 0.5 ng/mL, LH of 26.9 mIU/mL and FSH 16.5 mIU/mL. She was given 10,000 unites of human chorionic gonadotropins. Her dominant follicle measured 18mm. The serum E2 rose the next day to 355 pg/mL. One oocyte was retrieved and frozen by vitrification. She tried one more time. She got to a 16.6mm dominant follicle at age 14 with a serum E2 of 205 pg/mL but the oocyte was degenerating so freezing was not performed.

Discussion: The technique of reversing menopause by restoring sensitivity of the few remaining follicles was first published in 1984 and there have been many anecdotal reports of ovulation induction and successful pregnancy since that time. Suppressing FSH release from the pituitary by the negative feedback effects of high dose estrogen was the first technique described. However, suppression of FSH by gonadotropin releasing hormone agonists or antagonists have also been published. There have also been 2 cases reported...
of ovulation induction, and successful pregnancies despite streaked gonads, but they did not have Turner’s syndrome. Though sexual infantilism is the most common presentation for classic Turner’s, there are a few cases of spontaneous menses in the teen years with subsequent premature menopause. Even some rare successful spontaneous pregnancies have been reported. The child and mother were advised that if the egg did fertilize, and become an embryo, a female offspring would have a 50% chance of Turner’s syndrome.

**Conclusion:** The first case of reversal of menopause in a classic 45X Turner’s syndrome patient is reported. Furthermore, the first case of oocyte cryopreservation in a young teenager with classic Turner’s syndrome is reported.

**Abstract #902**

**INHIBITING MITOCHONDRIAL PERMEABILITY BY TREATING WITH SYMPATHOMIMETIC AMINES MAY REVERSE THE ADVERSE EFFECT OF AGE AND DIMINISHED EGG RESERVE ON FECUNDITY**

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**Objective:** Based on completely reversing 25 years of marked paresis in a wheelchair ridden woman (who had a mitochondrial disorder known as the syndrome of mitochondrial encephalopathy, lactic-acidosis, and stroke-like symptoms [MELAS]) following treatment with dextroamphetamine sulfate, which resulted in resuming completely normal walking, a decision was made to see if the marked adverse effect of advanced age and diminished oocyte reserve related to aging mitochondria on subsequent fecundity could be reversed by similarly using sympathomimetic amine therapy.

**Methods:** Subject – A 46.5 year old woman with a serum anti-mullerian hormone level of 0.09 ng/mL with 6 years of secondary infertility. She was treated with ethinyl estradiol 20mcg orally daily to lengthen her follicular phase. Dextroamphetamine sulfate extended release capsules 15mg daily was also given to possibly improve mitochondrial function.

**Case Presentation:** She spontaneously ovulated on day 11. The follicle was mature (18.8mm average diameter with serum estradiol 256 pg/mL). She conceived with natural intercourse in her second treatment cycle and was treated with both vaginal and oral progesterone during the luteal phase and throughout the first trimester. She delivered a full-term healthy boy. She continued the dextroamphetamine sulfate until 12 weeks from conception.

**Discussion:** One case does not prove that the dextroamphetamine sulfate contributed to the success. Nevertheless, if she had the one oocyte retrieved by in vitro fertilization, and the egg injected with donor mitochondria, almost everyone would be convinced that the injection of donor mitochondria was responsible for the success. Interestingly, she had one previous pregnancy resulting in a live delivery following natural intercourse and progesterone support in the luteal phase plus the addition of dextroamphetamine sulfate when she was age 40, but still showing marked diminished oocyte reserve with a day 3 FSH level of 46.5 mIU/mL. Hopefully, this case will influence our institutional review board to allow the evaluation of a larger series to determine if treatment with dextroamphetamine could improve fecundity of women of very advanced reproductive age, including those with marked diminished oocyte reserve.

**Conclusion:** The aging of mitochondria responsible for diminished oocyte quality and poor fecundity in women of advanced reproductive age may be related to increased permeability of the mitochondria with infusion of unwanted elements leading to disruption of function. Dextroamphetamine is hypothesized to correct cellular permeability defects by releasing more dopamine from sympathetic nerve fibers.

**Abstract #903**

**SYMPATHOMIMETIC AMINES IMPROVES RECURRENT ASCITES, PLEURAL EFFUSION AND PELVIC PAIN RELATED TO WIDELY DISSEMINATED ENDOMETRIOSIS**

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**Objective:** To describe a unique treatment for a very rare form of endometriosis presenting as pseudo-primary peritoneal cancer.

**Methods:** A 35 year old woman who had multiple admissions for marked ascites with the suspicion of primary peritoneal cancer (and was being considered to start chemotherapy by a major university medical center) was eventually diagnosed with widely disseminated ectopic endometriosis causing ascites, multiple pulmonary nodules and pleural effusions. She also complained of severe pelvic pain that occurred after her menses ended for 3-4 days followed by 3-4 days of severe dysuria (endometriosis found in urinary bladder also). She was treated with 15mg dextroamphetamine sulfate immediate release (IR) tablets increasing to 30mg IR tablet daily.
**Abstract #904**

**A VIABLE TRIPLET PREGNANCY RESULTING FROM OVULATION INDUCTION WITH LETROZOLE WITH A MAXIMUM PEAK MID-CYCLE ESTRADIOL APPROPRIATE FOR JUST ONE FOLLICLE**

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**Objective:** To report a viable triplet pregnancy resulting from ovulation induction with letrozole with a maximum peak mid-cycle estradiol appropriate for just one follicle.

**Methods:** An anovulatory 31 year old woman with oligomenorrhea was given letrozole 7.5mg/day for 8 days because she failed to ovulate with lower dosages, including 7.5mg x 5 days. She was monitored by serial pelvic sonography and serum estradiol (E2), and progesterone (P).

**Case Presentation:** She formed 4 dominant follicles of 37, 28.3, 19.3, and 21mm 8 days after stopping letrozole. However, her peak serum E2 was 268 pg/mL. All 4 follicles showed release by ultrasound 2 days later as evidenced by shrinkage of more than 5mm. However, based on the serum E2 level, the patient was advised that there was very little risk of multiple births because probably only 1 follicle was present, and the other cystic structures were non-functional cysts. However, she conceived triplets, which were very viable with appropriate heart rates and size at both 7 weeks and 8 weeks by pelvic sonography.

**Discussion:** Studies have shown lower pregnancy rates in a natural cycle if the serum E2 does not exceed 200pg/mL E2 at the time of peak follicular maturation. Thus, it was quite surprising that she conceived viable triplets since the assumption was made that there was only 1 good follicle with 1 good oocyte amongst the 4 follicles.

**Conclusion:** A precedent has been set that a viable triplet outcome is possible with multiple dominant follicles seemingly present by pelvic sonography, but a serum E2 level consistent with only 1 good dominant follicle. Thus, a patient very concerned about risk of multiple births could withhold contact with sperm if sonography suggests multiple follicles but the serum estradiol suggests that only one viable follicle is present. The triplets all have separate gestational sacs, and thus it is clear that 3 separate oocytes were fertilized.

**Abstract #905**

**POSTMENOPAUSAL HYPERANDROGENISM CAUSED BY A RARE OVARIAN TUMOR**

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**Objective:** To present a case of postmenopausal hyperandrogenism due to a benign steroid cell tumor, not otherwise specified (NOS).

**Case Presentation:** A 65 year old woman presented for Endocrinology evaluation with complaints of alopecia with a receding hairline and hirsutism managed via shaving and evolving over the preceding 6 to 12 months. She also endorsed a 20 pound weight gain over the past few years. She denied exogenous testosterone exposure. Vital signs included a blood pressure of 156/84 mmHg, weight of 171.8 pounds, and BMI of 31.93 kg/m2. On exam her skin was without significant striae but terminal chin hair was present. Prior labs included a testosterone of 183 (5-32 ng/dL) with repeat of 355 (12-36 ng/dL), DHEAS of
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87.0 (20.4-186.6 µg/dL), 17-hydroxyprogesterone of 60 (15-290 ng/dL), prolactin of 6.8 (4.8-23.3 ng/mL), and TSH of 0.819 (0.360-3.740 mIU/mL). Additional labs ordered as part of her Endocrinology evaluation revealed a testosterone of 269.6 (7.0-40.0 ng/dL), free T4 of 1.08 (0.70-1.55 ng/dL), IGF-1 of 218 (75-263 ng/mL), and cortisol of 5.5 (6.2-19.4 µg/dL). Based on her presentation, further testing for hypercortisolism was deferred. Previous imaging included a transabdominal ultrasound with limited visualization of her ovaries, a transvaginal ultrasound which did not visualize the ovaries but revealed a thickened endometrial stripe of 2.5 cm, and a noncontrasted CT scan of the abdomen and pelvis which was negative for an adrenal mass. Due to these findings, a repeat transvaginal ultrasound was ordered at a specialized imaging center and revealed an 11 mm left ovarian cyst and 7mm right ovarian cyst with an 11 mm thickened endometrial stripe. The patient was ultimately referred for hysterectomy and oophorectomy. Pathology showed a left ovarian 1.6 mm steroid cell tumor, NOS with pelvic washout negative for neoplastic or atypical cells. Months later, the patient endorsed symptomatic improvement and her total testosterone was 13.1 (7.0-40 ng/dL).

Discussion: There are several possible causes of hyperandrogenism in a postmenopausal woman although rapid onset raises concern for adrenal and ovarian tumors. Classically testosterone values > 200 ng/dL and DHEAS values > 700 µg/dL have been associated with such tumors although these criteria are not definitive. Imaging may detect a tumor source although some are difficult to localize. Steroid cell tumors can present in this manner and represent 0.1% of all ovarian tumors with 60% subcategorized as NOS.

Conclusion: In the presence of postmenopausal hyperandrogenism of a suspected ovarian tumor source, having ruled out adrenal pathology, hysterectomy with oophorectomy is to be considered even in the absence of a tumor on imaging.

Abstract #906

A CASE OF SECONDARY HYPOGONADISM IN A MALE WITH AN EATING DISORDER

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Case Presentation: A 45 year old male presented for evaluation of hypogonadism. He also had a preceeding weight loss and a BMI of 18. At his peak he was exercising upto 90 minutes a day and also had limited his caloric intake significantly. He complained of marked fatigue, low libido and erectile dysfunction. He was found to have very low serum gonadotropins and very low total and free testosterone levels. Remainder of the anterior pituitary gland function was intact. His blood glucose levels were normal.

He was referred for nutrition counseling and to the eating disorders clinic. Over the next few months he regained some weight. Given his symptoms we started him on topical gel androgen replacement as well. His testosterone levels improved but remained low and required several titrations of the dose of testosterone gel. Over time his androgen levels did return to the normal range.

He was advised continued nutrition counseling and psychotherapy. However, a return to excess exercise did result in weight loss again and androgen levels were lowered again. His doses for testosterone gel required titration.

He continues to receive nutrition counseling and encouragement to have a balanced exercise regimen and caloric intake. However, it has been a challenge to maintain this long term. A withdrawal of androgen therapy has so been not possible.

Conclusion: This case outlines the marked and sustained effect of an eating disorder with marked weight loss in a male patient on the hypothalamic-pituitary-gonadal axis. It has not been possible to withdraw androgen therapy due to persistent secondary hypogonadism.

Abstract #907

NORMAL PREGNANCY DESPITE ABNORMALLY ELEVATED SERA HUMAN CHORIONIC GONADOTROPIN LEVELS IN THE FIRST TRIMESTER

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Objective: To determine if an abnormally elevated sera beta human chorionic gonadotropin (beta-hCG) levels in a singleton pregnancy may be associated with an abnormal pregnancy.

Methods: One thousand singleton pregnancies achieved in natural cycles where the precise day of ovulation was determined by follicular maturation studies (i.e., serial pelvic sonography and sera levels of estradiol (E2), progesterone (P), and luteinizing hormone (LH)). All pregnancies were monitored by serial ultrasounds, E2, P, and beta-hCG levels during the first trimester.

Case Presentation: There was only one case found with abnormally high beta-hCG levels during the first trimester. When she was 15 days from conception her serum beta-hCG level was higher than expected (850 mIU, expected 100). At 22 days the beta-hCG was 21,926 (expected
~1000) and at 28 days the beta-hCG level was 109,695 (expected 10,000 mIU/mL). Throughout the first trimester all fetal ultrasounds appeared normal. Her cell free DNA test at 10 weeks showed no trisomy 13, 18, and 21. She has completed 14 weeks of pregnancy and the fetus looks perfectly normal with only a choroids plexus cyst noted. **Discussion:** Slow rising serum beta-hCG levels signal a poor pregnancy outcome in a high percentage of cases (either spontaneous miscarriage or ectopic pregnancy). A literature search did not find any publications dealing with sera beta-hCG levels much higher than expected in the presence of a singleton pregnancy with evidence of a fetus (i.e., not a molar pregnancy). Partial molar pregnancies are usually associated with low serum beta-hCG levels. In the 1000 singleton pregnancies evaluated, where the precise date of ovulation was determined by follicular maturation studies (similar to the case presented), there was not one patient whose serum beta-hCG level exceeded 10,000 21 days from conception or exceeded 100,000 28 days from conception. Interestingly her gestational sac was about 1 week advanced over the crown-rump length (CRL), and the CRL was more appropriate for the true gestational age. At least based on this one case an abnormally high sera beta-hCG level does not signify an abnormal pregnancy. **Conclusion:** Abnormally elevated beta-hCG levels in a singleton pregnancy are rare. There is no evidence that it prognosticates a poor outcome.

**Abstract #908**

**PITUITARY IMAGING BY MRI AND ITS CORRELATION WITH BIOCHEMICAL PARAMETERS IN THE EVALUATION OF MEN WITH HYPOGONADOTROPIC HYPOGONADISM**

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**Objective:** A significant ambiguity still remains about which patient deserves an MRI [magnetic resonance imaging] of the hypothalamic-pituitary region during evaluation of hypogonadotropic hypogonadism [HH]. In this study we aimed to evaluate the relevance of MRI in patients with HH and also tried to establish the relationship between MRI findings and the biochemical parameters.

**Methods:** This was a retrospective case series of men who were referred to our endocrinology department with clinical and biochemical evidence of HH (total testosterone level (TT) < 10 nmol/L and with low (< 10 IU/L) or inappropriately normal levels of LH between 2010 and 2016. Patients clinical, biochemical and MRI details were obtained from the departmental database and hospital clinical portal. Out of 233 men referred, 175 with isolated HH were included for this study.

**Results:** The mean age of men was 50.9 ± 13.7 years. Our patients were predominantly obese (BMI of 34.1 ± 5.9 kg/m2). The mean TT was 5.1 ± 2.1 nmol/L and LH was 3.0 ± 1.8 U/L. Only 87 (49.7%) men had TT levels lower than the Endocrine society threshold of 5.2 nmol/L. About 81.2% of men had normal pituitary imaging and the remainder had different spectrum of abnormalities [macro adenoma–8; micro adenoma–8; partial or complete empty sella – 16 and one had pituitary cyst]. Comparison between groups [Table 1] showed that patients in the higher age group were more likely to have a macro adenoma or empty sella. Likewise patients with higher BMI [36.3 ± 6.7 kg/m2] had higher rates of empty sella detected on MRI. The TT; LH; FSH; IGF1 and TSH were lowest in patients with macro adenoma and they also had the highest prolactin levels. We also found that a greater number of men who had MRI abnormalities had their TT levels in the lower quartiles (Q1-0.2 to 3.8 nmol/L, n=10 and Q2-3.9 to 5.2 nmol/L, n=9) in comparison to men who had TT in the higher quartiles (7 each in Q3 and Q4). A linear regression analysis showed that likely predictors of an abnormal MRI imaging are age (p=0.04), IGF1 (p=0.03) and prolactin (p=0.004) levels and not TT (p=0.44) or LH (p=0.73).

**Conclusion:** Our study confirms that an MRI of pituitary is not warranted in all patients with HH as the yield of identifiable abnormalities is quite low and there is little clinical benefit of identification of empty sella or a non-functioning micro adenoma. Clinicians should have a higher index of suspicion of an underlying anatomical lesion like macro adenomas only when low levels of TT (<5.2 nmol/L) are associated with abnormal levels of prolactin and IGF1 and consider imaging these patients only.
Abstract #909

SERUM FOLLICLE STIMULATING HORMONE VS. ANTI-MULLERIAN HORMONE LEVELS AS A PROGNOSTICATING FACTOR FOR SUCCESS FOLLOWING IN VITRO FERTILIZATION IN WOMEN WITH DIMINISHED OOCYTE RESERVE

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Objective: 1) To determine to what degree does measuring both day 3 serum follicle stimulating hormone (FSH) and serum anti-mullerian hormone (AMH) increase the detection of women with diminished ovarian reserve (DOR) as opposed to measuring only 1 of these predictors. 2) To determine if women with increased FSH and decreased AMH have a worse prognosis compared to those with only one parameter abnormal. 3) To determine in women with only one parameter abnormal, which one better predicts poor pregnancy outcome. 4) To determine if women with both parameters abnormal have a significant decrease in number of eggs retrieved compared to those with only 1 parameter abnormal.

Methods: Ovarian reserve determined by day 3 serum FSH and AMH – All patients used the same assay. Only mild controlled ovarian hyperstimulation was used. The age cut-off was <43. A serum FSH >12 mIU/mL or a serum AMH <1.0 ng/mL was considered consistent with DOR. Embryos transferred day 3. Comparison of 3 groups: 1) DOR suggested by high FSH and decreased AMH, 2) DOR suggested by high FSH, normal AMH, and 3) DOR suggested by normal FSH but low AMH.

Case Presentation: There were a total of 86 women evaluated. Assuming that if either FSH is elevated or AMH is low, if one determined DOR by high FSH only, 22 of 86 (25.5%) of cases would not have been detected for DOR. 8 of 86 (9.3%) would not have been detected if DOR was determined by low AMH only.. When both FSH and AMH suggest DOR, there were 402 metaphase II (MII) eggs retrieved (2.4 per retrieval), normal AMH but high FSH averaged 3.8 MII eggs/retrieval vs. 3.0 eggs when there was low AMH but normal FSH. The respective clinical and delivered pregnancy rates/transfer for these 3 groups were: 22.0% and 19.0%, 71.4% and 57.0%, and 25.0% and 16.6%. For those having transfers, the percentage with women aged <35 and 40-42 was 28% and 44% for grp 1, 43% and 43% for grp 2, and 25% and 16% for grp 3. Thus, an age advantage would not explain the trend for better pregnancy rates for grp 2.

Discussion: The groups were too small for statistical comparison. However, preliminary results suggest the women with DOR, evidenced by high FSH, but not low AMH, tend to have more oocytes retrieved and a better pregnancy rate than when the AMH is subnormal.

Conclusion: Measuring both AMH and day 3 FSH can help a given couple decide whether to pursue IVF-ET with their own oocytes, or consider donor oocytes.

Abstract #910

INSIGHT INTO THE MECHANISM OF THE EVOLUTION AND SUBSEQUENT REGRESSION OF A FOLLICULAR CYST SECRETING HIGH LEVELS OF ESTRADIOL

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Objective: To describe follicular maturation events leading to the development of a high estrogen-secreting follicular cyst.

Methods: A woman with left sided pain at mid-cycle was found to merely have a dominant follicle as determined by measurement of the size of the follicle by transvaginal sonography and sera levels of estradiol (E2), progesterone (P), luteinizing hormone (LH), and follicle stimulating hormone (FSH).

Case Presentation: At the time of the left sided pain a cyst was seen measuring 23mm. Since the serum E2 was 224 pg/mL, serum P 0.47 ng/mL, LH 7 mIU/mL and FSH 3.6 mIU/mL, the cyst was assumed to be a dominant follicle on the left and the pain “mittelschmerz”. Five days later the cyst grew to 30mm, E2 increased to 1079 pg/mL, serum P 1.04 ng/mL, LH 3.4 mIU/mL, and FSH 1.7 mIU/mL. The cyst eventually grew to 41.3mm 3 days later with the serum E2 at 1071 pg/mL and serum P 0.54 ng/mL. Two weeks later the cyst decreased to 32.6mm with a drop in serum E2 93 pg/mL and serum P 0.27 pg/mL. One week later the cyst disappeared without any intervention.

Discussion: This case demonstrates that a functional ovarian cyst secreting high levels of estrogen can develop from a dominant follicle that does not luteinize. The woman had been on oral contraceptives (OC) when the cyst developed. The OC may not have prevented follicular recruitment, but inhibited an LH surge.

Conclusion: At least one cause of an estrogen secreting cyst is the formation of a dominant follicle without an LH surge to cause luteinization. Expectant therapy may be all that is required.
Abstract #911

PREGNANCIES IN A TURNER MOSAIC PATIENT AT A RELATIVELY ADVANCED AGE

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**Objective:** To report a case of a Turner mosaic who successfully conceived at age 38 and had a phenotypically normal baby without evidence of Turner’s syndrome.

**Methods:** A 38 year old woman was evaluated for secondary infertility of 1 year duration. She had tried to conceive for 6 months at age 37 when she spontaneously conceived but miscarried (gestational sac without a fetal pole). She was unsuccessful for 1 year when she sought help in conceiving. She made a mature follicle without follicle maturing drugs so her sole treatment was with progesterone supplementation in her luteal phase. As part of her evaluation for miscarriage, she had a chromosome evaluation.

**Case Presentation:** The chromosome results showed that she was a Turner mosaic with 22% of the cells tested showing 45X. Options were discussed, including in vitro fertilization with pre-implantation genetic sampling. However, the patient-doctor decision was to proceed with a natural cycle. She conceived on her third progesterone treatment cycle. She delivered a phenotypically normal female baby whose chromosomes showed 46XX. A repeat chromosome analysis on the mother confirmed that she is a phenotypically normal Turner mosaic.

**Discussion:** A search of the literature failed to find a case of a Turner mosaic successfully conceiving at age 38. Most Turner mosaic women are sterile from premature ovarian failure. There are some cases reported of successful pregnancy, more in turner mosaics than when 100% of the cells are showing 45X (Turner’s syndrome). However, some very rare cases of patients with 100% Turner karyotype have delivered a live baby with their own oocytes. Thus, they may be undetected.

Abstract #912

THE FIRST REPORTED CASE OF 2 SUCCESSFUL PREGNANCIES FOLLOWING FOLLICLE MATURATION BY FSH DOWN-REGULATION WITH ETHINYL ESTRADIOL FOLLOWED BY IN VITRO FERTILIZATION OF SINGLE OOCYTES IN A WOMAN WITH PREMATURE MENOPAUSE

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**Objective:** To report 2 successful pregnancies, 1.5 years apart, in a woman in premature menopause following follicular maturation by FSH down-regulation with ethinyl estradiol followed by in vitro fertilization-embryo transfer (IVF-ET).

**Methods:** Based on persistent amenorrhea, estrogen deficiency and marked increase in her serum FSH and very low anti-mullerian hormone (AMH) levels (FSH 105 pg/mL and AMH undetectable), a 29 year old woman with premature ovarian failure consulted our group to determine if she could conceive using her own oocytes. Other reproductive endocrinologists advised her that her only option was to use donated oocytes. However, she did her own literature search and consulted our reproductive endocrine center because of extensive published case reports of reversing menopause with ovulation induction and pregnancies by restoring follicular sensitivity to endogenous or exogenous gonadotropins by up-regulating down-regulated FSH receptors on the few follicles remaining by lowering the elevated serum FSH levels. She was started on ethinyl estradiol 20 micrograms per day.

**Case Presentation:** She achieved one dominant follicle without the use of any exogenous gonadotropins. She chose IVF-ET to maximize her chances of conception. She was successful with one good quality embryo transferred on day 3 and she delivered a full-term healthy baby. She wanted a second child and she realized her best chance would be to start as soon as possible after delivery before she totally exhausted her oocyte supply. Thus six months after delivery she attained a mature follicle in a natural cycle using just ethinyl estradiol to restore FSH sensitivity, and again did IVF-ET transferring one embryo. She has successfully completed the first trimester.

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**Discussion:** The first case report of this technique of using ethinyl estradiol to reverse menopause was published in 1984. The first case of the exclusive use of ethinyl estradiol without exogenous gonadotropin followed by IVF-ET for tubal occlusion with a successful delivery was published
Case Presentation:
A 36 year old male presented to endocrinology clinic for evaluation of elevated testosterone (T) and infertility despite normal sexual function and normal puberty. His past medical history included epilepsy and phenytoin and levetiracitam; and surgical history included mammoplasty and ACL repair. On exam he had normal male pattern hair, no acne, descended testis and a normal penis with no hypospadias present. Laboratory testing revealed total T >1500 ng/dL, unquantifiably high free T, elevated SHBG 86.6 nmol/L, normal estradiol, normal DHEA, elevated LH 11.2 mIU/mL, normal FSH and TSH. Ultrasound showed normal testicular volume with several microcalcifications. Over 8 months his medications were simplified to levetiracetam and there was no change in his T, SHBG and LH levels. A karyotype confirmed 46, XY genotype. He had two semen analyses demonstrating azoospermia. He was diagnosed with mild androgen insensitivity syndrome and confirmatory genetic testing with possible testicular biopsy was recommended.

Discussion:
Virilization in utero is dependent on androgens and their receptors. Androgen resistance due to defects in the androgen pathway lead to varying phenotypes including complete, partial or mild Androgen Insensitivity Syndrome (AIS). Complete AIS presents with female external genitalia, a blind vagina, breast development and is usually identified by primary amenorrhea. Partial AIS has phenotypic expression of ambiguous genitalia with varying degrees of labial scrotal fusion, clitoromegaly and hypospadias. Mild AIS is the rarest form presents with gynecomastia and infertility. Androgen resistance is present in 40% azoospermia cases. The diagnosis of AIS requires 46 X,Y karyotype, normal or increased serum T, normal conversion of T to dihydrotestosterone and increased LH due to absence of negative feedback. An elevated androgen sensitivity index, a product of T and LH, is also seen in AIS. Our patient has mild AIS presenting with gynecomastia and azoospermia. In addition to biochemical evaluation, genotyping may reveal a mutated androgen receptor gene on chromosome Xq11-12. Over 800 mutations have been reported and 70% are germ line mutations. Genetic testing is not consistently confirmatory as only 25% of patients with partial AIS have known mutations.

Conclusion:
In couples undergoing infertility evaluation it is important to consider male causes of infertility. One rare cause of azoospermia is mild AIS that should be considered in the presence of elevated androgen sensitivity index and normal virilization.

Abstract #914

ELEVATED SERUM TESTOSTERONE LEVELS IN A PATIENT WITH CHRONIC LIVER DISEASE: IS IT CLINICALLY RELEVANT?

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Objective:
In chronic liver disease, testosterone levels are typically low and decline with progression of disease. Testosterone is highly protein-bound and has particularly high affinity for sex hormone binding globulin (SHBG). In cirrhosis, SHBG levels are elevated, and total testosterone levels may be normal or high in the setting of hypogonadism. This case demonstrates a clinically insignificant elevation of serum testosterone in a man with untreated cirrhosis.

Case Presentation:
A 66-year-old man with untreated hepatitis C (HCV) cirrhosis was referred to endocrinology for elevated testosterone levels. He denied fatigue, vision changes, heat or cold intolerance, excessive hair growth, easy bruising, weight changes or erectile dysfunction. He took a multivitamin including 600mcg of biotin. He did not have thyromegaly, gynecomastia or other stigmata of advanced liver disease. His testicular exam was normal. His labs showed total testosterone 1360ng/dL (240-950ng/dL), free testosterone 13.6ng/dL (3.47-13.0ng/dL), and SHBG 132nmol/L (10-57nmol/L). Follicle stimulating hormone (FSH) was 12.8mIU/mL (0.9-15mIU/L) and luteinizing hormone (LH) was 13.0 mIU/mL (1.3-13.0mIU/mL). Dehydroepiandrosterone-S was 83.5mcg/dL (25-131mcg/dL), androstenedione was 218ng/dL (40-150ng/dL), and estradiol was 61pg/mL (10-40pg/mL). After biotin supplementation was stopped, his total testosterone was 1130ng/dL, free testosterone was 9.04 ng/dL, and SHBG was 132nmol/L. FSH and LH levels
Abstract #915

DECREASE IN AMP KINASE EXPRESSION AND ACTIVITY IN DIABETIC PATIENTS WITH HYPOGONADISM: INCREASE FOLLOWING TESTOSTERONE SUPPLEMENTATION

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Objective: AMP kinase is a key enzyme involved with energy regulation, the intake of macronutrients, the uptake of glucose and fatty acids by cells and the metabolic combustion of fatty acids. We hypothesized that in patients with hypogonadism associated with diabetes, its expression and activity are diminished since there is a quantitative and qualitative loss of skeletal muscle function.

Methods: Twenty-two men with HH and T2DM were compared with 20 eugonadal men with T2DM at baseline. From the HH patients, 12 were treated with testosterone 200mg every 2 weeks injected intramuscularly for 24 weeks, during which their plasma concentrations were maintained in the physiological range. Hyperinsulinemic euglycemic clamps (HEC) were carried out prior to and after testosterone replacement and fat (abdomen) and muscle (quadriceps) biopsies were carried out prior to and following HEC procedure on each occasion.

Results: In the hypogonadal state, the expression and the activity (measured as phoso-T172-AMPK-α) of AMP kinase-α was significantly lower in HH patients than eugonadal diabetics both in adipose tissue and skeletal muscle by 37% and 29%, respectively, for expression and by 22.1% and 28%, respectively for activity. Following testosterone, there was no change in expression but there was a significant increase in AMP kinase activity by 69±31% (from 14.9±2.8 to 22.8±2.2U/ml, p<0.05) in the muscle but not in the adipose tissue. At the end of the treatment and following the hyperinsulinemic euglycemic clamp, there was a significant increase in AMP kinase expression by 41±9% and 46±11% in adipose tissue and muscle, respectively, while there was only a modest increase (NS) in activity in both tissues.

Discussion: This effect of testosterone may contribute to the increase in glucose uptake and an improvement in insulin sensitivity since AMP kinase also induces an increase in Akt-2 and GLUT-4 expression.

Conclusion: Clearly, therefore, testosterone is an important modulator of AMP kinase activity.

Abstract #916

TOTAL PARENTERAL NUTRITION (TPN) INTERFENCES WITH TESTOSTERONE ASSAY

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Objective: To Increase Awareness of the Interference of Total Parenteral Nutrition (TPN) with Laboratory Assay.

Case Presentation: A 67 year-old male with primary hypogonadism on topical testosterone replacement therapy with a good clinical response was started on TPN for short gut syndrome. Subsequent labs demonstrated an elevated Total Testosterone level at 2760 (240 - 950 ng/dL) and free Testosterone at 105 (3.47-13.0 ng/dL). After holding testosterone therapy, the repeated testosterone level was persistently elevated at 4280 ng/dL. The test was repeated at an alternate lab which showed low total Testosterone at 80 (241-827 ng/dL) and free Testosterone at 0.60 (3.70-23.28 ng/dL). When we further investigated this discrepancy between the two labs results, we found that the first lab obtained the blood sample from the PICC line that was also being used for TPN delivery (TPN infusion held prior to blood draw), whereas the latter obtained the sample from peripheral blood. To confirm, the same blood sample from the PICC line was analyzed at both labs and the testosterone
level was elevated in both. We subsequently obtained a peripheral blood sample and analyzed it at the first lab which demonstrated a low total Testosterone level of 14 ng/dL, and a free Testosterone level of 0.22 ng/dL - consistent with being off testosterone therapy.

Discussion: Clinical use of TPN is common in patients with certain gastroenterological conditions. Laboratory monitoring of these patients is important. We present a case which demonstrates blood collection from a PICC line in which TPN being infused could interfere with the laboratory assay, resulting in false results despite the infusion being held prior the blood draw. In our case, the patient was off testosterone therapy for several months with persistently elevated testosterone levels when the blood was collected from the PICC line. We postulate that contamination of the blood with TPN content in the PICC line resulted in pre-analytical error in laboratory testing. There is need for further research regarding this interaction. To our knowledge, this is the first reported case of TPN Interference with Testosterone assay.

Conclusion: Blood collection from the PICC line contaminated with TPN may falsely elevate testosterone levels leading to suboptimal treatment of hypogonadism. Increased awareness of this interference is important so that health care providers and laboratory personnel collect blood samples from peripheral blood to avoid contamination in such situations.
THYROID DISEASE

Abstract #1000

GRAVES’S DISEASE IN A PATIENT WITH HASHIMOTO’S THYROIDITIS AND BREAST CANCER

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Case Presentation: Graves’s disease presenting in a patient with Hashimoto’s thyroiditis is an uncommon phenomenon in the literature. Graves’s disease and Hashimoto’s thyroiditis fall in the spectrum of autoimmune thyroid dysfunction which is caused by genetic predisposition in about 70-80% of the cases. We present a 41 year old female with a history of BRCA1 positive breast cancer and Hashimoto’s thyroiditis diagnosed two years’ prior who presented with hyperthyroid symptoms and found to have Graves’s disease. Patient had been on levothyroxine 50mcg which was tapered off after a year from diagnosis of Hashimoto’s as her thyroid functions improved. Patient had a strong family history of thyroid dysfunction in her siblings. With the eventual diagnosis of breast cancer patient had a left breast mastectomy and received four cycles of adjuvant chemotherapy. Patient then presented to the ER six months after the breast cancer treatment with insomnia, palpitations, anxiety, sweating, and neck tenderness. On physical exam patient was mildly tachycardic and had right eyelid retraction and ptosis on the left eye. Lab work showed, thyroid stimulating hormone (TSH) level of <0.005 uIU/ml, free thyroxine (FT4) 2.4 ng/dL and total triiodothyronine (TT3) 235 ng/dL, thyroid stimulating immunoglobulin (TSI) elevation at 404% (nL <140%), thyroid peroxidase (TPO) antibodies at 579 IU/mL (nL <9IU/mL). Thyroid ultrasound showed heterogeneous echotexture and hypervascularity of the thyroid gland. Patient underwent a radioactive iodine scan which revealed a 24 hour iodine uptake of 51% with diffuse uptake compatible with Graves’ disease. Patient’s symptoms were improved by propranolol alone.

Conclusion: In our case we demonstrate the co existence of both Graves’ disease and Hashimoto’s thyroiditis likely secondary to autoimmunity in the patient which is also supported by her strong family history of thyroid disease. Her chemotherapy presented as a trigger to either development of autoimmunity or promotion of preexisting autoimmune antibodies to produce TSI and eventual hyperthyroid state.

Abstract #1001

THYROTOXICOSIS FROM METASTATIC CHORIOCARCINOMA

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Objective: Identify thyrotoxicosis as a potential complication of metastatic choriocarcinoma.

Case Presentation: A 31 year old woman with history of molar pregnancies presented with 3 months of worsening dyspnea. She underwent dilation and curettage for molar pregnancy in 2014 and 2016 but was subsequently lost to follow-up. Pathology was consistent with complete hydatidiform mole. At presentation, she had significant weight loss of 30 lbs over a 3 month period along with palpitations and chest discomfort. Her heart rate was 143/min and lid lag was observed. Thyroid exam was normal without goiter or nodules. CT imaging showed invasive uterine mass with innumerable pulmonary metastatic lesions. Human chorionic gonadotropin (HCG) was greater than 200,000 mIU/mL. TSH was undetectable, and free T4 and T3 levels were both elevated to 3.46 ng/dL (0.89-1.76 ng/dL) and 11.06 pg/mL (2.18-3.98 pg/mL), respectively. Her clinical picture was consistent with thyrotoxicosis due to metastatic choriocarcinoma. The patient was started on methimazole 20mg daily, propranolol 20mg TID, along with chemotherapy with etoposide, methotrexate, actinomycin, cyclophosphamide and vincristine (EMA-CO). After completing her first chemotherapy cycle, her serum HCG decreased to 176,000 mIU/mL, and was 288 mIU/mL by the end of cycle 3. Given that serum HCG levels had come down significantly, methimazole was discontinued after just 2 weeks of therapy with normalization of all thyroid studies.

Discussion: Human chorionic gonadotropin shares a homologous beta-subunit with TSH, and is able to cross react at the TSH receptor. Both TSH and HCG contain 12 half-cysteine residues with three disulphide bonds forming a cysteine knot structure, which is integral for binding to the receptor. In a human thyroid cell culture assay, 1 microU of HCG was equivalent to 0.0013 microU of TSH. As such, physiologic increase of HCG during a normal pregnancy results in rise in T4 and T3 levels and relative suppression of TSH. Multifetal pregnancies are associated with higher HCG levels, resulting in transient hyperthyroidism; HCG level is directly correlated with the degree of hyperthyroidism. Thus, thyrotoxicosis may occur in the setting of neoplasms that secrete HCG. The definitive treatment of the neoplasm will result in treatment of the hyperthyroid state, as demonstrated by this case. However, patients may require antithyroid agents and beta-blockade transiently to control symptoms of thyrotoxicosis.

Conclusion: It’s important to consider thyrotoxicosis as a complication in conditions with high serum HCG levels such
as choriocarcinoma. Management includes surveillance of HCG and appropriate discontinuation of antithyroid medications as HCG levels downtrend.

Abstract #1002

HYPERTHYROIDISM DUE TO A PARTIAL MOLAR PREGNANCY

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Case Presentation: A 27-year-old gravida 2, para 1 female presented to her obstetrician at 12 weeks gestation with a complaint of persistent headache. She was found to be hypertensive and started on labetalol. Headache persisted, and the patient also noted the onset of chest discomfort, dyspnea and palpitations. She denied vaginal bleeding or discharge. Reevaluation at 14 weeks gestation revealed continued hypertension (164/97 mm Hg), but resting heart rate was 64 and no goiter, thyroid nodules, murmurs, cracks, or lower extremity edema were present. Serum β-human chorionic gonadotropin (β-hCG) was 1,125,000 IU/L (up to 200,000 IU/L at 13-16 weeks gestation), and sonographic evaluation of the uterus showed an enlarged, cystic placenta, bilaterally enlarged ovaries with theca lutein cysts, and a single fetus with cystic hygroma. Partial molar pregnancy was diagnosed. Thyroid function tests were notable for TSH 0.03 mIU/L (0.35-4.94), free T4 2.1 ng/dL (0.9-1.5), and free T3 5.6 pg/mL (1.7-3.7). Methimazole 20 mg TID was started, with treatment continued for one week after induced delivery of uterine contents. Obstetrical ultrasound after the procedure confirmed complete evacuation of the uterus. Three weeks following termination of pregnancy, the patient was clinically and biochemically euthyroid, with TSH 1.23 mIU/L.

Discussion: Hydatidiform moles occur in approximately 1 in 1,200 pregnancies. This patient’s presentation was unusual because 80-90% of molar pregnancies present with vaginal bleeding. Biochemical hyperthyroidism is diagnosed in about 5% of cases before 10 weeks gestation but nearly 30% of cases after 10 weeks gestation with this patient. However, only 2-3% of patients have clinical hyperthyroidism. The patient was treated with a thioamide due to the possibility that her symptoms were due to hyperthyroidism, with heart rate controlled by labetalol. Structural homology between β-hCG and TSH is responsible for cross-reactivity of β-hCG with the TSH receptor, and severe elevations of β-hCG in molar pregnancies increase risk of hyperthyroidism. Levels of β-hCG return to normal 8-12 weeks after evacuation of the hydatidiform mole, though hyperthyroidism usually resolves sooner.

Conclusion: Endocrinologists need to consider hydatidiform mole in the differential diagnosis of hyperthyroidism in pregnancy, even when there is no vaginal bleeding. Inappropriate elevation of β-hCG for gestational stage is an important clue to the diagnosis. Depending on the severity, hyperthyroidism may require treatment with β-blockers and thioamides before termination of the pregnancy. Evacuation of the hydatidiform mole leads to prompt resolution of hyperthyroidism.

Abstract #1003

HEPATIC DYSFUNCTION IN GRAVES’ DISEASE: TWO CASE REPORTS

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Objective: HEPATIC DYSFUNCTION IN GRAVES’ DISEASE: TWO CASE REPORTS

57-year-old man presented with palpitations and dyspnea for one week. Review of systems was positive for heat intolerance, anxiety and unintentional weight loss. On physical exam tachycardia with an irregularly irregular rate, lid lag, lid retraction, non-tender thyromegaly was noted; abdominal exam was unremarkable. Laboratory data: TSH 0.006 mIU/L, free T4 6.69 ng/dL, AST 1893 U/L, ALT 872 U/L, serology for viral hepatitis was negative. Transthoracic echocardiogram showed a left ventricular ejection fraction (LVEF) of 20%. 31-year-old female presented with gradual onset painless jaundice, pruritus and dark urine. Review of systems was positive for neck swelling, heat intolerance, tremors, and unintentional weight loss. Physical exam was pertinent for sclera icterus, exophthalmos, lid retraction, lid lag, large non-tender thyroid gland with bilateral bruit, and an unremarkable abdominal exam. Laboratory data: TSH 0.006 mIU/L, free T4 3.47 ng/dL, total bilirubin 13.3 mg/dL, direct bilirubin 8.7 mg/dL. Abdominal ultrasound without evidence of biliary disease.

In both cases thyroid stimulating immunoglobulin was >500% and TSH binding inhibitory immunoglobulin >40 IU/L. They were diagnosed with Graves’ disease and after two months of methimazole therapy their LFTs normalized.

Discussion: Hyperthyroidism has been associated with hepatic dysfunction ranging from mild LFTs abnormalities to liver failure and death. Prevalence of hepatic dysfunction in hyperthyroidism has been reported as high as 76%, with normalization of LFTs
ABSTRACTS – Thyroid Disease

after improvement of thyroid function. The mechanism behind this association is not well understood and may be due either indirect pathways or direct hormone effects. Hypothyroidism interferes with bilirubin metabolism by decreasing its conjugation; also hyperthyroidism causes relative liver hypoxia, by increasing hepatic metabolic activity without an appropriate increase in blood flow. Furthermore, hyperthyroidism may cause heart failure with resultant liver congestion; nonetheless, there does not appear to be a correlation between LVEF and the degree of hepatic dysfunction.

Conclusion: Awareness may prevent delayed diagnosis, misdiagnosis and unnecessary investigations. Prompt recognition and treatment of hyperthyroidism can lead to resolution of LFTs abnormalities.

Abstract #1004

A RARE CASE DEMONSTRATING AN OVERLAP OF AUTOIMMUNE THYROID DISEASE WITH IMMUNE THROMBOCYTOPENIA

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Objective: Immune Thrombocytopenia (ITP) is an acquired thrombocytopenia caused by autoantibodies against platelet antigens. Rarely, patients with autoimmune thyroid disease (ATD) may present with mild thrombocytopenia. When associated together, ITP and ATD could reflect a more significant defect in the immune self-tolerance of these patients compared with those who have primary ITP alone. Such patients are often refractory to standard ITP therapy.

Case Presentation: We present a case of a 32-year-old female with hypothyroidism, who was admitted to the hospital with thrombocytopenia found on a routine blood work. She had symptoms of fatigue, cold intolerance, menorrhagia, weight gain, gingival bleeding, and skin bruising for the past two months. She was non-compliant with her thyroid medication. She was hemodynamically stable with no evidence of hypothermia, edema, or altered mentation. Her physical examination revealed multiple bruises on the skin, however no hepatosplenomegaly or lymphadenopathy was noted.

Initial blood work revealed thrombocytopenia without anemia or leukopenia. Her INR, renal, and liver function tests were normal. Her thyroid studies supported a diagnosis of Hashimoto’s thyroiditis (Refer to table 1). Secondary causes for ITP were ruled out by negative results of ANA, HIV, HBV, HCV, H. Pylori Ab, and DIC panel. The diagnosis of primary idiopathic ITP was made. Peripheral blood smear showed markedly decreased platelets with increased mega-thrombocytes and increased immature platelet fraction, consistent with peripheral destruction as seen with ITP. She was started on intravenous levothyroxine and dexamethasone. By day 3 of admission, thyroid function studies had improved along with the platelet count (Refer to table 1). This eliminated the need for IVIG. The patient was discharged on a 2-week course of prednisone 60mg daily and levothyroxine 150mcg daily. She was asymptomatic without any skin bruising during her outpatient follow-up.

Conclusion: When ITP co-exists with ATD, solely directing standard treatment at correcting the thrombocytopenia may be ineffective as these patients demonstrate a more widespread immune defect. The platelet count in this patient showed a significant improvement with levothyroxine in addition to steroids within 48 hours, without necessitating IVIG. Prompt diagnosis and treatment of underlying hypothyroidism can prevent unnecessary splenectomies and the use of medications that often have significant side effects such as azathioprine, danazol, rituximab, and thrombopoietin agonists. In addition, patients with ITP often have recurrent thrombocytopenia, and maintaining their euthyroid state can improve their platelet counts, thus preventing relapse.

Abstract #1005

AN UNREPORTED COMPLICATION OF THYROID STORM: REFEEDING SYNDROME

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Objective: Thyroid storm is a rare condition within the spectrum of thyrotoxicosis that reflects an extreme physiological state. Most commonly seen with Graves’ disease, its presentation is related to the increased hypermetabolic state in a thyrotoxic environment. We present an unusual case of refeeding syndrome (RFS) triggered during management of a thyroid storm.

Case Presentation: This is the case of a 41-year-old Hispanic woman with a recent diagnosis of Graves Disease, who presented to the hospital after being found unresponsive in her house. Her primary care physician started therapy with methimazole 9 months prior, but she was non-adherent to regimen. Relatives reported development of erratic behavior with visual hallucinations and social withdrawal over the course of
1 year. On examination, she was cachectic with a BMI of 16 kg/m², stuporous, with sinus tachycardia of 168 bpm, temperature of 39°C, and 25 rpm. Her thyroid was diffusely enlarged with bilateral exophthalmos; lungs were clear to auscultation. Reported TSH level was <0.01 mIU/L (nl, 0.5-5.0) with free T3 and free T4 markedly elevated at >65pg/mL (nl, 2.3-4.2) and >16ng/dL (nl, 0.8-1.8) respectively. Burch-Wartofsky-Score was 80 points (nl, <25) with clear diagnosis of thyroid storm. She was admitted to ICU and required immediate intubation. Glucocorticoids, propylthiouracil, cholestyramine, Lugol’s iodine and propranolol were initiated. Baseline work-up showed leukocytosis, elevated liver enzymes, negative blood cultures and no electrolyte abnormalities. Early peptide-based enteral feeding was initiated at slow rate of 15ml/hr. Six hours later, she was found with bibasilar crackles and diminished bowel sounds. Follow-up labs showed potassium of 2.3mEq/L (nl, 3.5-5.1), magnesium of 1.1mEq/L (nl, 1.5–2) and phosphorus of 1.0 mEq/L (nl, 1.8-2.3). New diffuse ST depressions were noted on EKG with no cardiac enzyme elevation. Suspecting RFS, diet was stopped immediately and electrolytes were replaced aggressively. After repletion, normalization of EKG was achieved and enteral feeding was initiated meeting less than 50% of estimated requirements. Diet was progressed in two-to-three day intervals along with electrolyte replacement without major complications.

**Conclusion:** Refeeding syndrome is caused by severe electrolyte shifts during reintroduction of nutrition in malnourished patients. Hypermetabolic states, such as long-standing untreated thyrotoxicosis, are risk factors. Moreover, acute hypophosphatemia, hypokalemia and hypomagnesemia can result in fatal pulmonary, hematologic and cardiac complications. Early identification of high-risk patients and its treatment is crucial to reduce the mortality associated with the syndrome.

**Abstract #1006**

**WOMAN WITH HASHIMOTO’S ENCEPHALOPATHY**

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**Objective:** Present an interesting case of Hashimoto’s encephalopathy (HE).

**Methods:** The clinical and paraclinical findings of the patient are shown

**Case Presentation:** A 50 y/o woman, previously healthy without history of thyroid disease, who 7 weeks ago presented an episode characterized by a fixed gaze, generalized tonic-clonic movements, loss of consciousness of spontaneous recovery, without sphincter relaxation. Relatives refer behavioral changes. Patient adds decreased strength in right lower limb making walking difficult. A few days later, she presented disorientation, decreased left-sided strength to predominance of the lower limb, tendency to sleep and delusions. She was admitted to a clinic where they diagnose viral encephalitis and prescribe acyclovir, dexamethasone and topiramate, she was discharged with acyclovir PO- But due to behavioral disorder, decreased strength of the lower limbs and tremor of the extremities, she was admitted to our hospital; on examination: dry skin on extremities, goiter 1b; awake, oriented in time and person; no meningeal signs; bradypsychia, bradydalia; tremor in tongue and lower limbs; muscle strength decreased in right lower limb; hyperreflexia in upper limbs; slow gait, slight extension of lift point, with tendency to drag the lower right limb. Analytical: BC, G, electrolytes (N), ANA, TORCH/HIV in blood (-). TSH: 14uUI/ml; FT4: 1.55ug/dl; AbTPO 370U/ml. CSF transparent, 74 leukos/mm³, G: 60mg%, Pr: 86mg%; TORCH/TB in CSF(-). CT: discrete loss of the interface between cortical gray matter and white matter. MRI: Hypoxic-ischemic lesions at the level of the basal ganglia, thalamus and hippocampal gyrus; EEG: symptomatic epilepsy vs. paroxysmal, non-epileptic disorder. MTP pulses of 1 gr IV/d for 3 days followed by PDN 1mg/kg PO with progressive decrease in 3 months and LT4 75 µg PO. Currently she is developing normally, has not repeated seizures or involuntary movements

**Discussion:** HE is a rare encephalopathy with AbTPO (+) and usually normal thyroid function associated with a variety of neuropsychiatric symptoms that should be considered in patients who do not have previous neurological pathology. The prevalence is 2.1/100,000, it’s diagnosed predominantly in the adult population and the average age of onset is 50 years, with a predominance of females 5:1.

**Conclusion:** Clinical cases like this suggest that this disease is probably under-diagnosed. So that each patient with an unexplained encephalopathy, particularly in women, should think about ruling out HE. The AbTPO(+), an EEG with slow waves and focus of activity that suggests the presence of epileptogenic focus, a normal MRI or with findings of vasculitis, as well as, the response to corticotherapy it’s very suggestive of HE.
Abstract #1007

COEXISTING ANAPLASTIC THYROID CARCINOMA AND RECURRENT PAPILLARY THYROID CARCINOMA: A DIAGNOSTIC DILEMMA

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Case Presentation: A 74-year-old woman presented with dysphagia, dyspnea, and hemoptysis. She previously underwent total thyroidectomy and I-131 treatment for stage III (T1, N1a, M0) papillary thyroid carcinoma with TSH goal < 0.1 mU/L. She also had a known history of untreated chronic lymphocytic leukemia with diffuse adenopathy which complicated routine monitoring and rendered a pre-hospitalization nodal sonogram unreliable. Three months prior to presentation, Thyrogen rTSH prepped I-123 whole-body imaging was negative for local or distant uptake and thyroglobulin tumor marker level was 2.8 ng/mL (baseline 2.4 ng/mL). On admission, CT chest exhibited a heterogenous, enlarged, multinodular mass extending into the upper mediastinum and significant narrowing of the distal trachea. Cervical lymph node biopsy was performed with pathology consistent with metastatic papillary thyroid carcinoma. She subsequently underwent tracheostomy for continued airway protection with simultaneous pretracheal mass biopsy; the pathology from this location was consistent with anaplastic thyroid carcinoma.

Discussion: Papillary thyroid carcinoma is the most common thyroid malignancy whereas anaplastic thyroid carcinoma is the least common, accounting for 89.4% and 0.8% of all thyroid cancers, respectively. Papillary thyroid carcinoma is well-differentiated and relatively slow growing with low rates of recurrence in ATA low risk (0.8%) and ATA intermediate risk (2.5%) cases. In contrast, anaplastic thyroid carcinoma is rapidly growing, aggressive, and represents the progression of a primary neoplasm to histologically undifferentiated tissue with resulting lack of thyroid functionality. According to multiple longitudinal single-institution reviews, 23-39% of patients have well-differentiated thyroid carcinomas present at the time of anaplastic thyroid carcinoma diagnosis.

Conclusion: Although the overall prognosis of anaplastic thyroid carcinoma is poor, the aggressive nature of the disease makes early diagnosis and treatment imperative. The undifferentiated nature of anaplastic thyroid carcinoma results in tissue loss of thyroid functionality and subsequent loss of cellular iodine concentration and thyroglobulin production. This complicates conventional diagnostic methods as screening for recurrence and disease progression may result negative in the setting of active disease. In addition to these screening challenges, approximately 1/3 of anaplastic thyroid carcinoma cases exist simultaneously with well-differentiated tumors at the time of diagnosis. As demonstrated in this case, biopsies of separate tumor sites may be necessary for accurate diagnosis and prompt treatment of thyroid carcinomas.

Abstract #1008

THYROTOXICOSIS FROM “PROPER” USE OF AN OTC PREPARATION: A CASE REPORT

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Case Presentation: Over the counter nutritional supplements are not regulated by any federal authority. Consumers often misinterpret that as implying that they are safe and free of potential side effects. Ingredients as innocuous as iodine (Tri-iodine(R), for instance) have been associated with hyperthyroidism. Other OTC which contain levothyroxine, triiodothyronine (or both in the form of dessicated thyroid) have also been confirmed as causing hyperthyroidism. A recent survey by AACE yielded 91 cases of thyroid supplements causing alterations in TSH, 65% of which were in the hyperthyroid direction, and 68% of which were symptomatic, including two cases of arrythmias. In these reported cases, it was not established conclusively whether the patients were taking the supplements as directed, or taking more than the recommended daily doses. Also, it is not explicit whether they were also taking prescription LT4 or T3.

T.P. is a 77 year old woman with a history of postsurgical hypothyroidism for benign disease. She weighs 146 pounds and was not taking any medications or supplements known to interfere with thyroid function. Her most recent TFTs included TSH=0.34 U/ml (0.40 - 4.00) and Free T4 =1.73 ng/dl (0.89 - 1.76) while taking levothyroxine 112 mcg daily. She was advised to reduce to levothyroxine to 112 mcg five days a week, and 100 mcg two days a week. Instead, she consulted with the proprietor of a vitamin store, who told her to discontinue the levothyroxine, and instead take “Thyro 300 IC with cytodextran technology -- a dietary supplement." Each capsule contained 800 mg of a “proprietary blend” of “L-tyrosine, Thyroid, kelp (Atlantic whole), Cycodelxtran.” The patient took two capsules a day as recommended.

Approximately three months later, the patient described hair loss, shaking, crying easily, and a 5 pound weight loss. Labs showed TSH <0.01, Free T4=2.53 (0.89-1.76). Labs repeated seven days later (while still taking...
the supplement) TSH <0.01, Free T4=2.34 and Free T3=13.80 pg/ml (1.80 - 4.20). The patient was advised to stop the supplement. Labs repeated 14 days later showed TSH=1.66, Free T4=0.54, and Free T3=2.60. The patient subsequently resumed her usual dose of levothyroxine and follow up labs a month later were completely normal. All of her symptoms resolved.

Conclusion: In this case, we have documentation that the patient was taking the “supplement” as prescribed, and no other potentially interfering medications or supplements were present. One needs to be cautious that even seemingly innocuous “dietary supplements” may contain active ingredients in sufficient quantities as to cause frank thyrotoxicosis. This can be especially dangerous in the elderly.

Abstract #1009

A CHALLENGING CASE OF AMIODARONE INDUCED THYROIDITIS WITH PROTRACTED DISEASE COURSE

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Objective: Amiodarone induced thyrotoxicosis (AIT) is a diagnostic and therapeutic dilemma. It is often challenging to treat in patients with congestive heart failure. We present a unique case of AIT Type 2 with prolonged course requiring 6 months of treatment before becoming euthyroid.

Case Presentation: This is a case of a 58-year-old male with history of advanced heart failure secondary to ischemic cardiomyopathy on Left Ventricular Assist Device, atrial fibrillation on amiodarone for last 2 years admitted with shortness of breath. His workup showed thyroid stimulating hormone was suppressed and free T4 was elevated (>6.0 ng/dL). He had no other symptoms of hyperthyroidism except palpitations. He had no personal or family history of thyroid problems or radiation exposure. Doppler thyroid ultrasound revealed goiter with normal vascularity. Thyroid stimulating antibodies were negative. Thus, the etiology of his hyperthyroidism was thought to be AIT type 2. He was started on high doses of steroids with no change in thyroid function. Subsequently, thionamides, initially methimazole and later propylthiouracil was added with no improvement. He was also started on cholestyramine and continued on carvedilol. The lack of improvement over 1.5 weeks with thionamide therapy and steroids suggested that this was not a self-limited process. Subsequently, amiodarone was stopped and he was started on potassium iodide to prepare him for thyroidectomy. He also received three sessions of plasmapheresis with no improvement. He was then started on lithium for about 1 week with no change in thyroid function. Free T4 started to trend down after 2 months of treatment while he was on steroids and propylthiouracil. Thyroidectomy could not be performed, as he was later considered high risk for the procedure. Patient was discharged home on 40 mg prednisone and became euthyroid after 6 months of initial presentation.

Discussion: Studies have shown that thyroid function returns to normal within 30 days or less in 60% of patients with AIT type 2 treated with steroids. The case presented above had AIT type 2 initially refractory to medical therapy with return of thyroid function to normal after 6 months of treatment.

Conclusion: Disease course in patients with AIT can be unpredictable requiring prolonged course of treatment. More research is warranted in this field to better treat patients with destructive thyroiditis on amiodarone with underlying congestive heart failure.

Abstract #1010

A RARE CASE REPORT OF GRAVES' DISEASE WITH COEXISTING TSH PRODUCING PITUITARY ADENOMA

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Objective: Only 10 cases of Graves’ disease coexisting with a TSH-secreting pituitary adenoma (TSHoma) have been reported to date. We present a patient with a TSHoma identified based on the biochemical pattern developing while on treatment with anti-thyroid medications initiated after establishing the diagnosis Graves’ disease.

Case Presentation: A 44-year-old Caucasian lady presented with unintentional weight loss. Physical examination revealed diffuse goiter without bruit. TSH was 0.158 mIU/L (0.4-4.5), free T4 (FT4) 3.5 mg/dL(0.8–1.8) with TSI antibodies elevated 345 %(<140%). I-123 thyroid uptake and scan showed a diffuse uptake of 84% ( 8-35%) at 24 hours. While on treatment with Methimazole(MMI), thyroid function tests (TFTs) normalized initially, however, a pattern of elevated FT4 with inappropriately normal TSH was noted. Assay interference and thyroid hormone resistance were ruled out by negative HAMA antibodies and negative RTH mutation analysis. Alpha subunit was1.2 ng/ml (normal <1.02) with elevated a-TSH/TSH molar ratio at 5 (normal range <1). MRI revealed a 1.7X1.4X1.6 cm pituitary macroadenoma. Transphenoidal resection of the pituitary adenoma was done. TFTs normalized postoperatively without medications. However, four months after surgery, FT4 was found to be elevated at 6.5 with suppressed TSH <0.005. Patient was treated again with MMI with
successful achievement of biochemical and clinical euthyroid state.

**Discussion:** Hyperthyroidism caused by excess TSH is uncommon. TSH-secreting pituitary adenoma accounts for less than 2% of pituitary adenomas. The association of TSHoma with Graves’ disease is exceedingly rare. It is recommended that surgery as primary therapy for TSHoma but there is no established management guideline for coexisting condition of Graves’ disease and TSHoma at this time.

In our case, it is possible that the coexistence of the two conditions is incidental. However, the interruption of normal negative feedback mechanism caused by antithyroid medications leading to the progression of preexisting TSHoma has been postulated. Similarly, it has been postulated that a rapid decrease TSH level after pituitary tumor removal may induce autoimmune activation against the thyroid gland.

**Conclusion:** We emphasize the importance of reevaluation of the primary diagnosis and consideration of coexisting diagnoses including rare entities if there is any deviation of clinical and laboratory findings from the primary diagnosis.

Abstract #1011

**DIAGNOSIS OF RESISTANCE TO THYROID HORMONE DUE TO A RARE MUTATION IN THE THRb GENE IN A PATIENT PREVIOUSLY PRESUMED TO HAVE HYPERTHYROIDISM**

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**Objective:** Resistance to thyroid hormone (RTH) is caused by mutations in the thyroid hormone receptor beta (THRb) gene and over 100 mutations have been identified. There has been only one published case of a novel point mutation, the p.Ile250Thr variant (c.749T>C) with 50% reduction in THRb binding affinity to T3. Impaired sensitivity to thyroid hormone can be misdiagnosed as hyperthyroidism.

**Methods:** A 66-year old man, with a history of non-ischemic cardiomyopathy, ventricular tachycardia and atrial fibrillation, was referred for concerns about a possible TSH adenoma. His TSH and FT4 were elevated. Pituitary imaging was negative. He was treated for presumptive Graves’ disease >20 yrs earlier. Further evaluation indicated that RTH was most likely. RTH mutation analysis - Heterozygous positive for p.Ile250Thr variant in the THRb gene.

**Case Presentation:** A 66-year old man was referred by his cardiologist with concerns about a possible TSH adenoma. He has a history of non-ischemic cardiomyopathy, ventricular tachycardia and atrial fibrillation and was to be started on amiodarone. His TSH was 5.04 mIU/mL and FT4 1.83 ng/dL. Pituitary imaging was negative. More than 20 yrs ago he was diagnosed with Graves’ disease because of elevated thyroid hormone, and treated with I-131. No known family history of thyroid disease. Examination revealed a diffuse thyroid gland enlargement with no nodules; heart rate was controlled with metoprolol. THR was suspected. Repeat TSH, FT4 and with FT3 were 7.8 mIU/mL, 1.84 ng/dL and 4.7 pg/mL respectively. Alpha subunit (1.4 ng/ml) and SHBG (66.3 nmol/L) levels were both normal. HAMA was negative. Thyroid antibodies were negative. Genetic testing was done; family members were not available. The patient was heterozygous positive for p.Ile250Thr THRb gene variant.

**Discussion:** The clinical and biochemical phenotype, and the genotype of this patient are consistent with RTH-beta, the p.Ile250Thr variant. He was erroneously diagnosed with hyperthyroidism in the past and treated as such. Thyroid ablation should generally be avoided in RTH. Differential diagnoses include a TSH-secreting tumor but a high alpha subunit to TSH ratio, pathognomonic of the condition, is absent in this patient; also pituitary imaging did not show an adenoma. Although family history seemed negative, RTH is sometimes asymptomatic. Occurrence of atrial fibrillation in RTH-beta patients is not uncommon. Tachycardia occurs because of high serum T4 and T3 in the heart which predominantly expresses the alpha isoform of the TR.

**Conclusion:** RTH can be misdiagnosed as hyperthyroidism with consequent inappropriate treatment. This RTH-beta patient has the rare p.Ile250Thr variant in the THRb gene, second reported case in the literature.

Abstract #1012

**A CASE OF BOTH SECONDARY AND PRIMARY HYPOTHYROIDISM FOLLOWING CHECKPOINT INHIBITOR THERAPY FOR METASTATIC MALIGNANT MELANOMA**

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**Objective:** The use of checkpoint inhibitor therapy for the treatment of malignancy has increased in the last several years. This group of monoclonal antibodies whose targets include cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1), and programmed cell death protein ligand 1 (PDL-1) can cause both primary and secondary hypothyroidism. We present a case of a patient who developed ipilimumab induced central hypothyroidism followed by thyrotrope recovery.
and later primary hypothyroidism.

Case Presentation: A 67 year old male with history of recurrent melanoma underwent treatment with 4 cycles of adjuvant ipilimumab. Three months after therapy he began to experience increasing fatigue, cold intolerance, and skin dryness. Physical exam was notable for mild skin dryness and no palpable thyromegaly. Initial laboratory findings were notable for TSH of 1.25 mcIU/L (ref 0.27-4.2), FT4 of 0.67 ng/dL (ref 0.93-1.7), and FT4 by direct dialysis of 0.67 ng/dL (ref 0.8-1.7). His remaining anterior pituitary axis was within normal limits. A brain MRI did not show pituitary pathology. He was treated with levothyroxine with normalization of his FT4 levels and symptom improvement. Two years later the patient received 5 cycles of nivolumab therapy followed by pembrolizumab and low dose ipilimumab for recurrence. Two months after treatment he was noted to have an undetectable TSH with a FT4 of 2.22 ng/dL. He was instructed to discontinue his levothyroxine. Repeat labs at 4 weeks showed a TSH of 50.62 mcIU/ml with FT4 level of 0.14 ng/dL and positive thyroid peroxidase antibodies. His levothyroxine was re-started for treatment of primary hypothyroidism.

Discussion: This case highlights the effects that newer classes of oncologic medications can have on the endocrine system. Ipilimumab has been associated with the development of anterior pituitary dysfunction. Although rare, recovery of thyrotrope function after ipilumumab therapy has been reported and in this case 2 years after initial therapy. While primary hypothyroidism and thyroiditis have been seen with CTLA-4 agents they are more commonly associated with anti PD-1 agents such as nivolumab and pembrolizumab. This case demonstrates that multiple immunotherapy mediated endocrinopathies can occur in the same patient.

Conclusion: As the use of checkpoint inhibitor therapy becomes more common clinicians should be familiar with the endocrine dysfunction that can occur. This patient developed central hypothyroidism followed by thyrotrope recovery and autoimmune thyroiditis. These patients should therefore be monitored serially for the development of these complications both during and after therapy.

Abstract #1013

THYRODECTOMY FOR THE TREATMENT OF THYROID STORM

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Objective: Thyroid storm is a rare endocrine emergency characterized by dysfunction of multiple organ systems; diagnostic criteria are largely clinical and include thermoregulatory, central nervous system, gastrointestinal, and cardiovascular dysfunction. Thyroid storm can be precipitated by untreated Graves’ disease, surgery, infection, iodine load, and parturition. Medical treatment is targeted at synthesis and release of thyroid hormone and attempts to decrease circulating hormone. In refractory cases, plasmapheresis or thyroidectomy has been used.

Case Presentation: A 29 year old female with untreated Graves’ disease presented to an outside hospital for dyspnea and agitation. She was found to be febrile (105.5F), hypertensive (188/86 mmHg), TSH <0.01 U/mL and FT4 4.05 ng/dL. Chest x-ray revealed pulmonary edema. She was intubated and treated with hydrocortisone, methimazole, and empiric antibiotics and transferred to University of Vermont Medical Center (UVMMC). Physical exam was significant for an intubated young female with a diffusely enlarged thyroid. She was tachycardic with a regular rhythm, had coarse crackles, and 2+ pitting edema up to the thighs. Her TSH was <0.02 mlU/L and thyrotropin receptor antibody level was 29 IU/L (nl <1.75IU/L). Echocardiogram showed diffuse hypokinesis. Her Burch-Wartofsky score (80/140) was highly suggestive of thyroid storm, thus medical management with hydrocortisone, methimazole, potassium iodide drops and cholestyramine was continued. Her hospital course was complicated by hypotension, intermittent atrial fibrillation with rapid ventricular response, and difficulty weaning from the ventilator. Despite aggressive medical treatment and a decrease in her thyroid hormone levels, she did not improve clinically after 1 week. Plasmapheresis was not deemed a treatment option due to pulmonary and cardiovascular instability, thus thyroidectomy was performed on hospital day 8. The patient’s post op course was uncomplicated, she improved clinically, and her thyroid hormone levels normalized.

Conclusion: Medical therapy for thyroid storm is well established in the literature; it involves blocking synthesis and release of thyroid hormone and the recycling and peripheral conversion of circulating thyroid hormones. Treatment for refractory cases is less clear. Plasmapheresis has been used to remove bound thyroid hormone, but
guidelines for safe use are few. Despite the risk of surgery in the critically ill, early thyroidectomy has been shown in retrospective studies to reduce mortality, even when euthyroidism is not achieved. This case illustrates thyroidectomy as a successful option for medically refractory cases of thyroid storm.

**Abstract #1014**

**KEEP ARMOUR THYROID PRESCRIPTION AWAY FROM DOGS**

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**Objective:** To alert endocrinologists to the risk of dog poisoning with Armour Thyroid, if the medication prescription container is not properly stored.

**Case Presentation:** A 30-year-old female with hypothyroidism has been doing well on replacement with Armour Thyroid, 120 mg daily. Considering that this medication needs close monitoring, the patient was informed and she agreed with more frequent than average lab monitoring, and agreed to report any symptom suggestive of hyperthyroidism. She has felt very well on Armour with normal thyroid function tests and regular office follow up. About 2 years later, the patient requested a refill for her Armour Thyroid, although it was just refilled few days earlier. When the patient was asked why she ran out of the medication that soon, she explained the situation having brought the medication bottle to the clinic. The patient stated that her dog attacked the bottle that she had forgotten on the kitchen counter. The dog survived the ingestion of almost 90 tablets of the Armour Thyroid.

**Discussion:** Accidental pet animal poisoning with human medications include both over the counter and prescription medications. Among over the counter human medications/supplements, nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly encountered in accidental pet poisoning, with ibuprofen being the commonest culprit. Of human prescription medications, the Pet Poison Helpline publishes the top 10 classes that are poisonous to pets. This list is outlined below, in the order of prevalence (per annual calls to the helpline) with brands encountered in each class (2):

- NSAIDs (e.g. Advil, Aleve and Motrin)
- Acetaminophen (e.g. Tylenol)
- Antidepressants (e.g. Effexor, Cymbalta, Prozac, Lexapro)
- ADD/ADHD medications (e.g. Concerta, Adderall, Ritalin)
- Benzodiazepines and sleep aids (e.g. Xanax, Klonopin, Ambien, Lunesta)
- Birth control (e.g. estrogen, estradiol, progesterone)
- ACE Inhibitors (e.g. Zestril, Altace)
- Beta-blockers (e.g. Tenormin, Toprol, Coreg)
- Thyroid hormones (e.g. Armour desiccated thyroid, Synthroid)
- Cholesterol lowering agents (e.g. Lipitor, Zocor, Crestor)

**Conclusion:** Endocrinologists should educate their patients to properly store Armour Thyroid, away from pets, especially dogs. Because Armour is made from porcine thyroid extracts: In fact, it has a characteristic and strong odor that can attract dogs (not unlike the smell of dog treats). The therapeutic requirements for thyroid hormones in dogs are much higher than that of requirements in humans. Nevertheless, fatal poisoning with thyroid hormone medications has been reported.

**Abstract #1015**

**COMPUTERIZED CYTOLOGIC FEATURES OF THYROID CANCER DIAGNOSIS**

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National Taiwan University

**Objective:** Fine needle aspiration cytology (FNAC) is known to be accurate for diagnosis of certain types of thyroid cancers and has an essential role in evaluation of thyroid nodules. However, even with the current FNAC practice, the percentage of excised nodules that are malignant only surpasses 50%. According to a meta-analysis studying publications between 2008 and 2011, though the sensitivity of FNAC can reach 97% in average, the average specificity is only about 50% resulting an overall accuracy less than 70%. Therefore, researchers are seeking ways to further improve cytological findings with computerized cytological features.

**Methods:** Totally 167 resected thyroid nodules, including 70 benign and 97 papillary thyroid cancers (PTC), were included in this study. Digital images of the FNAC specimens by Riu’s stain, a type of Romanowsky stain, were obtained from these nodules. With an effective segmentation algorithm, the cytoplasm and the nuclei were automatically identified to allow computation and clustering of cell colors in the Hue, Saturation, and Value (HSV) color space. A total of 18 quantified cytological features, including 12 morphological and 6 chromatic features were computed and analysed. A logistic regression model was then established using 3 quantified features, i.e., mean of ellipticity, mean of circularity, and nuclear-cytoplasmic saturation ratio (Figure 1) and validated for diagnosis of thyroid nodules.

**Results:** Among the 18 quantified features, 10 morphological features and 2 chromatic features were
shown to be statistically significant in differentiating malignant cells with p-value ranging from less than 0.0001 to 0.0181. The logistic regression model was tested to show an AUROC of 0.927, a sensitivity of 89.7%, and a specificity of 91.4%.

Discussion: With the visualization of clinical features, cytologists were alerted to the cytological characteristics suspicious for malignant cells. In addition, quantification of the features showed that some of the computerized features were useful in assisting diagnosis of the thyroid nodules. With only 3 significant computerized features selected into the regression model, the diagnostic accuracy was shown to be comparable to an experienced cytologist.

Conclusion: Our study has shown that the visualization and quantification of the cytology morphological and chromatic features have the potential of being developed as a computer-aided diagnosis tool for diagnosis of thyroid nodules

Abstract #1016

A RARE CASE OF IMPAIRED SENSITIVITY TO THYROID HORMONE

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Objective: Reduced sensitivity to thyroid hormones (RTH) is a rare autosomal dominant disorder with reduced end-organ responsiveness to thyroid hormone. It manifests as persistent hyperthyroxinemia and non-suppressed TSH with variable clinical presentation. We present a challenging case of hyperthyroxinemia and non-suppressed TSH in a patient with hyperthyroid symptoms. Our case highlights the utility of THR gene analysis for diagnostic confirmation in such rare patients.

Case Presentation: A 62-year old Caucasian female was seen in the endocrine clinic for evaluation of abnormal thyroid function tests (TFT’s). She reported history of hyperthyroidism, treated with RAI, in 1982. She denied being treated with thyroid replacement therapy post-RAI ablation. She was euthyroid until 2013 when she noticed hyperthyroid symptoms. Clinical examination showed mild goiter without any other signs of hyperthyroidism. TFT’s showed elevated Free T4 3.32 ng/dl (0.78-2.20 ng/dl), elevated total T3 202 ng/dl (97-170 ng/dl) and non-suppressed TSH 0.87 mIU/L (0.45-4.70 mIU/L). All thyroid antibodies and RAI uptake scan were normal in 2013. The patient was prescribed variable doses of methimazole without improvement in TFT’s or in her symptoms. She admitted noncompliance with methimazole. She reported history of brain tumor, diagnosed in 2011. MRI brain was normal in 11/2016, making TSH producing adenoma less likely. The patient reported multiple family members including her mother, sister, and daughter with thyroid disorder. Gene testing for THRβ (thyroid hormone receptor beta) showed THRβ mutation confirming thyroid hormone resistance syndrome. Methimazole was stopped and the patient was treated with beta blocker only. Gene counseling for family members was offered.

Discussion: RTH should be considered in all hyperthyroxinemic patients who have nonsuppressed TSH with variable clinical presentation. Mutations interfering with major steps required for TH action on target tissues have been, so far, identified (TR-β, TR-α, MCT8, SPB2). TR-β mutation is responsible for RTH and 122 different mutations involving 300 families have been identified. Differential diagnosis includes TSHoma, endogenous antibodies against T4 and T3 and primary thyrotoxicosis.

Conclusion: Our patient’s clinical presentation and pattern of TFT’s were suggestive of RTH syndrome, which was confirmed by gene analysis. Because of the rarity of this disorder and variable presentation, diagnosis requires a high degree of suspicion and is often delayed or misdiagnosed, resulting in inappropriate treatment. Goals of management are to maintain a normal serum TSH level and a eumetabolic state. Gene counseling for appropriate patients should be offered.

Abstract #1017

PARATHYROID FUNCTION IN HYPERTHYROIDISM IN RELATION TO CALCIUM-PHOSPHORUS METABOLISM

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Objective: Various studies have reported conflicting results on parathyroid function in hyperthyroidism. Some results showed low, normal and high levels of PTH. This research aimed to evaluate parathyroid function in relation to calcium and phosphorus and vitamin-D levels in thyrotoxicosis in Nigerians

Methods: This was a cross-sectional study of forty hyperthyroid subjects with clinical and biochemical hyperthyroidism and age and sex -matched healthy controls. Only subjects who met exclusion criteria were recruited. Fasting blood sample was analysed for serum calcium,
albumin, phosphorus, intact Parathyroid Hormone (PTH), Free thyroxine (T4), Free Triiodothyronine (T3), Thyroid Stimulating Hormone (TSH), creatinine and 25-Hydroxyvitamin D levels. Early fasting urine sample was analysed for calcium, phosphorus, creatinine, laboratory parameters were compared between hyperthyroid and controls. Statistical analysis done using SPSS 21. P<0.05 set as level of significant

**Results:** The age distribution of studied was 36.13 (+8.43) years with M: F ratio of 1:4. The mean corrected calcium showed tendency to hypercalcemia in the test group compared to controls 2.3(+0.19) vs 2.2 (±0.22) mmol/l p=0.08. 7.5% of test population had hypercalcemia. The serum phosphorus was comparable between the two groups 1.43(+1.28) vs 1.47 (+0.4) p=0.87. Renal calcium excretion was significantly elevated in comparison to controls 590.95 (+506.71) vs 396.10 (+103.22) mg/24hrs p=0.02. Although phosphorus excretion was high in thyrotoxicosis, the difference was insignificant. More than one-third of studied (37.5%) had reduced PTH and none had hyperparathyroidism. The mean serum 25-Hydroxylvitamin-D of the hyperthyroid and controls were comparable between the two groups, p=0.5.

**Discussion:** Various studies have published either decreased or increased levels of PTH in thyrotoxicosis. In our research, serum PTH concentration in thyrotoxic patients was lower with 37.5% of our studied showing suppressed PTH levels. This could be attributed to tendency to higher free and total serum calcium concentrations in thyrotoxicosis {secondary to bone demineralization} and resultant negative feedback inhibition of parathyroids. The changes in serum phosphorus were also related to suppressed PTH levels probably due to direct effects of thyroid hormones on tissue phosphate metabolism and renal phosphate handling. This altered calcium-phosphorus metabolism was unrelated to serum 25-Hydroxyvitamin D levels in our study.

**Conclusion:** Thyrotoxicosis is a risk factor for altered calcium-phosphorus metabolism and the resultant suppressed parathyroid function.

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**Abstract #1018**

**ARE DIFFERENT LEVOTHYROXINE BRANDS INTERCHANGEABILITY?**

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**Objective:** To evaluate the effects of switching levothyroxine brands in patients whose TSH have been stable.

**Methods:** A retrospective, single-center study was performed in patients with differentiated thyroid cancer or primary hypothyroidism who had taken a stable dose of levothyroxine in the Thyroid Clinic of Chiang Mai University Hospital between January 2012 and December 2016. In the patients who changed the brand of Levothyroxine, TSH levels before and after the brand change, doses of drug A, drug B and adjusted doses of drug B in two consecutive visits after changing the brand were recorded. TSH goals were set differently according to the patient’s diagnosis and staging of disease.

**Results:** By retrospective reviews, 102 patients were included. Ninety-five percent were female and mean age was 57.94 ± 10.94 years. Thyroid cancer occurred in 19 patients while primary hypothyroidism was present in 83 patients of which the most common cause was post-I131 treatment (51.96%). When switching brand, 40 patients (39.22%) needed a dose adjustment because TSHs were not at the desired levels. The geographic mean of TSH while using drug A was significantly lower to that while using drug B (1.06 mIU/ml vs 1.80 mIU/ml, p < 0.01). The difference in TSH was significant in the thyroid cancer group (0.23 mIU/ml vs 1.19 mIU/ml, p < 0.01) and the post-I131 treatment group (1.52 mIU/ml vs 2.38 mIU/ml, p < 0.01). There were 39 patients (38.24%) whose TSH levels were out of the treatment goal even when doses of drug B were adjusted. Optimal doses of drug A and drug B were significantly different (510 mcg/week vs 521 mcg/week, p < 0.01) especially in the post-I131 treatment patients (486 mcg/week vs 498 mcg/week, p = 0.03)

**Discussion:** Our study demonstrated different TSHs when switching brands even with the same doses of levothyroxine, clearly shown in the thyroid cancer and post-I131 treatment groups. The other groups had a small number of the patients, thus the differentiation was unclear. Levothyroxine dose adjustment was up to 39.22%. We also found different optimal doses in the different brands. Our research strengths were (1) the same patient took drug A then switched to drug B so we can eliminate the pharmacokinetic interpersonal variation, (2) we excluded the patients who took the levothyroxine with interfering drugs. The disadvantages were a small number of cancer
Conclusion: Different brands of levothyroxine result in different TSH levels. Brand change should be avoided in clinical practice. If the brand is changed, serum TSH should be checked earlier and dose adjustment done as soon as possible.

Abstract #1021

A PROLONGED SILENT THYROIDITIS WITH SEVERE HYPERTHYROIDISM: A CASE REPORT

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Temple University Hospital

Objective: Present an unusual case of silent thyroiditis (ST) associated with severe hyperthyroidism, hypercalcemia and a very prolonged course.

Case Presentation: A 63 year-old female with advanced CKD was referred to endocrinology for hyperthyroidism. She complained of a 60 pound weight loss over three months, decreased appetite, palpitations, loose stools, and heat intolerance. She had no family history of thyroid disease. On exam the patient had a top-normal sized thyroid gland, with no neck tenderness, bruits or eye finding suggestive of Graves’ disease. Thyroid function tests (TFTs) confirmed hyperthyroidism: TSH 0.02 mIU/mL, FT4 3.6 ng/dL, FT3 720 pg/dL, Total T3 271 ng/dL. Thyroid stimulating immunoglobulin (TSI) was 26, TPO 2 IU/mL, thyroglobulin (Tg) elevated at 105.9 ng/mL, and Tg antibody <1 IU/mL. Thyroid uptake and scan showed 2% uptake at 2 hours and less than 2% uptake at 24 hours. Nuclear medicine questioned whether low uptakes were from iodine exposure in spite of no history of this. She was presumed to have ST and was treated with a two-week course of prednisone due to severity of hyperthyroidism. She was admitted twice over the next two months due hyperthyroidism related issues and developed hypercalcemia with calcium of 13.0 mg/dL with PTH 17 pg/mL. Due to nuc med concern that this could be Graves’ masked by iodine load, methimazole (MMI) 30 mg daily was begun. Urinary iodine was not elevated and MMI was ultimately stopped. Hyperthyroid phase lasted seven months after onset of symptoms, at which time she had lab evidence of transition to the hypothyroid phase. She has had a prolonged hypothyroid phase as well and has required management with levothyroxine (LT4) replacement at 50 mcg daily. Hypercalcemia resolved spontaneously with resolution of the hyperthyroid phase. Her total course from onset of symptoms to resolution of hypothyroid phase was over 18 months.

Discussion: ST frequently follows a progression of a hyperthyroidism, often followed by hypothyroidism, and finally recovery. It accounts for approximately 0.5 to 5% of hyperthyroidism. In most cases, hyperthyroid symptoms last for 2-8 weeks. ST is thought to be an autoimmune condition, with 50% of patients having positive anti-thyroid peroxidase (TPO) antibodies. It is unclear if the advanced CKD contributed to the severity and prolonged course in this patient.

Conclusion: Silent thyroiditis can rarely have a prolonged and severe course, requiring therapy with steroids, cholestyramine and beta blockers.

Abstract #1022

PLASMAPHERESIS AS A TREATMENT FOR AMIODARONE-INDUCED THYROTOXICOSIS IN A PATIENT WITH DYSPHAGIA

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Objective: To present a case in which plasmapheresis was used to treat Amiodarone-induced thyrotoxicosis (AIT) in a nonagenarian. She presented with dysphagia and inability to manage hyperthyroidism with oral anti-thyroid medications.

Case Presentation: A 93-year-old female with a history of subclinical hyperthyroidism secondary to Grave’s Disease presented to the ED with dysphagia, weight loss, fatigue, nausea, vomiting and palpitations. She was started on Amiodarone for atrial fibrillation 3 months prior to the onset of symptoms.

Physical examination revealed tachycardia, exophthalmos, hand tremor, lower extremity edema and a non-tender thyroid gland. TSH was less than 0.005 micro IU/mL (0.36 to 3.74) and free T4 was greater than 7.70 ng/dL (0.76 to 1.46). She had a positive TSI and thyroid ultrasound showed multinodular goiter with diffuse increased vascularity on doppler.

She was admitted to the ICU and started on Methimazole, potassium iodide, corticosteroid, and propranolol. Throughout the following week, she had worsening dysphagia and lethargy. A nasogastric tube was inserted to administer medications and nutrition. Despite 2 weeks of conventional treatment, her symptoms and laboratory values had not improved. Given her age and comorbidities, she was not a candidate for thyroidectomy. As a result, plasmapheresis was initiated.

TSI prior to the plasmapheresis peaked at 201% (less than 140) and declined to 100% post-treatment. Free T3 and free T4 were 3.33 pg/mL (2.18 to 3.98) and 2.79 ng/dL (0.76 to 1.46) respectively after treatment. Eight days after plasmapheresis, her TSH was 0.44 mIU/mL (0.36 to 3.74), FT4 1.20 ng/dL (0.76 to 1.46), FT3 2.4 pg/dL (2.3 to 4.0), and T3 0.4 ng/dL (0.25 to 0.85). Her TSH and FT4 normalization was complete by 3 weeks post-plasmapheresis.
the plasmapheresis, her mental status improved and her dysphagia resolved. She was able to tolerate conventional oral therapy and discharged home.

**Discussion:** Dysphagia can be a primary symptom of hyperthyroidism in the elderly which can lead to treatment challenges with oral anti-thyroid medications. Plasmapheresis is a treatment reserved for resistant thyrotoxicosis and is usually a bridge to thyroidectomy. It was used in our patient as an alternative treatment for hyperthyroidism which resulted in clinical improvement and the ability to safely discharge the patient.

**Conclusion:** This case highlights the utilization of plasmapheresis as the main treatment for hyperthyroidism in patients who are not surgical candidates. It also outlines the possibility of shortening the hospital stay in patients with hyperthyroidism.

**Abstract #1023**

**FEVER OF UNKNOWN ORIGIN: A RARE THYROID CAUSE**

*Andrea George, MD, Noor Addasi, MD, Mohsen Zena, MD*

Creighton University

**Objective:** Fever is a known symptom of thyrotoxicosis and subacute thyroiditis. We report a case with subjective fever for 3 months, who had extensive work-up, later found to have Fibrosing Variant of chronic lymphocytic thyroiditis (FVCLT) with differential including Reidel’s thyroiditis (RD).

**Case Presentation:** 43 year-old female evaluated for a 3 month history of flu-like symptoms including subjective fever, chills, fatigue, sore throat and odynophagia. She denied sick contacts, recent travel or Intravenous drug use. She resided on a farm with rabbits and cows. Infectious disease work-up which included the following: Urinalysis, Blood cultures, Chest X-ray, CT Abdomen/Pevlis, Ebstein barr virus, Francisella tularensis, Brucella, Coxiella, HIV, Tuberculosis and histoplasmosis. All was negative. CBC showed mild leukocytosis 13,000. Pro-calcitonin was low. She had elevated ESR >115 and elevated CRP 106 mg/dl. Rheumatology work-up for elevated ESR was also negative. She was started on Prednisone 80 mg daily and for temporal arteritis, however temporal artery biopsy was found to be negative. A trial of antibiotics did not resolve her sympotms. To further evaluate for malignancy a PET/CT was done, which showed asymmetric thyroid with larger right than left lobe with diffusedly increased in metabolism in the right and left lobe. Thyroid ultrasound showed a right lobe 52 x 38 x 25 mm and the right lobe was replaced by a mass heterogeneous with coarse microcalcifications. Thyroperoxidase(TPO) Antibodies were negative. She had normal TSH and Free T4. She underwent FNA of the thyroid nodule, which showed atypia of undetermined significance. Affirma was suspicious and therefore she underwent Right lobectomy. Pathology findings reported FVCLT with differential including RD. Post-operatively patient’s symptoms resolved, her CRP normalized to <9 mg/L.

**Discussion:** FVCLT a rare condition occurring in about 10% cases, mainly middle age people and Riedel’s thyroiditis is reported in 0.05% of thyroid surgery. Most common presenting symptoms for FVCLT includes dysphagia, hypothyroidism and positive TPO Ab. We present a patient with persistent subjective fever and elevated inflammatory markers, negative TPO antibody, biochemically euthyroid found to have FVCLT.

**Conclusion:** FVCLT should be considered in the differential diagnosis along with subactue thyroiditis and thyrotoxicosis in patients with persistent fever and elevated inflammatory markers.

**Abstract #1024**

**AN OVERLOOKED ETIOLOGY OF HYPERTHYROIDISM: THE JOD-BASEDOW PHENOMENON WITH CHORINC IODINATED MOUTH WASH USE IN A PATIENT WITH GRAVES’ DISEASE**

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University of Florida, Jacksonville

**Objective:** Contrast and Amiodarone are commonly suspected sources of excess iodine exposure. However, other iodine sources causing hyperthyroidism are often overlooked.

**Case Presentation:** A 55-year-old woman with a history of atrial fibrillation presented to Endocrine clinic after a recent ED visit for thyrotoxicosis. Presenting symptoms were palpitations, shortness of breath, and atrial fibrillation. TSH was 0.01uIU/mL. She received IV contrast for 3 CTAs, 4 months before initial presentation. TSH 1 month prior to contrast was normal, 0.93uIU/mL. She was discharged on Lopressor, with improvement of palpitations. Her brother had Graves’ disease and ophthalmopathy. She denied thyroid medication use and OTC supplements. Vital signs and physical exam were normal.

A thyroid uptake and scan 5 months after presentation showed a normal homogenous gland with 3 & 24Hr uptake of 7.2% & 23.7%. Labs showed TSH 0.01uIU/mL, FT4 1.3ng/dL, FT3 4.6pg/mL and TSI 305%. Lopressor was continued and methimazole was started. Repeat uptake & scan, 6months after treatment initiation, revealed normal homogenous uptake of 6.1% & 4.3% at 4 & 24Hr. She became biochemically and clinically euthyroid and methimazole was stopped after 7 months of therapy. She was lost to follow up for 1.5 years when she presented...
again for recurrence of hyperthyroidism 7 days following a CT with contrast. Methimazole therapy was restarted. Upon further questioning, she admitted to using iodinated mouthwash for years. She stopped iodine solution and 5 months later the following labs were obtained: FT4 1.4ng/dL, FT3 5.0pg/mL, and TSH 0.006mIU/L, 24Hr Urine iodine 98.2ug/24Hr, and Cr 0.8g/24Hr. A repeat RAIU showed 23.2% and 51.3% uptake at 4 and 24Hrs. 1 month later she received 15.923mCi of I-131 RAI ablation for Graves' disease.

Discussion: Graves’ disease in the setting of exogenous iodine intake and possible Jod-Basedow phenomenon was diagnosed. Iodinated mouthwash is an underappreciated cause of excess iodine exposure. Iodine induced hyperthyroidism, the Jod-Basedow phenomenon, should be suspected in individuals presenting with hyperthyroidism who are at risk for underlying thyroid disease. Due to decreased iodine uptake by the thyroid gland, our patient could not be definitively treated until cessation of iodinated mouthwash.

Conclusion: This is a case of thyrotoxicosis caused by Graves’ disease in the setting of both chronic and acute exogenous iodine exposure that delayed the definitive treatment with RAI ablation.

Abstract #1025

THYROID DISEASE AFTER IMMUNE CHECKPOINT INHIBITOR THERAPY

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Objective: Checkpoint inhibitor immunotherapy has significantly improved the prognosis for patients with advanced melanoma. The combination of an anti-cytotoxic T lymphocyte antigen 4 (CTLA4) mAb such as ipilimumab, and an anti-programmed cell death 1 receptor (PD1) antibody as nivolumab, is commonly used. Nevertheless, much toxicity has been described, with primary thyroid dysfunction and hypophysitis increasingly recognized.

Case Presentation: Case of a 55 year-old-male with history of uveal melanoma diagnosed at the age of 53, who was initially treated with left eye enucleation and adjuvant radiotherapy. Metastatic melanoma to pancreas, bone and liver was subsequently detected and he was started on combination therapy with ipilimumab 3 mg/kg and nivolumab 1 mg/kg, on 21-day cycles. Three weeks after receiving his third dose of therapy, he developed new-onset symptoms of diaphoresis, palpitations, and weight loss but no headache. On examination, he was afebrile, normotensive, and tachycardic. Dermatitis was noted on chest, back and extremities. There was no evidence of goiter or thyroid tenderness. Neurological exam revealed normal extraocular movement and intact visual fields with no evidence of tremors and adequate deep tendon reflexes. Laboratory evaluation revealed a TSH of <0.015 μUI/ml (nl, 0.40- 4.0), free T4 of 2.77 ng/dl (nl, 0.71- 1.85) and three-fold elevation of transaminases. Baseline thyroid function tests were normal prior to therapy. Thyroid scintigraphy was consistent with thyroiditis. Anti-thyroglobulin and thyroid peroxidase antibodies were negative. Due to adverse effects of dermatitis, transaminitis and thyroiditis, immunotherapy was discontinued. High dose steroids (prednisone 1mg/kg) were given for two weeks with significant improvement of symptoms. No clinical or biochemical evidence of pituitary dysfunction was present. Four weeks later, he was found to have subclinical hypothyroidism, and levothyroxine treatment was eventually started due to progressive increase in TSH up to a level of 10.8 μUI/ml. The patient remained on thyroid replacement therapy. Nivolumab alone was restarted two months later without further complications.

Conclusion: An increasing number of patients will receive anti-CTLA-4 and PD1 therapies for metastatic melanoma. Both, transient hyperthyroid phase of a destructive thyroiditis with eventual permanent hypothyroidism, and autoimmune hyperthyroidism secondary to Graves’ disease, can occur. If combination therapy is used, the incidence of such disorders has been reported to increase 2 to 4-fold. It is critical for endocrinologists to acknowledge the potential adverse endocrine effects of these new therapies since management can differ greatly.

Abstract #1026

SURGICAL MANAGEMENT OF AMIODARONE INDUCED THYROIDITIS IN TWO PRE-HEART TRANSPLANT PATIENTS

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Objective: Amiodarone can cause thyrotoxicosis that can trigger fatal arrhythmias. We present two pre heart-transplant cases, one with a favorable outcome and one with an unfortunately poor outcome to demonstrate the importance of considering a total thyroidectomy.

Case Presentation: Patient 1: A 66 year old male with kidney disease, pulmonary hypertension, end stage non-ischemic dilated cardiomyopathy, left ventricular assist device and ventricular arrhythmias presented after an ICD shock for ventricular tachycardia (VT). At presentation, labs showed...
hyperthyroidism but previously had been normal. He was on amiodarone 200mg for the last 3 years and was listed for a heart transplant. Repeat TSH = 0.01 (0.3-4.2mIU/L) and FT4 = 5.9 (0.9-1.7ng/dL), FT4 by dialysis = 8.7 (0.8-2.0ng/dL), TT4 = 24.9 (4.5-11.7mcg/dL), thyroglobulin antibody <1.8 IU/mL, thyroid stimulating immunoglobulin (TSI) <1.0, thyroperoxidase antibody (TPO) =0.5 IU/mL. A thyroid ultrasound showed minimal doppler flow. Methimazole (MMI) 10mg TID and prednisone 40mg were started. MMI and prednisone were increased with no improvement. MMI was further increased still with FT4 of 4.5 mg/dL and FT3 of 6.5 (2.8-4.4pg/mL). After discussion with the transplant and otolaryngology teams, total thyroidectomy was arranged. Metoprolol was changed to propranolol and cholestyramine was started. Total thyroidectomy was complicated by hematoma but otherwise uneventful. He is now euthyroid and underwent a heart transplant 5 months later.

Patient 2:
A 49-year-old male with hypertrophic cardiomyopathy, congestive heart failure and VT status post ICD started to have symptoms suggestive of hyperthyroidism. TSH = 0.06 uIU/mL, TT4 = 10.8 mcg/dL, FT3 = 3.3 and TT3 = 121 (80-200ng/dL) with normal thyroid tests prior. He had been on amiodarone therapy since 2008 and was listed for a heart transplant. Repeat TSH <0.01 mIU/mL and free T4 = 13.4 mcg/dL with negative TSI and TPO. Thyroid ultrasound showed normal vascularity. Prednisone 20mg and MMI 10mg BID was started. Shortly after, he was admitted for recurrent VT causing ICD firing. While initially his TSH, FT4 and FT3 normalized, they again started to worsen despite prednisone 60mg, MMI 20mg BID and metoprolol XL 200mg BID. Urgent decision to proceed with thyroidectomy was made but the patient developed recurrent episodes of VT and despite resuscitative efforts expired the morning of planned thyroid surgery.

Conclusion: These cases demonstrate that amiodarone induced thyroiditis may be difficult to manage medically. Pre-heart transplant patients are complicated surgical candidates but thyroidectomy may be the only definitive and life-saving treatment.

Abstract #1027

GRAVES DISEASE RELAPSE DURING PREGNANCY PRESENTING WITH T3 THYROTOXICOSIS

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Objective: Thyroid disease is the second most common endocrine disorder affecting women of reproductive age. Untreated thyroid disease during pregnancy is associated with an increased risk of complications. Differentiating physiologic patterns of thyroid dysfunction during gestation and intrinsic hyperthyroidism could be challenging, but important due to the possible consequences.

Case Presentation: 35 years old female with history of Graves’ disease who presented on week 13th of pregnancy complaining of palpitations, anxiety, tremors, and insomnia. On physical examination the patient had a mild goiter, but not exophthalmos. Her initial TSH was 0.006 mcIU/mL (0.270 - 4.200), Free T4 0.86 ng/dL (0.8 - 1.77), Total T4 8.8 mcg/dL (6.75 - 18.0) and total T3 of 450 ng/dL (106.0 - 270.0), Free T3 356 ng/dL (2.0-4.4). TSI 585 (<140 %) and TRAb 56 (<16.0 %). She was started on 300 mg daily of PTU and was progressively increased to 400 mg daily. The thyroid ultrasound showed an enlarged gland with increased vascularity, but no cysts or nodules. The patient was switched to methimazole 20mg daily on week 19th. On week 21th her TSH was <0.006 mcIU/mL, FT4 1.24 ng/dL, T4 13.9 mcg/dL, T3 356ng/dL, based on this, her methimazole was increased to 30mg daily. On week 25th her weight gain was appropriate and the palpitations improved significantly. Her Free T4 1.2 ng/dL, free T3 3.8 pg/mL, Total T3 277 ng/dL, TSI 396 and TRAb 3.59 and her dose methimazole was decreased to 20mg daily. On week 31th her Free T3 2.5 pg/mL, T3 199 ng/dL and the methimazole dose was decreased to 10mg daily. The patient is currently asymptomatic and also continues to follow closely with her perinatologist.

Discussion: Hyperthyroidism in women of childbearing age is most often due to Graves’ disease, which has an incidence of 55–80/100000/year in women older than 30 years. The prevalence of overt thyrotoxicosis in pregnancy ranges from 0.2 to 0.7%. T3 thyrotoxicosis occurs only in 5% of these patients. Clinical management of these patients is challenged by the understanding that maternal antibodies, as well as antithyroid medication, may differentially affect maternal and fetal thyroid function. But while mild hyperthyroidism appears safe for the mother and fetus, moderate to severe hyperthyroidism can prove dangerous. To our knowledge, the association of T3 thyrotoxicosis and pregnancy is very rare and seldom
described in the literature.  

**Conclusion:** Described cases of T3 thyrotoxicosis during pregnancy are rare. It is important to check T3 levels in patients with Graves’ disease and normal Free T4 levels. Awareness of maternal and fetal complications of pregnancy associated with hyperthyroidism is important as well as close follow-up visits.

**Abstract #1028**

**RECURRENT HYPERTHYROIDISM AFTER NEAR TOTAL THYROIDECTOMY IN A PATIENT WITH GRAVE’S DISEASE**

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SUNY Upstate Medical University

**Objective:** Introduction:  
Recurrent hyperthyroidism after thyroidectomy is rare. We report a case of recurrent hyperthyroidism with hyperplasia of remnant thyroid tissue after near total thyroidectomy in a patient with a history of grave’s disease.  

**Case Presentation:** Case: A 24-year-old female was referred for evaluation of hyperthyroidism. She had a history of Grave’s disease with near total thyroidectomy six years prior. Near total rather than total thyroidectomy was done due to a highly vascular gland and difficulty finding the left recurrent laryngeal nerve. Following surgery, she started Levothyroxine 137 mcg. Over the past year her dose was reduced several times due to low TSH, down to 25 mcg daily.  

On presentation, she had symptoms of hyperthyroidism including tremor, diarrhea, heat intolerance and mood swings. Labs showed suppressed thyroid stimulating hormone <0.01 (TSH, 0.35-4.94 uIU/mL), elevated free T4 1.55 (FT4, 0.7-1.48 ng/dL) and free T3 3.78 (FT3, 1.71-3.71 pg/mL). Levothyroxine was stopped; repeat labs showed persistent hyperthyroidism: TSH <0.030 (TSH, 0.27-4.94 uIU/mL), FT4 2.56 (0.9-1.7 ng/dL), FT3 6.59 (2.2-4.4 pg/mL). Thyroidectomy was stopped; repeat labs showed thyroid stimulating hormone <0.01 (TSH, 0.27-4.94 uIU/mL), elevated free T4 1.55 (FT4, 0.7-1.48 ng/dL) and free T3 3.78 (FT3, 1.71-3.71 pg/mL). Thyroid stimulating Immunoglobulin was normal (TSI 78, 1-139%). Thyroid Receptor Antibody was high (TRAb 14.89, 0.0-1.75 IU/L). Thyroid ultrasound showed bilateral thyroid lobes with bilateral solid hypervascular nodules. Thyroid uptake scan showed residual thyroid tissue with increased uptake and possible functioning nodules. Methimazole 20 mg daily was started and her symptoms improved. She desired permanent treatment and underwent radioactive iodine therapy with 20.7 mCi of I-131. Two months later, she was started on levothyroxine 137 mcg for post ablative hypothyroidism.  

**Discussion:** Surgical management of hyperthyroidism provides rapid and definitive treatment and is associated with lower recurrence compared to other modalities. Our patient had recurrence of hyperthyroidism six years after near total thyroidectomy. This may be due to inadequate initial resection, however the time course argues against this. Another possibility is that continued stimulation of her thyroid remnant by TRAb led to her recurrence.  

**Conclusion:** Recurrent hyperthyroidism after thyroidectomy is rare and may be associated with the continued presence of thyroid autoantibodies. More studies are needed to evaluate this association.

**Abstract #1029**

**MULTIVITAMINS, A GRAVE PHENOMENON!**

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**Objective:** Multivitamins account for one sixth of all purchases of dietary supplements nationwide. Biotin is a water-soluble vitamin that plays a role in gene expression, gluconeogenesis and fatty acid synthesis and is a common component in multivitamin preparations. We present an interesting case of a biotin-related phenomenon in order to increase awareness of an easily missed entity in clinical practice.  

**Case Presentation:** A 30-year-old male with a past medical history of adrenal leukodystrophy, hypothyroidism, seizures, blindness, and intellectual disability presented to his endocrinologist’s office for a routine follow-up. His home medications included risperidone, oxcarbazepine, vitamin D, calcium, biotin, hydrocortisone, levetiracetam and levothyroxine. On physical examination vitals were stable and revealed a restless, malnourished male without any hypo/hyperpigmentation, thyromegaly, exophthalmos, or tremors. Labs included a TSH of 0.009 mcIU/ml and free T4 7.8 ng/dl. In light of an absence of clinical suggestion of hyperthyroidism, interference with the assay was suspected and the endocrinologist recommended stopping biotin supplements for a few days before retesting thyroid functions. Repeat labs one month later showed a normalized TSH of 0.580 mcIU/ml and free T4 1.06 ng/dl. He was advised to stop biotin supplements for a few days prior to thyroid testing in the future.  

**Discussion:** Our patient presented with biotin-induced pseudo-thyrotoxicosis. Biotin may interfere with the most commonly used thyrotropin and thyroid hormone assays and anti-thyrotropin antibodies. The mechanism seems to be a biotin/streptavidin interaction, affecting streptavidin hormone binding, which normally plays the key role in assays for thyroid and other testing. This may lead to falsely abnormal thyroid function tests mimicking Graves’ disease. In most cases, levels normalize within 24-48 hours after discontinuation of biotin, but sometimes persist for several days after ingestion. This may lead to
unnecessary treatment and iatrogenic hypothyroidism.

**Conclusion:** At moderate doses biotin has been reported to cause interference in immunoassays leading to abnormal thyroid function tests. Similar interference has been noted in PTH, ACTH, FSH, LH, troponin and Vitamin D assays. We report this case to increase general awareness about this interaction. With the current widespread use of multivitamins, clinicians must be careful while interpreting thyroid function tests and consider interference in assays if lab results do not correlate with the clinical picture.

Abstract #1030

**A CASE OF SEVERE THYROTOXICOSIS CAUSED BY IMMUNE CHECKPOINT INHIBITORS**

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The Ohio State University

**Case Presentation:** Immunotherapy is becoming increasingly popular due to its remarkable therapeutic benefit, including remission of some cancers. These monoclonal antibodies block the CTLA-4 and PD-1 immunologic checkpoints and lead to immune related adverse events (irAEs). Hypophysitis and thyroiditis are among the most recognized endocrinopathies associated with CTLA-4 and PD-1 immunotherapy. However, patients with irAE related thyroiditis rarely require hospitalization and generally need replacement therapy as outpatient. Here we present a patient with severe irAE related thyroiditis who required hospitalization due to sudden and drastic change in her thyroid function.

A 58 year old female with metastatic colon cancer presented to the hospital with acute onset of fever, neck enlargement and tachycardia 10 days after her first dose of Ipilimumab and Nivolumab, anti-CTLA4 and anti PD1 immunotherapy. Her thyroid function test (TFTs) were normal on the day of infusion but her symptoms started 3 days after the immunotherapy. She was noted to have TSH 0.026 uIU/mL (0.55-4.78), freeT4 >6 ng/dL (0.89 – 1.76) and Total T3 of 5.31 (0.6-1.81) on day of presentation with a persistent heart rate of 130. The thyroid antibodies were noted to be negative. She was treated with Propylthiouracil, cholestyramine, propranolol and Dexamethasone. On day 3 of hospitalization, she was discharged with Propranolol, Methimazole and a rapid steroid taper. The TFTs were drastically different 4 weeks after discharge: TSH 0.01, FT4 6.85, and TSI <1. Thyroid function tests (TFTs) were normal on the day of infusion but her symptoms started 3 days after the immunotherapy. She was noted to have TSH 0.026 uIU/mL (0.55-4.78), freeT4 >6 ng/dL (0.89 – 1.76) and Total T3 of 5.31 (0.6-1.81) on day of presentation with a persistent heart rate of 130. The thyroid antibodies were noted to be negative. She was treated with Propylthiouracil, cholestyramine, propranolol and Dexamethasone. On day 3 of hospitalization, she was discharged with Propranolol, Methimazole and a rapid steroid taper. The TFTs were drastically different 4 weeks after discharge: TSH 73.152 uIU/mL, freeT4 0.71 ng/dL (0.89 – 1.76) and total T3 of 0.27 ng/dL (0.6-1.81). Replacement with levothyroxine was initiated and her TFTs remain stable on 112mcg of levothyroxine daily.

**Conclusion:** Immunotherapy has advanced cancer management significantly and is used world-wide for the treatment of many aggressive cancers. The irAE thyroiditis commonly occurs in 3-6 months but can happen with or without antibodies anytime from 1 day to 13 months after immunotherapy. As noted in this case, the patient required very close monitoring, treatment and follow-up due to the severe derangement and rapid change of her TFTs. The irAE will continue to become more common as the use of immunotherapy becomes more prevalent given their remarkable efficacy as cancer therapy. Physicians need to be well aware of the irAE, vigilant about screening of irAE and ready to start treatment if necessary to avoid adverse outcomes.

Abstract #1031

**A CASE OF RELAPSING AMIODARONE-INDUCED THYROTOXICOSIS**

**Jessica Watari, DO, Anupa Sharma, DO**

Rutgers Robert Wood Johnson Medical School

**Objective:** Amiodarone-induced thyrotoxicosis (AIT) may be secondary to increased thyroid hormone synthesis (AIT-1) or destructive thyroiditis (AIT-2). We present a case of AIT presenting one year after cessation of amiodarone that was exacerbated by a brief course of glucocorticoids and required prolonged treatment.

**Case Presentation:** A 63-year-old male with a history of atrial fibrillation previously treated with 10 months of amiodarone and completed one year prior to presentation, presented with 6 months of weight loss, fatigue, and tremor. Thyroid function tests (TFTs) revealed suppressed TSH 0.03 mIU/L (0.35-5.50) and elevated FT4 2.37 ng/dL (0.90-1.80). His primary care physician prescribed methimazole 20 mg daily and a one week course of methylprednisolone for suspected AIT. Two months off treatment, symptoms worsened and he was referred for endocrinologic evaluation. Labs revealed TSH 0.01, FT4 6.85, and TSI <1. Thyroid ultrasound showed mild thyromegaly, 0.34 cm noncalcified hypoechoic heterogeneous solid right lobe nodule, and a 1.03 cm noncalcified solid left lobe nodule without mention of vascularity. Methimazole was increased to 40 mg daily and prednisone 40 mg daily was started for presumed AIT-2. Over the next month, FT4 decreased and symptoms improved. TFTs remained normal as methimazole and prednisone were tapered over 3 months and 6 months, respectively. Two weeks following discontinuation of prednisone, the patient reported weight loss. Repeat labs showed FT4 2.04. He was restarted on prednisone 7.5 mg daily for presumed recurrent AIT-2 with immediate normalization of TFTs. Prednisone was tapered over 3 months and he remained euthyroid.
Discussion: Thyrotoxicosis is reported in 3% of patients on amiodarone. AIT-1 is associated with underlying thyroid pathology and caused by high iodine load in amiodarone while AIT-2 is destructive thyroiditis secondary to toxic drug effect. Based on literature for AIT-2, the expected median cure time is 30 days, as predicted by baseline FT4 levels and thyroid volume. High dose steroids for at least 1 month, if not 3 months, are recommended for AIT-2. We hypothesize that our patient’s prolonged treatment course may be secondary to an enhanced immune response resulting in a rebound thyroiditis and could not be predicted by FT4 levels.

Conclusion: Our case demonstrates that a short course of glucocorticoids with early withdrawal in patients with AIT-2 may result in an extended treatment course longer than 3 months. When treating AIT-2, abrupt withdrawal of glucocorticoids can worsen thyrotoxicosis, resulting in a prolonged duration of treatment.

Abstract #1032

HYPERTHYROIDISM ASSOCIATED WITH HYPEREMESIS GRAVIDARUM; TO TREAT OR NOT TO TREAT?

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Objective: Hyperemesis gravidarum occurs in 0.5-10 per 1000 pregnancies and has been associated with gestational transient thyrotoxicosis (GTT). We report a case of hyperemesis gravidarum presenting with hyperthyroidism and acute liver dysfunction.

Case Presentation: 26-year-old female at 13 weeks of gestation was admitted for 40 lb weight loss, nausea, vomiting and abdominal pain. Review of symptoms was significant for palpitations, anxiety, and heat intolerance. She had mild thyromegaly. Laboratory evaluation showed suppressed TSH <0.01 mU/L (0.27-4.20) and elevated Free T4 (FT4) 3.67 ng/dl (0.8-1.90), Free T3(FT3) 5.0 pg/ml (2.3-4.2), transaminases (AST 805 U/L (10-50), ALT 897 U/L (10-50)), and Bilirubin 2.5 mg/dl (0.2-1.0). Her hCG levels were very elevated at 96,282 mU/ml. Supportive treatment was started with IV fluids, electrolytes replacement and antiemetics. She was started on methimazole 10 mg daily due to concern for symptomatic hyperthyroidism possibly worsening liver dysfunction. Her Thyroid stimulating immunoglobulins (TSI) were not available at that time and later were found to be normal. Her transaminases improved and FT4 and FT3 levels normalized after 1 week of therapy and methimazole was tapered off in 3 weeks. Her TSH improved to 0.32 mU/L at 20 weeks of gestation.

Discussion: GTT complicates 1-3% of pregnancies. Excessive circulating levels of hCG weakly bind the TSH receptor and have a thyrotrophic effect leading to stimulated thyroid hormone production and suppressed TSH levels. The elevated hCG levels have been implicated in pathophysiology of hyperemesis gravidarum. Prior history of hyperthyroidism, ophthalmopathy, goiter, persistent symptoms and elevated TSI favor diagnosis of Graves’ hyperthyroidism over GTT. Elevated hCG level > 40,625 mIU/mL can interfere with the TSI bioassay and may give false negative results. Majority of patients with GTT do not require anti-thyroid drugs (ATD) and thyroid hormone levels normalize by mid-2nd trimester of pregnancy when hCG levels trend down. A short course of ATDs can be considered when it is difficult to achieve a definitive diagnosis.

Conclusion: It is important for medical providers to distinguish between physiological changes in thyroid hormone concentrations during pregnancy, GTT and overt hyperthyroidism. GTT can be optimally managed with supportive therapy while untreated hyperthyroidism can lead to adverse maternal and fetal outcomes.

Abstract #1033

PAPILLARY THYROID CANCER AS CAUSE OF NIGHTSPELLS

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Objective: To present an unusual case of nocturnal paroxysms due to intermittent left vagal nerve compression by papillary thyroid cancer.

Case Presentation: This is a 43-year-old Caucasian female nurse who presented for a second opinion on her nontoxic multinodular goiter. She reported ongoing nightly “spells” that routinely woke her from sleep. These spells had been ongoing for the previous two years and only happened at night. She described the episodes as a cold sensation that started in her chest and moved throughout her body. They were associated with palpitations, tachycardia upon waking to 180 bpm, diaphoresis, anxiety, flushing, lightheadedness, and pre-syncope. Immediately following each episode, she noted significant diarrhea. She had no history of external beam radiation therapy and no family history of medullary thyroid carcinoma or multiple endocrine neoplasia (MEN) syndrome. Her TSH was 4.61 mIU/mL, calcitonin was undetectable, and plasma metanephrines were normal. An in-office real-time ultrasound revealed a suspicious, hypoechoic nodule in the posterior left lateral lobe abutting the left carotid sheath.
FNA was performed and diagnostic for papillary thyroid carcinoma (PTC) (Bethesda Category VI). Consideration was made for intermittent left vagal nerve compression as cause of her paroxysms while sleeping, particularly on her left side. She underwent total thyroidectomy and central neck dissection that demonstrated a T3 N0 MX classical PTC at that location. Since surgery, her symptoms have completely resolved.

**Discussion:** This is a rare case of nocturnal positional vagal nerve compression due to papillary thyroid carcinoma. Although pathology demonstrated minimal extrathyroidal extension, there was no invasion into the vagal nerve itself as has been described in other case reports. Therefore, we hypothesize that laying on her left side for prolonged time at night caused intermittent vagal nerve compression and nocturnal vasomotor spasms. These vasomotor spasms constituted classic symptoms of rebound tachycardia (i.e. vagal escape phenomenon), diaphoresis, temperature change, decreased vascular tone, and diarrhea.

**Conclusion:** Thyroid tumors located close to the carotid sheath may cause vasomotor symptoms associated with vagal nerve compression.

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**Abstract #1034**

**WHEN THE THYROID GLAND GOES SILENT: A 36-YEAR-OLD WITH MYXOEDEMA CRISIS**

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**Objective:** Myxedema crisis is a rare, life-threatening endocrine emergency that represents decompensated hypothyroidism, leading to decreased mentation, hypothermia and symptoms related to slowed function of multiple organs. We present a 36-year-old black female with no prior diagnosis of hypothyroidism.

**Case Presentation:** A 36-year-old female presented with a 2-year history of cold intolerance, progressive weight gain and recurrent breathlessness. On examination, she was stuporous, pale (Hemoglobin was 9.6gm/dl), with swelling of the face and extremities, thick coarse skin, a hoarse voice and macroglossia. Temperature was 35.8°C, pulse rate 56 beats per minute (bpm) and a blood pressure (BP) of 100/60 mmHg. Thyroid Stimulating Hormone (TSH) was elevated > 45 mIU/L (0.35 - 5.3 mIU/L), with suppressed triiodothyronine (T3) < 1.9 pmol/L (3.8 - 6.0 pmol/L) and thyroxine (T4) = 1.7 pmol/L (7.2 - 16.4 pmol/L). Complete Blood Count (CBC) showed leucopenia and neutrophilia. Thyroid tissue biopsy showed normal thyroid tissue. Anti-thyroid peroxidase assay done was within normal limits. ECG revealed low voltages. She was managed with intra-gastric levothyroxine 400ug daily, parenteral antibiotics, intravenous hydrocortisone 100mg 6hourly, and oxygen therapy.

**Discussion:** Myxedema crisis is common among females from the 6th decade of life; in Caucasians and Hispanics than blacks, and often found in patients with a prior history of hypothyroidism. Remarkably, our index patient is a 36 year old black female with no prior diagnosis nor family history of hypothyroidism.

**Conclusion:** Diagnosis of myxoedema crisis is challenging due to its rarity, varied presentation and a low index of suspicion amongst physicians. It is imperative to treat suspected cases of myxoedema crisis based on clinical indices while awaiting confirmation via laboratory parameters. A high index of suspicion, accurate diagnosis and early intervention will aid favourable outcome in a condition associated with high mortality.

Keywords: myxoedema, hypothyroidism

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**Abstract #1035**

**SUPERIOR MESENTERIC ARTERY SYNDROME IN A HYPERTHYROID PATIENT: A RARE PRESENTATION OF A COMMON DISEASE**

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**Case Presentation:** A 24 year old female presented with recurrent progressive episodes of anxiety, nausea, vomiting, palpitations and tremors progressively worsening over three weeks. Her past medical history was significant for hepatitis C, and polysubstance abuse including heroin. Patient reported over 100 pounds of weight loss over the past year. Her vital signs on presentation were only notable for Heart rate of 120. Physical examination revealed severe cachexia with generalized muscle wasting, bilateral proptosis, lid-lag, and a non-nodular, non-tender diffuse goiter with audible bruit on auscultation of the thyroid gland. The abdomen was severely distended with hypoactive bowel sounds. Urine drug screen was positive for cocaine and opiates. Her thyroid stimulating hormone was 0.010 UIU/ML (Normal 0.34 - 5.60 UIU/ML), and the free T4 of 4.17 NG/DL (Normal 0.50 - 1.26 NG/DL) and positive thyroglobulin antibodies and thyroid peroxidase antibodies as well as thyroid stimulating hormone receptor antibodies consistent with Graves’ disease. The
diagnosis of heroin withdrawal was established along with a thyroid storm and was admitted to the medical intensive care unit but the patient continued to have worsening nausea and vomiting. A computed tomography scan of the abdomen and pelvis with contrast was performed and showed severe gastric and duodenal dilation with compression of the third part of the duodenum consistent with SMA syndrome (Figure 1, Figure 2). The patient was treated surgically with retrocolic duodenojejunostomy and jejunojejunostomy. Interestingly, the stomach had returned almost to a normal size and required no further intervention with uneventful discharge and follow-up.

Discussion: The duodenum is surrounded by fatty and lymphatic tissue known as the mesenteric pad. The presence of this pad helps maintain a wider angle between the vessels, generally between 38 to 65 degrees 3, 4. Compression typically occurs if the angle between the SMA and aorta is less than 25 degrees5. The biggest risk factor for SMA syndrome is significant and rapid weight loss most commonly due to severe illness, trauma, bariatric surgery, anorexia, and drug abuse and rarely uncontrolled hyperthyroidism5, 6. There have been very few cases reported of SMA syndrome as a result of thyrotoxicosis in the modern medical literature. A case of SMA syndrome was described in untreated hyperthyroidism in Japan in 2004 and was managed conservatively9. This syndrome is reportedly more common in young females.

Conclusion: SMA syndrome should be suspected in patients presenting with uncontrolled hyperthyroidism causing significant weight loss and persistent nausea and vomiting or signs of small bowel obstruction.

Abstract #1036

HYPOTHYROIDISM INDUCED BY MULTI DRUG RESISTANT TUBERCULOSIS (MDR-TB) TREATMENT

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Objective: Multi Drug Resistant Tuberculosis (MDR-TB) is one of the health problems in Indonesia because of its increasing number. Some causes are identified such as unstandardized treatment and also several comorbidities, like diabetes mellitus. One of the consequences of MDR-TB treatment is hypothyroid events. Test of thyroid function has not been routinely performed in our country

Case Presentation: A 59 year old male, with chief complaint weakness for 2 months and must use a wheelchair. The patient’s voice also becomes hoarse with easy to experience cold. In 2010, patients were diagnosed with tuberculosis and received antituberculosis drugs first category and then declared cured. In 2017 he diagnosed with MDR TB and received treatment (ethambutol, pyrazinamide, capreomycin, levofloxacine, cycloserine, and etionamide). We performed thyroid panel test, FT4: 0.47 ng/dl (0.82-1.51 ng/dl) TSHs > 100 µIU/ml (0.27-4.70 µIU/ml) and antiTPO was negatif. These patients had diabetes mellitus, and routinely injected insulin. We diagnose this patient with hypothyroid cause by the treatment for MDR TB. We gave low dose levothyroxin 25 mcg/day at the beginning and increased the dose slowly until 100 mcg/day in 6th month of treatment where the TSH level became normal.

Discussion: Treatment of MDR-TB has several side effects. One of them is hypothyroid. The incident reports are vary between 3.5% - 69%. It is said that ethionamide can lead to hypothyroidism by preventing the formation of thyroid hormone by inhibiting the organification of iodine. This is because the structure of ethionamide has similarities with other thionamide groups such as propylthiouracil and methimazole. This patient received treatment with etionamide which has a structure similar to methimazole, and has been known to inhibit thyroid hormone synthesis through the mechanism of inhibition of iodine organification. Patients may develop hypothyroidism within 3-5 months. Supplementation of levothyroxine drugs may improve the hypothyroid condition in these patients, as indicated by symptom improvement, as well as the improved thyroid function within one month of treatment. Therapy is continued and will be evaluated monthly. Evaluation should also be given at the end of treatment when the drug is stopped because most cases of drug induced hypothyroidism will be reversible when treatment is stopped.

Conclusion: We strongly recommend the measurement of thyroid function prior to the commencement of MDR TB management.

It is also necessary to increase knowledge from physician to recognize signs of hypothyroidism in patients receiving MDR TB treatment

Abstract #1037

AN UNUSUAL PRESENTATION OF GRAVES’ DISEASE

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Case Presentation: A 40-year-old healthy female presented with chest pain. She was a smoker but denied drug abuse or family history of premature coronary artery disease. Her pulse was 113/min, blood pressure 192/115 mm Hg and body
mass index, 23 kg/m2. Laboratory data showed Troponin I 0.36 ng/ml (0-0.08), Low Density Lipoprotein 73 mg/dl (<100), and negative urine drug screen. Electrocardiogram (EKG) was negative for acute changes and echocardiogram was normal. Coronary angiogram revealed no blockage. She was diagnosed with Non-ST segment elevation Myocardial Infarction (NSTEMI), managed with medical therapy and discharged home.

She returned three months later with recurrent chest pain and had higher markers of myocardial injury than before, Troponin I 1.99 ng/ml. EKG showed no acute changes. She was diagnosed with second episode of NSTEMI. Repeat coronary angiogram was nonrevealing. On questioning, she reported occasional hand tremor. Further lab testing revealed undetectable TSH <0.001 mIU/mL (0.3-5.3), elevated FT4, 4.3 ng/dL (0.7-1.9), Total T3 >651 ng/dL (80-200) and Thyroid Stimulating Immunoglobulin 409% (>122). She denied other symptoms of hyperthyroidism. Exam revealed fine hand tremor and brisk reflexes. She was diagnosed with Graves’ disease causing NSTEMI from demand ischemia.

**Discussion:** Our case is a rare occurrence of NSTEMI in the setting of patent coronaries with underlying Graves’ disease in a healthy young female. Thyrotoxicosis may induce symptomatic myocardial ischemia even in patients with angiographically normal coronaries. Excess thyroid hormones suppress myocardial oxygen supply due to hyperkinetic state from increased β-adrenergic receptors. This may cause a critical imbalance in coronary circulation leading to Myocardial Infarction (MI) in some patients. A case of transient STEMI with underlying Graves’ disease was diagnosed with second episode of NSTEMI. Repeat coronary angiogram was nonrevealing. On questioning, she reported occasional hand tremor. Further lab testing revealed undetectable TSH <0.001 mIU/mL (0.3-5.3), elevated FT4, 4.3 ng/dL (0.7-1.9), Total T3 >651 ng/dL (80-200) and Thyroid Stimulating Immunoglobulin 409% (>122). She denied other symptoms of hyperthyroidism. Exam revealed fine hand tremor and brisk reflexes. She was diagnosed with Graves’ disease causing NSTEMI from demand ischemia.

**Conclusion:** Hyperthyroidism may be an under recognized etiology of acute coronary events and should be considered in the differential diagnosis of angina.
in 4.4% of patients, but may be higher in patients with a history of cancer. Random bilateral cytopathologic sampling can be considered to rule out malignancy in patients who have FDG-PET/CT thyroid activity but no discrete nodule, especially for those who have a known non-thyroid malignancy.

Abstract #1039

BEXAROTENE-INDUCED CENTRAL HYPOTHYROIDISM MISINTERPRETED AS OVER SUPPLEMENTATION OF THYROID HORMONE

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Objective: Thyroid dysfunction has been identified as a side effect of several currently used anticancer medications. It is important for physicians to be familiar and up-to-date with these medications and their common endocrine side effects. This is a case of bexarotene-induced thyroid disorder.

Case Presentation: 66-year-old female with mycosis fungoides (cutaneous T-cell lymphoma), treated with bexarotene since 2010, presented to the endocrine clinic for evaluation of abnormal thyroid function. One year after initiating bexarotene, she was diagnosed with hypothyroidism by a free T4 of 0.71 (0.8-1.8 ng/dl) and started on levothyroxine. She was taking levothyroxine 125 mcg daily. Her TSH levels remained detectable ranging from 0.31 to 1.26 (0.3 – 5.00 uIU/mL) until from 1 year ago when TSH became undetectable at < 0.01 uIU/mL. Her primary care doctor interpreted the low TSH to be secondary to overreplacement of thyroid hormone. The levothyroxine dose was therefore lowered to 100 mcg and then 75 mcg, yet TSH remained suppressed and free T4 declined, prompting referral to endocrinology. Labs on initial presentation to our clinic were significant for TSH < 0.01 (0.45 – 5.33 uIU/mL) and free T4 of 0.59 (0.61 – 1.44 ng/dl). Thyroid ultrasound confirmed a normal homogeneous thyroid gland without nodules and without increased vascularity. We recognized her hypothyroidism was central in origin due to bexarotene and increased her dose to 100 mcg once daily with improvement of free T4 into the normal range.

Conclusion: Bexarotene was approved in 1999 by the US Food and Drug Administration as a second-line treatment for early- and late-stage refractory cutaneous T-cell lymphomas. The molecule is highly selective for the retinoid X receptor (RXR). Reversible, dose-dependent, RXR-mediated thyroid hormone-independent suppression of TSH gene expression is well described with this drug. Suppression of TSH can occur instantly even after the first dose of the medication. A second mechanism of hypothyroidism is increased peripheral degradation of thyroid hormones. Treatment of patients with bexarotene-induced hypothyroidism frequently requires higher doses of thyroid hormone, often twice the typical doses used to treat more common etiologies of hypothyroidism. Since bexarotene results in TSH suppression, TSH levels are an unreliable measure of thyroid function. Measurement of free T4 and T3 should be monitored to determine adequacy of supplementation. Increased awareness of this drug-induced endocrine side effect is important to avoid incorrect interpretation of a low TSH.

Abstract #1040

AUTOIMMUNE THYROIDITIS MIMICKING SUBACUTE THYROIDITIS

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Case Presentation: 45 year old female, married, hypertensive, presented with painful swelling in the right side of neck for the last 2 months. She had received treatment for subacute thyroiditis (SAT) by another physician, who prescribed her Prednisolone and an NSAID for 1 week. After stopping the steroid, the pain and systemic illness had progressively worsened with weight loss of 2 kg. On examination, she was febrile with a tender swollen multinodular goiter (MNG). Her ESR was 81 mm/1st hour, CRP was 2.28 (0-0.5 mg/dl) and TSH was 0.025 (0.4-4.2 uIU/ml). She was restarted on Prednisolone and advised further tests. Her FT4, FT3 and TSH were 2.7 (0.89-1.76 ng/dl), 6.7 (2.1-4.4 pg/ml) and <0.004 uIU/ml respectively. Tc-99m pertechnetate scan showed non-homogenous tracer uptake with multiple cold nodules. Ultrasound (US) thyroid showed MNG. Her thyroid antibodies were negative at this point. She was started on Carbimazole 20 mg/day along with steroids and beta-blockers. Over the next few weeks her symptoms improved but recurred whenever steroids were tapered or stopped. Her thyroid antibodies repeated from a different laboratory showed a positive anti-Thyroglobulin antibody (anti-TG). On follow-up a month later, she had a positive anti-TG, positive anti-TSH receptor antibody (TRAb), low FT4, FT3 and a suppressed TSH. The dose of Carbimazole was reduced to 10 mg/day. In an effort to understand the pathology, an FNAC was advised which showed atypical cells of unknown significance (AUS). The patient is currently better and off steroids.

Conclusion: Hashimoto’s Thyroiditis (HT) and Graves’ Disease (GD) are autoimmune disorders of the thyroid gland. There have been case reports of HT mimicking SAT
as well as cases of thyrotoxicosis occurring due to both HT and GD in the same patients. It has been suggested that these two pathologies are two ends of the same spectrum. The difference in diagnosing these two entities lies in the antibodies and the radioisotope scan. This patient presented as SAT with dramatic response to steroids but the antibody profile and radioisotope scan varied between HT and GD. The changing antibody profile and recurring symptoms of toxicosis made it a difficult case to diagnose and treat.

Abstract #1041

A CASE OF OSSEOUS METAPLASIA WITH MATURE BONE FORMATION AND EXTRAMEDULLARY HEMATOPOIESIS IN A THYROID NODULE WITH SUSPICIOUS AFIRMA® GENE EXPRESSION CLASSIFIER

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Objective: Osseous metaplasia (OM) with mature bone formation and extramedullary hematopoiesis (EMH) of the thyroid is a rare finding. It is defined as the presence of heterotopic bone formation within soft tissue. In OM, the bone matrix may be associated with osteoblasts, osteoclasts, adipocytes and hematopoietic stem cells. We present a patient with indeterminate cytology on thyroid nodule FNA and a suspicious Afirma® Gene Expression Classifier (GEC) who underwent total thyroidectomy revealing OM and benign pathology.

Case Presentation: A 47-year-old female with iron deficiency anemia was found to have a palpable left-sided thyroid nodule on routine physical exam. She reported no compressive symptoms and was clinically and biochemically euthyroid. Thyroid ultrasound revealed a 1.1cm hypoechoic nodule with microcalcifications and poorly defined borders. FNA showed tight clusters of follicular cells with nuclear overlap and crowding which was read as FLUS. Afirma® GEC was suspicious (~40% risk of malignancy). She underwent total thyroidectomy. Grossly, a 0.8x0.5x0.4cm tan-white calcified nodule was noted in the lower portion of the left lobe. Microscopically, the nodule showed an area of dense fibrosis and OM with mature bone and bone marrow. There was no evidence of neoplasia.

Discussion: OM of the thyroid is rare and has been previously described in case reports associating it with both neoplastic and benign disease. The pathophysiology is poorly understood, but is felt to be part of the degenerative changes which occur in thyroid nodules including hemorrhage, hyalinization, fibrosis, cystic degeneration and calcification. Bone morphogenetic protein plays a role in inducing bone formation followed by deposition of calcium salts. EMH is defined as abnormal development and growth of hematopoietic tissue in sites other than those that are normally active, common sites being liver, spleen and lymph nodes. EMH occurring in the thyroid is rare. Case series of soft tissue EMH have described an association with myeloproliferative disorders, hematologic malignancies and chronic anemias. Our patient has iron deficiency anemia, which is consistent with previously reported cases.

This is the first reported case of suspicious FNA molecular testing showing OM on final pathology. Afirma® GEC uses cells obtained at the time of biopsy to screen for molecular markers that are associated with thyroid cancer. We pose the question if OM is a confounder in the genomic testing or an indicator of neoplastic transformation. Further studies are required to identify the molecular profile of OM vs. malignancy.

Conclusion: This case highlights a rare association of OM in a benign thyroid nodule with suspicious molecular testing on FNA.

Abstract #1042

A CASE OF RAMUCIRUMAB INDUCED THYROIDITIS

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Case Presentation: Background: Ramucirumab is a monoclonal antibody approved for the treatment of advanced gastric adenocarcinoma. Prior studies have reported hypothyroidism in association with Ramucirumab use. No reports currently exist on Ramucirumab-induced thyroiditis as an etiology for hypothyroidism. We report the first case of Ramucirumab-induced thyroiditis in a patient treated for gastric carcinoma.

Case study: A 65-year-old man with history of stage IIa gastric cancer presented with subacute weight loss of 15 lbs, and progressive dysphonia and dysphagia over two weeks. He denied fevers, cough or upper respiratory tract infection symptoms. Of note, patient had been initiated two months prior on Ramucirumab therapy, with completion of four cycles of therapy. His physical examination was notable for a tender and enlarged thyroid, estimated to weigh 35 grams. His thyroid labs drawn at admission indicated a low TSH (0.014 U/mL, reference range 0.4- 55 U/mL), elevated free T3 (>29 pg/mL, reference range 2.3- 4.1 pg/mL), and elevated free T4 (>7.8 ng/dL, reference range 0.9-1.7 ng/dL). Of note, he had no personal or family history of thyroid disease, with
ABSTRACTS – Thyroid Disease

laboratory data from 2011 documenting a normal TSH of 2.149 U/mL and free T4 level of 1.05 ng/dL. A thyroid ultrasound on presentation revealed a heterogeneous, mildly enlarged thyroid gland with diminished vascularity. His thyroid receptor and microsomal antibodies were both negative. Given his presentation in relationship to initiation of Ramucirumab therapy, patient was suspected to have thyroiditis secondary to Ramucirumab use. Patient was initiated on corticosteroid therapy and beta-blockers, with subsequent significant symptomatic relief. He was discharged on a taper dose of prednisone therapy. At his most recent outpatient follow up, his thyroid was no longer tender to palpation, with full recovery of his dysphagia and dysphonia. Repeat labs revealed TSH <0.005 U/mL, free T4 at 3.3 pg/mL, and free T3 at 1.7 ng/dL.

**Conclusion:** With the widespread use of novel monoclonal antibody therapies, a wide range of thyropathies have emerged. Clinicians should have a low threshold to test thyroid function in symptomatic patients receiving such therapies.

**Abstract #1043**

A CASE OF IMMUNE-MEDIATED HYPERTHYROIDISM SECONDARY TO ATEZOLIZUMAB USE

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Cleveland Clinic

**Case Presentation:** Background: Programmed Death 1 (PD-1) is an inhibitory checkpoint expressed on the surface of several immune cells that modulate immune responses. Antibodies that block PD-1 represent a new approach in immunotherapy treatment of solid tumors. With the increase in utilization of PD-1 inhibitors, a number of emerging endocrinopathies have been identified. Herein, we report a novel case of immune-mediated hyperthyroidism in association with Atezolizumab use. Case Study: An 82-year-old man, with no prior personal or family history of thyroid disease, presented with progressive 15 pound weight loss with no changes in appetite, and with palpitations. His medical history was notable for metastatic non-squamous cell lung cancer, recently initiated on Atezolizumab therapy, and had completed one cycle of therapy. His physical examination was notable for tachycardia with no palpable thyroid nodules. Initial workup revealed elevated free T3 (6.8 pg/dL, reference range 2.3-4.1 pg/dL), elevated total T4 (11.4 ng/dL, reference range 5.5-10.4 ng/dL), and suppressed TSH (<0.005 U/mL, reference range 0.400 -5.500U/mL). Further testing revealed elevated thyroid stimulating immunoglobulins (TSI) (1581%, reference range < 150%), TSH binding inhibitory antibodies (TBI Ab) (8.6 U/L, normal <1.0 U/L), and microsomal antibodies (176.4 IU/mL, normal <5.6 IU/mL) that were not previously present. Patient was subsequently initiated on methimazole therapy at 10 mg three times daily, and a beta-blocker for symptomatic relief. Follow up blood work three days later showed improvement in thyroid hormone levels, with free T4 documented at 2.5 ng/dL, and free T3 at 3.7 pg/dL. At his most recent outpatient follow up, the patient reported significant improvement in symptoms, and had gained 12 lbs since discharge. His free T4 measured 1.3 pg/dL, free T3 at 2.3 pg/dL, and TSH 0.011 U/mL. His dose of methimazole was reduced to 10 mg daily. He is being continued on this dose at the present time.

**Conclusion:** We reported a novel case of immune-mediated hyperthyroidism in association with the PD-1 inhibitor Atezolizumab. A plausible mechanism underlying this phenomenon is loss or reduction of self-tolerance in patients treated with immunomodulatory agents, making such individuals more susceptible to developing autoimmunization.

**Abstract #1044**

QUANTITATIVE ANALYSIS OF TALLER THAN WIDE SHAPE FOR PATIENTS WITH THYROID NODULES

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**Objective:** A taller than wide (T/W) shape refers to a nodule with an anteroposterior diameter that is longer than the transverse diameter on a transverse, which is a useful feature for diagnosis of thyroid cancer. T/W shape feature, compare to other features, interobserver and intraobserver variability should be less because this is relatively measurable and quantitative. But in truth, the selected length of so-called tall or wide is always operator dependency. New quantitative T/W indexes are proposed here to study the shape of thyroid nodule. The aim of this study was to clarify whether these quantitative T/W indexes are useful for the detection of malignant thyroid nodules.

**Methods:** Overall, 196 patients with 229 thyroid nodules were included in the final analysis. Quantification of T/W was performed using commercial software (AmCAD-UT;AmCad BioMed,Taiwan). Quantitative T/W indexes includes TTW=ROIY/ROIX, Long Axis/Orthogonal Axis ratio (LO ratio) and tumor orientation angle.

**Results:** The average value of TTW, LO ratio and orientation angle were 0.685, 0.571 and 0.708, respectively. Ultrasound T/W shape (US-T/W), as assessed...
by clinicians, defined T/W shape as an independent factor for malignancy. The value of TTW and orientation angle between the benign and malignant nodules were all significantly different, with higher values for malignant nodules. All of the quantitative T/W indexes showed similar percentages of sensitivity and specificity and had better accuracies than US-T/W.

Discussion: We proposed a computerized method to evaluate ultrasound T/W shape quantitatively. From our study, using T/W indexes, a statistically significant difference was observed between the benign and malignant nodules. The results of this quantitative evaluation also supported the usefulness of T/W in the diagnosis of thyroid nodules. To our knowledge, this is the first study to report that the quantitative measurement of ultrasound T/W could be a helpful approach in the diagnosis of thyroid nodules using a computerized method.

Conclusion: In conclusion, the proposed quantitative T/W indexes seems more promising to constitute an important advancement than the conventional qualitative T/W shape in allowing for a more reliable distinction between benign and malignant thyroid nodules.

Abstract #1045

MULTIMODAL TREATMENT IN A PATIENT WITH 3 DIFFERENT TYPES OF THYROID CANCER.

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Objective: Thyroid carcinomas have been classified into two major groups: well-differentiated, composed of papillary or follicular cells and undifferentiated, composed of anaplastic and poorly differentiated cells. The prognosis for the former is generally good, and typically much worse for the later subtype. Managing these cancers can be a challenge. Proper pathological diagnosis is essential as less differentiated cancers warrant prompt and more aggressive treatment. How does one decide on the most appropriate treatment when 3 different types of thyroid cancer are present in one patient?

Case Presentation: An 83-year-old male with history of hypertension and dyslipidemia presented for a second opinion for a recently discovered large right thyroid nodule. A FNA performed at another facility was concerning for follicular thyroid cancer. Thyroid ultrasound revealed a hypoechoic mass measuring 4.6 x 3.2 x 4.2 cm, in the right lower thyroid lobe. He underwent total thyroidectomy and the pathology report noted a 7.2 cm mixed poorly differentiated insular carcinoma (60%), papillary thyroid carcinoma, mixed type (follicular, oncocytic, classical - 35%) and focal anaplastic carcinoma (5%). Extensive lymphovascular invasion, capsular invasion and focal extrathyroidal extension was identified. No lymph nodes were involved.

A PET/CT scan showed a 4 cm left renal mass and subcentimeter pulmonary nodules in bilateral lung bases. I-123 whole body imaging showed multiple foci of increased radionuclide activity in the lungs, predominantly in the lower lobes. The renal mass did not demonstrate increased radiotracer activity and MRI results were consistent with a renal cell carcinoma.

The patient underwent rhTSH stimulated I-131 therapy with 156 mCi with post therapy images redemonstrating pulmonary metastases and minimal thyroid bed uptake. No additional distant metastases were identified.

Subsequently, the patient received treatment with intensity modulated radiation therapy (6600 cGy) of head and neck. Systemic therapy was offered due to the anaplastic component, but the patient declined and is under close surveillance.

Repeat PET/CT scan done 2 months post I-131 treatment redemonstrated metabolic activity in the left renal mass. Seven months following the thyroidectomy, he underwent left nephrectomy. Pathology revealed a 5.5 cm metastatic papillary thyroid carcinoma.

Conclusion: Our patient presented with 3 histotypes of thyroid cancer within his thyroid tumor. Comprehensive imaging permitted proper thyroid cancer staging [Stage IVA for anaplastic and IVC for differentiated] and timely management for both. Genetic test of this patient’s tumor may help clarify the process of de-differentiation in thyroid cancer.

Abstract #1046

INCIDENTAL FINDING OF COEXISTENT PAPILLARY THYROID CARCINOMA AND SQUAMOUS CELL CARCINOMA OF TONGUE; REPORT OF A CASE

Wajiha Gul, MBBS, MRCP¹, Mahmoud Zirie, MD, FACE¹, Hossein Gharib, MD, MACE²

1. Hamad Medical Corporation, 2. Mayo Clinic College of Medicine

Objective: To report the incidental finding of metastatic papillary thyroid cancer [PTC] in the lymph node specimen during surgical resection and staging workup of squamous cell carcinoma [SCC] of tongue.

Case Presentation: An 83-year-old male with history of hypertension and dyslipidemia presented for a second opinion for a recently discovered large right thyroid nodule. A FNA performed at another facility was concerning for follicular thyroid cancer. Thyroid ultrasound revealed a hypoechoic mass measuring 4.6 x 3.2 x 4.2 cm, in the right lower thyroid lobe. He underwent total thyroidectomy and the pathology report noted a 7.2 cm mixed poorly differentiated insular carcinoma (60%), papillary thyroid carcinoma, mixed type (follicular, oncocytic, classical - 35%) and focal anaplastic carcinoma (5%). Extensive lymphovascular invasion, capsular invasion and focal extrathyroidal extension was identified. No lymph nodes were involved.

A PET/CT scan showed a 4 cm left renal mass and subcentimeter pulmonary nodules in bilateral lung bases. I-123 whole body imaging showed multiple foci of increased radionuclide activity in the lungs, predominantly in the lower lobes. The renal mass did not demonstrate increased radiotracer activity and MRI results were consistent with a renal cell carcinoma.

The patient underwent rhTSH stimulated I-131 therapy with 156 mCi with post therapy images redemonstrating pulmonary metastases and minimal thyroid bed uptake. No additional distant metastases were identified.

Subsequently, the patient received treatment with intensity modulated radiation therapy (6600 cGy) of head and neck. Systemic therapy was offered due to the anaplastic component, but the patient declined and is under close surveillance.

Repeat PET/CT scan done 2 months post I-131 treatment redemonstrated metabolic activity in the left renal mass. Seven months following the thyroidectomy, he underwent left nephrectomy. Pathology revealed a 5.5 cm metastatic papillary thyroid carcinoma.

Conclusion: Our patient presented with 3 histotypes of thyroid cancer within his thyroid tumor. Comprehensive imaging permitted proper thyroid cancer staging [Stage IVA for anaplastic and IVC for differentiated] and timely management for both. Genetic test of this patient’s tumor may help clarify the process of de-differentiation in thyroid cancer.

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1. Hamad Medical Corporation, 2. Mayo Clinic College of Medicine

Objective: To report the incidental finding of metastatic papillary thyroid cancer [PTC] in the lymph node specimen during surgical resection and staging workup of squamous cell carcinoma [SCC] of tongue.

Case Presentation: A 42 years old Asian male presented with painful non-healing ulcer on left posterolateral side of the tongue of one month duration. Clinical examination revealed 2x2 cm ulcer on left lateral tongue with indurated
base and everted margins. Punch biopsy and histopathology of the lesion was suggestive of moderately differentiated invasive SCC. MRI tongue showed neoplastic mass along the left posterior aspect of the tongue with associated metastatic cervical lymphadenopathy. PET scan revealed the same findings with uptake in bilateral submandibular, submental and parajugular lymph nodes, suggestive of possible metastasis. Patient underwent left glossectomy and left neck lymph nodes dissection. Histopathology was consistent with moderately differentiated SCC. 1 out of 17 lymph nodes was positive for metastatic PTC. Despite negative preoperative thyroid ultrasound he underwent total thyroidectomy and histopathology showed pT1aN1M0 PTC (tumour size 0.8cm). Post therapy scan after 150 mCi radioiodine showed uptake in thyroid bed and submental lymph nodes. He underwent 60 sessions of external beam radiotherapy for SCC. He was kept on percutaneous endoscopic gastric [PEG] tube feeding allowing the time for oral wound to heal. After wound healing, PEG tube was removed and he was started on oral feed which he tolerated well apart from mucositis because of radiotherapy. He developed fibrotic bands as a complication of radiotherapy that were treated with local triamcinolone injections. Repeat PET scan after 1 year of treatment was unremarkable showing no evidence of PTC or SCC. 

**Discussion:** Synchronous occurrence of primary thyroid malignancy and head and neck squamous cell carcinoma [HNSCC] is a rare condition with incidence of 0.3-1.9%. There are a few reported cases of SCC of tongue and metastatic PTC. Due to paucity of information it is not clear what is the best management strategy for metastatic PTC. Based on present case it appears that node-positive PTC has good short term prognosis.

**Conclusion:** The association of papillary thyroid carcinoma and SCC of tongue is rare, few case reports are available, and further information is needed to elucidate the optimal management of PTC in this setting.

**Abstract #1047**

**HYPERTHYROIDISM? THE SIMPLEST EXPLANATION IS NOT ALWAYS THE CORRECT ONE**

*Andres Ortiz, MD, Margarita Ramirez-Vick, MD, Milliette Alvarado Santiago, MD, Loida Gonzalez-Rodriguez, MD*

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**Objective:** Thyroid hormone resistance (THR) is a rare syndrome, and may be confused with other forms of thyroid hormone excess due to biochemical profile, nonspecific symptoms, and imaging studies. If there is not a high index of suspicion, the syndrome may be treated incorrectly, changing long term management and follow-up.

**Case Presentation:** 66 y/o female was treated since 2004 for goiter and hyperthyroidism by her primary care physician. She initially presented with goiter, palpitations, cold intolerance, anxiety, and daily loose stools. Patient was treated with methimazole, since TSH was 0.2 uIU/mL (nl, 0.358-3.74) with free T4 of 1.65 ng/dL (nl, 0.76-1.46), Anti TPO antibodies 714.5 IU/ML (nl, <20), TG-Ab 99.9 IU/ML (nl, <45). Thyroid scan/uptake was consistent with diffuse toxic goiter, showing increased radiotracer uptake with 88% uptake at 24 hours. The patient was treated with methimazole. Three years later, the patient received Radiiodine (RAI) therapy due to persistent disease. After treatment, she continued with elevated free thyroid hormone levels regardless of high or low TSH levels, for which she was intermittently switched between L-T4 therapy and methimazole, depending on biochemical status, but with minimal clinical improvement. During treatment with low dose methimazole (< 5 mg daily), the patient developed frank clinical hypothyroidism with normal free T4; and when taking low dose L-T4 treatment she had inappropriately normal TSH with high free T4 levels. After second thyroid ablation, hypothyroidism worsened, and levothyroxine was re-started, developing an inappropriately high TSH 21.8 uIU/mL despite a high free T4 of 1.55 ng/mL. In order to rule out other diagnoses, further work-up revealed truly elevated free T4 by equilibrium dialysis of 3.9 ng/dL (nl, 0.8-2.7), normal sex hormone binding globulin levels, and TSH alpha subunit of 2.1 ng/mL (nl, <3.56) ruling out TSH-secreting adenoma, for which a diagnosis of THR was entertained by exclusion. Due to financial constraints, the patient was unable to have genetic testing performed. She continued treatment with L-T4 therapy at a dose of 1.6 mcg/kg/day, with clinical euthyroidism and a normal TSH level, despite a slightly free T4.

**Conclusion:** Biochemical and clinical findings of THR may be confused with other etiologies of thyroid gland hyperactivity. Patients are often mistreated inappropriately given such hormonal patterns. It is of utmost importance to have a high degree of suspicion, since management options range from no treatment to lifelong L-T4 replacement therapy.
Abstract #1048

CORRELATION BETWEEN ROSETTAGX REVEAL TESTING OF BETHESDA INDETERMINATE THYROID NODULES AND SURGICAL PATHOLOGY

Juman Takeddin, MD, Sumi Thomas, MD, Stanley Trooskin, MD, Sara Lubitz, MD

Rutgers Robert Wood Johnson Medical School

Objective: To describe the outcomes of patients with Bethesda indeterminate thyroid nodules who underwent testing with microRNA classifier RosettaGX Reveal. We will compare the molecular test results to surgical pathology after thyroidectomy, and report other relevant clinical outcomes for patients who did not undergo surgery.

Methods: A retrospective chart review was conducted to identify all patients who had testing of indeterminate thyroid nodules with RosettaGX Reveal at Robert Wood Johnson University Hospital. Data gathered included patient demographics, risk factors for thyroid cancer, nodule features by ultrasound, FNA results, molecular test result, and surgical pathology when available.

Case Presentation: We identified 22 patients with indeterminate thyroid FNA samples tested with RosettaGX Reveal. On initial cytology, 20 were Bethesda category III and two were Bethesda category IV. Molecular testing classified seven samples as suspicious, all were Bethesda category III. Out of the seven patients with suspicious molecular classifier, five underwent surgery and two are awaiting surgery. Final pathology identified one Hürthle cell adenoma, one noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), one multi-nodular goiter, and two cases of micropapillary thyroid cancer (micro-PTC). Out of the 15 patients with indeterminate nodules with benign molecular classification, one underwent thyroidectomy and was found to have multiple nodules with incidental micro-PTC. Clinical follow-up of other Bethesda III nodules with benign molecular testing showed that three patients had multinodular goiter with benign FNA of the other nodules, and two patients had repeat FNA of the same nodule within one year read as benign.

Discussion: The published positive predictive value (PPV) of RosettaGX Reveal is 59%. In our small sample of 20 patients with Bethesda III, seven (35%) were classified as suspicious, in contrast to the established rate of malignancy of 5-15% in this category. A number of false positive results is anticipated and concordant with the PPV of the test.

Conclusion: Molecular testing is an additional tool that helps evaluate the risk of malignancy in indeterminate thyroid nodules, and should be used in combination with clinical data. Results from our small sample showed that it overestimated the risk of malignancy, and this is concordant with the PPV of the test. We do not have enough data to comment about the negative predictive value. We plan to collect data for patients who had other types of molecular tests and follow them longitudinally to further evaluate the clinical utility of molecular testing at our institution.

Abstract #1049

FOLLICULAR THYROID CARCINOMA WITH LATE METASTASIS TO KIDNEY IN A PATIENT WITH ELEVATED THYROGLOBULIN LEVELS OF UNKNOWN SOURCE

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Objective: Follicular thyroid cancer can metastasize hematogenously, most commonly to lung and bone. Here we present a case of follicular thyroid cancer with elevation of thyroglobulin (Tg, in ng/ml) detected almost 10 years after initial surgery and radioactive iodine therapy (RAI). The elevated Tg persisted for years before he was found to have a metastasis in his kidney 16 years after his initial cancer treatment.

Case Presentation: A 78 year old male had a total thyroidectomy followed by RAI therapy in 2001 for a 2.4 cm follicular thyroid cancer. His Tg became mildly elevated in 2009, and continued to rise gradually. Whole body 131-I imaging, PET scan and neck ultrasound did not find a source for the Tg. In 12/12 his Tg was 49.4 with a suppressed TSH. A thyrogen stimulated Tg in 2/13 was 930 and again ultrasound, 131-I imaging and PET scan were unrevealing. He was treated empirically with 210 mCi 131-I. His Tg level came down and remained <2 but a thyrogen stimulated Tg was 8.8 in 10/14. Tg antibodies have always been undetectable. Tg continued to rise to 96.5 on levothyroxine in 6/15. Again ultrasound, 131-I and PET scanning were unrevealing. On an abdominal CT scan for appendicitis in 10/15 a 1.4 cm right renal lesion was observed which remained stable on active surveillance. An increase in size of the renal mass was noted in June 2017, with further increase in Sept 2017 leading to right nephrectomy. The pathology of the right kidney showed a lobulated 2.7 x 2.4 x 2.0 cm mass. Histologic appearance and immunostains led to diagnosis of metastatic follicular thyroid carcinoma. Tg in 3/17 on levothyroxine was 63.4, and rose to 95.4 in 6/17, 267.5 in 9/17 and 190.9 in 10/17 before his nephrectomy.

Interestingly, the presence and change in the renal mass corresponded to his Tg levels all along. In retrospect,
the small renal mass could be seen on his PET CT films from 2012. The FDG uptake in the kidney lesion appears to have been missed due to normal FDG concentration in the urinary tract. At the time of his last whole body 131-I scan in 2015 the renal mass was only 1.4 cm on CT and likely below the detection of the 131-I. A Tg level after nephrectomy is pending.

**Conclusion:** Given the rarity of thyroid cancer metastases to the kidney, and the normal concentration of FDG in the urinary tract, a renal metastasis may be missed during evaluation of patients with persistent elevations of thyroglobulin.

**Abstract #1050**

**JOD-BASEDOW AFTER RADIOIODINE ABLATION**

*Harris Baloch, MD, Mark Cruz, MD, Alicia Warnock, MD, Thanh Hoang, DO, Vinh Mai, DO*

Walter Reed National Military Medical Center

**Objective:** Jod-Basedow phenomenon is hyperthyroidism following administration of iodine; previously it was described in iodine deficient area where administration of iodine led to the phenomenon. More recently, its been noted with the use of contrast mediums. Typically, this occurs in patients who have existing thyroid disease - such as Graves’ disease or toxic multinodular goiter. At the basic level, it is thought to occur due to over activation of the entire thyroid gland or autonomous nodules within it after iodine repletion without adequate feedback from the pituitary gland. Here, we describe a case where patient developed thyrotoxicosis following uterine ablation despite having had successful radioiodine ablation (RAI) induced hypothyroidism five months prior.

**Case Presentation:** 39 year old female with a 40 pound weight loss and hand tremors presented to the endocrine clinic. Initial laboratory evaluation showed TSH 0.005 mcIU/ml (0.27-4.2), FT4 > 7.77 ng/dL (0.93-1.7) and TSI of 570%. A diagnosis of Graves’ disease was made and patient was started on methimazole titrated to euthyroid state. Patient remained on it for 12 months prior to electing for RAI. A thyroid scan showed enlarged gland, with regular contour and heterogeneous trapping with 70% uptake at 4 hours consistent with Graves’ disease. Patient underwent RAI with 16.23 millicuries. Two months post-RAI, patient developed hypothyroidism with TSH 20.910 mcIU/ml (0.27-4.2), FT4 > 7.77 ng/dL and FT3 of 1.750 pg/mL (2.0-4.4). Patient was started on synthroid 100mcg. One month later patient underwent uterine ablation for uterine fibroids requiring administration of IV contrast of 60mL. Immediately post-contrast administration patient became tachycardic and hypertensive (HR 115, BP 167/101). Lab evaluation at this time showed TSH 0.016, FT4 2.18 with serum iodine of 1029.1 mcg/L and 24 hour urine iodine of >25,000 mcg/L suggestive of Jod-Basedow phenomena. Synthroid was discontinued while patient remained hyperthyroid with continued decrease in TSH and an increase in FT4 requiring methimazole for control of her thyrotoxicosis.

**Discussion:** Jod basedow is a rare presentation of thyrotoxicosis that occurs after IV contrast administration. Our case above highlights a rare occurrence of the phenomenon in a patient who had successful RAI ablation.

**Conclusion:** This case suggests that post-RAI patients continue to be at risk of developing thyrotoxicosis following contrast administration and close vigilance for it should be maintained.

**Abstract #1051**

**ONCE WEEKLY ORAL SUPERVIZED LEVOTHYROXINE ADMINISTRATION AS AN OPTION FOR POORLY COMPLIANT PATIENTS**

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San Juan City Hospital

**Objective:** Levothyroxine (LT4) replacement is the most common hormonal replacement therapy prescribed worldwide. Most of the patients TFT improve after replacement but some need further adjustment. This subgroup of patients requires more frequent medical visits, malabsorption workup, non-conventional replacement therapies such as combination therapy with LT4 plus Lt3 or intramuscular LT4. This may rise cost and if unclear diagnosis may signify harm to patient. When we encounter a patient with non-suppressible TSH and reporting adequate compliance with therapy, we should consider other etiologies such as assay interference, TSH secreting adenoma, TSH resistance syndrome, occult celiac disease, and medications interaction, among others. On this case series we demonstrate that non-compliance is the most common reason to TSH non suppressibility while on LT4 therapy even on those patients that refer extremely good adherence to therapy.

**Methods:** We selected 4 hypothyroid patients with either on high dose of LT4, Lt4/Lt3 and a non-suppressible TSH for > 12 months of therapy, with malabsorption workup done and with reported excellent medication adherence. We administered an oral Lt4 bolus at 1.6 mcg/Kg *7 once weekly upon direct supervision and measured TSH, free t4 and free T3 at specific intervals and repeat this procedure for 6 weeks.

**Case Presentation:** Patient 1: baseline TSH: 56.3 (0.34-5.60 uIU/MI) on LT4 2,975 mcg weekly (425 mcg daily). LT4 bolus of 700 mcg once a week achieved a TSH of 0.75 uIU/MI. Patient 2: baseline TSH: 57.41 uIU/Ml on LT4 2,975 mcg weekly (425 mcg daily). Patient 3: baseline TSH: 57.3 (0.34-4.2) on LT4 2,975 mcg weekly (425 mcg daily). Patient 4: baseline TSH: 56.3 (0.34-4.2) on LT4 2,975 mcg weekly (425 mcg daily).
**ABSTRACTS – Thyroid Disease**

Lt4 6,300 mcg/weekly (900 mcg PO daily) plus Lt3 700 mcg/weekly (50 mcg PO bid). LT4 bolus of 1500 mcg once a week suppressed TSH to 4.01 uIU/mL. Patient 3: baseline TSH: 17 uIU/mL on Lt4 1,400 mcg PO weekly (200 mcg PO daily). Lt4 bolus of 1150 mcg weekly showed over-suppression of TSH: 0.23 uIU/ml by week #3, therefore LT4 was decreased to 950 mcg and her TFT normalized with TSH: 4.68 uIU/ml. Patient 4: baseline TSH: 4.92 uIU/ml on Lt4 3,850 mcg/week (550 mcg oral daily). LT4 bolus 1400 mcg once a week maintained her TSH stable at 1.36 uIU/ml.

**Discussion:** All patients had TSH suppression (>90%) after 6 weeks of direct supervised oral LT4 administration with a weight-based bolus or less.

**Conclusion:** This approach is of useful clinical utility in terms of cost effectivity of therapy, to avoid workup of rare and/or subclinical conditions or utilization of more complex replacement therapies that will result in higher cost and not necessarily control TFT. More studies are needed in order to determine long term safety, lipids homeostasis, quality of life, and more important if it can be used to suppress TSH to the targets needed in thyroid cancer management.

**Abstract #1052**

**STROKE OR SOMETHING ELSE? EXPRESSIVE APHASIA IN A YOUNG PATIENT DUE TO ‘STEROID RESPONSIVE ENCEPHALOPATHY ASSOCIATED WITH AUTOIMMUNE THYROIDITIS’**

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**Objective:** To emphasize the importance of early diagnosis and appropriate management of Steroid Responsive Encephalopathy associated with Autoimmune Thyroiditis (SREAT) with atypical presentation in a young patient.

**Case Presentation:** A 28-year-old African American man with hypothyroidism due to ablative treatment of Graves’ disease, presented with sudden onset of aphasia and difficulty in walking. Patient was taking levothyroxine 88 mcg daily intermittently. His vital signs were normal. He had expressive aphasia, fasciculations around the mouth, decreased strength in lower extremities and ataxic gait.

Initial labs: TSH= 0.03 (0.4-4) mU/ml, Free T4= 1.22 (0.8-1.9) ng/dl, TT3= 86 (82-179) ng/dl. Levothyroxine was decreased to 50 mcg daily. Urine was positive for marijuana. CT and MRI of head did not reveal any evidence of stroke or vasculitis. CSF analysis and cultures were negative. EEG showed sharp and spike wave discharges over the biparietotemporal region and intermittent episodes of slow wave discharge.

He continued to have expressive aphasia, ataxia and fasciculations with no etiology found. However he had high titers of thyroid peroxidase antibodies (2552 IU/ml); SREAT was considered and he was started on IV methylprednisolone 1 gram/ day. His condition started to slowly improve. By the fifth day of therapy, he was able to express himself fully with minimal residual slurred speech. Patient was able to ambulate with a walker. He was discharged on prednisone 40mg twice a day.

Four weeks following discharge, he had normal gait with improved speech. We recommended continuing prednisone 40 mg twice a day for four more weeks.

**Discussion:** Pathogenesis of SREAT is controversial. However, it is associated with high anti-thyroid antibody titers. Thyroid hormone levels don’t correlate with the clinical presentation. Literature review of SREAT symptoms include not only neuropsychiatric syndromes with behavioral or cognitive abnormalities, but also tremor (80 %), stroke-like episodes including transient aphasia (80 %), myoclonus (65 %), gait ataxia (65 %), seizures (60 %), and sleep abnormalities (55 %). The most common finding in CSF is elevated protein. EEG findings are nonspecific with generalized slowing; spikes with epileptic activity can also be identified. Neuroimaging findings are normal in most of the patients; rarely there will be cerebral atrophy, diffuse or focal white matter changes. Most of the patients with SREAT respond to steroids.

**Conclusion:** This is a unique case of SREAT in a young man presenting with atypical stroke-like symptoms. Appropriate diagnosis and treatment led to a good neurological outcome in this patient.

**Abstract #1053**

**PREVALENCE OF THYROID MALIGNANCY AMONG THYROID NODULES IN THE UNITED ARAB EMIRATES: FIVE-YEARS TERTIARY CENTER ANALYSIS**

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Sheikh Khalifa Medical City

**Objective:** The incidence of thyroid malignancy is increasing worldwide, and it constitutes the sixth common cancer type in the United Arab Emirates (UAE) where its incidence is increasing worldwide. There are no epidemiological data outlining the prevalence of cancer in thyroid nodules, nor previous analysis of ultrasonographic features correlating with thyroid malignancy in the UAE. This study aimed to estimate the prevalence of thyroid malignancy in thyroid nodules and to describe
the demographic and ultrasonographic characteristics of thyroid nodules harboring malignancy.

**Methods:** Retrospective electronic medical records review of all thyroid nodules in patients aged 18 to 80 years with a normal TSH who underwent ultrasound guided fine needle aspiration biopsy (UGFNA) at Sheikh Khalifa Medical City (SKMC) during 2011-2015.

**Results:** A total of 573 nodules with normal TSH underwent UGFNA cytological examination. The overall crude prevalence of thyroid cancer in thyroid these nodules was 8.8% (95% CI 6.5-11.2). The age-adjusted prevalence of thyroid cancer in thyroid nodules detected among UAE nationals, Arabs, Far East Asians, and Caucasians was 8.1% (3.3-13.0), 9.2% (5.9-12.5), 13.3% (3.4-23.2) and 13.0% (1.2-25.5), respectively, with relatively higher cancer prevalence in nodules detected in male patients. Most of the cancerous nodules were hypoechoic or isoechoic compared to the noncancerous nodules (p=0.025). Cancerous nodules were most more frequently 2-4 cm in the size between 2-4 cm.

**Conclusion:** We reported a relatively higher prevalence of thyroid malignancy among thyroid nodules. Thyroid malignancy was higher among nodules in patients of Far East Asian and Caucasian certain ethnic backgrounds population. Nodules of size 2 cm or larger and being either complex or hypo echoic turned out to harbour thyroid malignancy.

**Abstract #1054**

**NIVOLUMAB-INDUCED THYROTOXICOSIS IN STAGE IV HEPATOCELLULAR CARCINOMA: PAINLESS THYROIDITIS OR GRAVES’ DISEASE?**

Rebecca Neril, MD, Gary Rothberger, MD, ECNU

NYU Winthrop Hospital

**Objective:** The immune checkpoint inhibitor nivolumab, a monoclonal antibody which blocks the programmed death-1 receptor (PD-1), has revolutionized the landscape of cancer therapy. Nivolumab is known to cause endocrine immune-related adverse events (IRAEs), including thyroiditis. This case aims to describe nivolumab-induced thyroiditis in a patient treated for stage IV hepatocellular carcinoma, as well as to highlight a diagnostic dilemma arising from the concurrent presence of Graves' antibodies.

**Case Presentation:** A 58-year-old female with stage IV hepatocellular carcinoma presented with complaints of fatigue, insomnia and an eight pound weight loss after two doses of nivolumab. Prior to her first dose of nivolumab, she was euthyroid with a TSH 4.95 µU/mL (reference range 0.4-4.8µU/mL). At the time of evaluation, she complained of fatigue, insomnia and weight loss. Laboratory analysis showed thyrotoxicosis with TSH of 0.07 µU/mL and free T4 of 15.79 ng/dL (reference range 0.8-2.7 ng/dL). Acorrelating thyroid ultrasound demonstrated an enlarged hypoecho heterogeneous avascular gland with fibrous stranding, consistent with painless thyroiditis. Further testing revealed elevated TSI of 348% (reference range <140% baseline) and TPO antibody of 383.8 IU/mL (reference range 0.0-5.0 IU/mL). Six weeks later, TSH rose to a peak of 382.2 µU/mL, requiring initiation of levothyroxine.

**Discussion:** Thyroid dysfunction is a known immune-related adverse event with nivolumab therapy, with a reported incidence of <1%. Given the recent FDA approval for nivolumab use in hepatocellular carcinoma, there have been no known reported cases of nivolumab induced thyroiditis in a patient treated for hepatocellular carcinoma. However, the mechanism responsible for nivolumab-induced thyroid dysfunction is largely unknown. The rapid progression suggests an inflammatory destructive process with a mechanism reflecting that of painless thyroiditis, which mirrors this patient’s clinical and biochemical picture.

**Conclusion:** This represents the first reported case of nivolumab-induced thyroiditis in a patient treated for stage IV hepatocellular carcinoma. It is imperative for practitioners to be aware of immune-related adverse events such as thyroiditis in patients being treated with PD-1 inhibitors for hepatocellular carcinoma. This case is also intriguing due to the presence of Graves’ antibodies, which could have led to an erroneous diagnosis of Graves’ disease. However, the ultrasound appearance favored painless thyroiditis, and the subsequent development of hypothyroidism confirmed this diagnosis.

**Abstract #1055**

**ENDOSCOPIC THYROIDECTOMY VIA AXILLARY AND BREAST APPROACH (ABA) VS BILATERAL AXILLARY AND BREAST APPROACH (BABA) FOR TREATMENT OF THYROID TUMORS: A RETROSPECTIVE STUDY OF A 4-YEAR EXPERIENCE**

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**Objective:** Endoscopic thyroidectomy allows surgeons to remove a thyroid tumor from a remote site, and provide excellent cosmetic outcome. Various endoscopic approaches have been performed and their applications has been recently extended. The Aim of this study was to compare the appropriateness and outcome of endoscopic thyroidectomy (ET) via Axillary and Breast Approach vs Bilateral Axillary and Breast Approach (BABA) for the treatment of thyroid tumors.
Methods: A total of 98 patients with thyroid tumors were operated endoscopically in our unit. Forty six patients underwent ET via ABA and Fifty Two underwent ET via BABA. Variables such as surgery related outcomes and post-operative complications, were compared between two groups.

Results: A unilateral lobectomy was performed in 37 patients (80.44%) of ABA group and in 25 patients (48.08%) in BABA group. A bilateral total thyroidectomy was performed in 03 patients (6.52%) in ABA group and 25 patients (48.08%) in BABA group. The mean size of tumor was 4.03cm in ABA group and 5.84cm in BABA group. The operative time in ABA was longer compared to BABA group (243 min vs 187 min, for total thyroidectomy; and 143 min vs 126min for unilateral lobectomy). The BABA group has longer mean hospital stay compared to ABA group (4.5 days vs 2.49 days). There was two case conversion in BABA group and six case conversion in ABA group. The Recurrent laryngeal nerve and parathyroid were identified and preserved in both the group. Two cases in each group reported temporary hoarseness of voice. Temporary post operative hypocalcaemia was noticed in all case of total thyroidectomy of ABA group and 21% in BABA group.

Discussion: The cosmetic outcome was excellent during 06 month follow-up in both the group.

Conclusion: We believe that endoscopic thyroidectomy through ABA and BABA have role in the treatment of selected thyroid tumors; however BABA endoscopic thyroid surgery approach is more appropriate for the large goiters.

Abstract #1056

MALIGNANT STRUMA OVARI WITH SYNCHRONOUS THYROID PAPILLARY CARCINOMA

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The Jewish Hospital/Mercy Health

Objective: This is a case presentation of a 52-year-old female that was incidentally found to have a rare ovarian tumor consisting of thyroid tissue from struma ovarii. This tumor accounts for approximately five percent of all teratomas and thyroid tissue must comprise more than half of the overall tumor to meet criteria. Patients typically present with abdominal pain and, less frequently, with ascites. Clinical and biochemical features of thyroid irregularities occur in less than five to eight percent of cases. The treatment of malignant struma ovarii requires surgical resection of the tumor with total abdominal hysterectomy (TAH) and unilateral or bilateral salpingo-oophorectomy (BSO) followed by complete thyroidectomy and radioactive iodine therapy once biopsies of thyroid tissues confirm thyroid cancer.

Case Presentation: Patient is a 52-year-old female that presented to her gynecologist for a routine pap smear, which showed the presence of endometrial cells. Endometrial biopsy was not obtained due to cervical stenosis. CT scan noted 14 x19 cm complex cyst with enhancing peripheral nodules and partially calcified septations that were concerning for malignancy. She underwent TAH, BSO, appendectomy, omenectomy and lymph node dissection. Pathology results revealed follicular variant of papillary thyroid carcinoma arising from struma ovarii. Patient was subsequently evaluated for thyroid dysfunction for which she denied any symptoms of hyperthyroidism. Ultrasound of the thyroid gland was unremarkable. Levels of free T3 were mildly low, otherwise free T4, TSH and thyroglobulin levels were normal. BRAF and KRAS mutations were undetectable. Patient underwent total thyroidectomy with biopsy of the thyroid tissue significant for micropapillary thyroid carcinoma and was treated with radioactive iodine ablation. Post-ablation thyroid scan showed residual thyroid uptake in the neck with no distant spread or uptake in the pelvis. She was placed on TSH suppression therapy.

Conclusion: This is a rare presentation of a malignant struma ovarii with biopsies consistent with follicular variant of papillary thyroid carcinoma. Surgical and medical modes of treatment include surgical resection of both ovarian mass and thyroid gland followed by TSH suppressive therapy. The goal of T4 therapy is to maintain TSH at levels between 0.1 to 0.5 mU/L for the first five years followed by levels in the conventional normal range given no evidence of disease. BRAF and KRAS mutations have been reported in tumors of patients with malignant struma ovarii. However, negative mutations do not exclude the diagnosis of this malignancy. Recurrence rate is typically low following surgical resection and T4 suppressive therapy.

Abstract #1057

THYROID DISEASES IN PHPT: A SINGLE CENTRE STUDY

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Objective: Primary hyperparathyroidism (PHPT) and thyroid diseases are common in the general population. It is difficult to establish whether they occur in the same patient because of a direct relationship or just due to the
widespread prevalence of both conditions. The reported prevalence of the concomitant occurrence of these two clinical conditions is widely scattered (ranging 17-84%), especially due to the heterogeneous criteria for patient selection. We aimed to evaluate in a large series of PHPT patients the prevalence of thyroid diseases and the clinical and biochemical presentation of PHPT in patients without or with concomitant thyroid diseases. Methods: We retrospectively evaluated an unselected and monocentric series of 434 outpatients with PHPT, attending our hospital between 1998 and September 2017. Patients with neither bone or kidney involvement, nor hypercalcemic symptoms were considered asymptomatic. The US thyroid pattern was considered abnormal if nodules or features of chronic lymphocytic thyroiditis were found. The histological report of patients submitted to thyroidectomy was then evaluated. Results: Thyroid diseases were found in 263/434 (60.6%) PHPT patients. Among them, over than 80% were affected by nodular goiter, that was toxic in almost 10% of cases. Thyroid autoantibodies were positive in 50 (19%) patients, all with an autoimmune US pattern. Thyroid cancer was diagnosed in 11/85 patients (12.9%) and it was a papillary microcarcinoma in all cases but one. Patients with thyroid diseases were older and more frequently female than the others, despite no difference in serum calcium, creatinine, 25OHD and TSH levels. PTH levels result significantly higher in patients without thyroid abnormalities. Anyway, no difference were found in the PHPT clinical presentation nor in the presence of osteoporosis at any site between the two groups. Discussion: Thyroid diseases, mostly nodules, were present in 60% of our patients with PHPT, consistently with the goiter endemic area where our study has been conducted. Moreover, a thyroid carcinoma was found in more than 10% of patients. The predominantly histotype was papillary microcarcinoma, in agreement with literature data. PHPT characteristics resulted biochemically and clinically similar in patients with or without thyroid abnormalities. Conclusion: In conclusion, the majority of PHPT patients have a thyroid disease. Our data confirm that thyroid diseases and PHPT are two conditions prevailing in specific population, thus making their association more frequent. Thyroid nodules could interfere in the diagnostic and therapeutic PHPT work up.

Abstract #1058

CASE SERIES OF THREE MYXEDEMA COMA PATIENTS TREATED WITH T4 AND T3

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Objective: Myxedema coma is an endocrine emergency that requires prompt treatment with medical stabilization and thyroid hormone replacement. It is seen more frequently in the winter months. Although there is no consensus on the exact treatment regimen, review of literature shows that myxedema coma patients have been successfully treated with oral or intravenous (IV) T4, and with or without T3. Under most circumstances the body is able to convert T4 to T3 as needed; however, this process can be delayed in the critically ill. This brings forth the question of when is it clinically prudent to administer T3. Case Presentation: We present three patients who were admitted to our hospital in the winter of 2016-17 who were ultimately diagnosed with myxedema coma. Patient 1 was a 64-year-old woman with Graves' disease and history of total thyroidectomy (TSH 28, FT4 0.12). Patient 2, a 34-year-old quadriplegic man (TSH 79, FT4 0.26), and Patient 3, a 69-year-old woman (TSH 67, FT4 <0.1), both presented with new onset autoimmune hypothyroidism. They were all admitted to the Intensive Care Unit with altered mental status, hypothermia, and hemodynamic and/or respiratory instability. They received IV T4 in initial bolus doses ranging from 100 to 300mcg. Due to clinical deterioration over the initial twenty-four hours and concern for inefficient conversion of T4 to T3 in the critically ill state, all three patients ultimately received T3 (oral or IV) doses of up 30mcg over a 24 hour period; they all had significant improvements within twelve hours of starting T3 after which the T3 dose was promptly reduced or discontinued. We did not see the development of new cardiovascular complications after starting T3. All three patients survived their hospitalization with recovery of mental status to normalcy.

Conclusion: Our case series brings forth three circumstances in which IV T4 was given as a bolus dose, and T3 added within or after twenty four hours due to concern for clinical deterioration. Whether the improvement within hours after T3 administration is the effect of T3 or simply coincided with the expected timeframe of T4 converting to T3 in the body, is unclear. Our cases highlight consideration of addition of T3 to IV T4 in myxedema coma patients that do not show improvement with T4 therapy alone, in accordance with the 2014 ATA Guidelines for the Treatment of Hypothyroidism.
Abstract #1059

PROGNOSTIC FACTORS OF METASTATIC THYROID CARCINOMA: A SINGLE CENTER RETROSPECTIVE STUDY

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Objective: To identify the most significant risk factors for mortality in patients with well-differentiated metastatic thyroid carcinoma.

Methods: This retrospective cohort review was comprised of patients with well-differentiated metastatic thyroid cancer seen at a tertiary care center between January 1990 to December 2010. Data was analyzed from this cohort in December 2017. Patients with the following carcinomas were excluded: anaplastic, medullary, poorly differentiated subtypes, or other primary. A 15-year Kaplan-Meier survival estimate was created for overall survival (OS) and cancer specific survival (CSS). Hazard ratios (HR) and p-values from Cox proportional hazard models were used with 95% confidence intervals (CI). A p-value less than 0.05 was set as statistically significant. Analysis was performed with SAS software (version 9.4; Cary, NC).

Results: There were 139 patients (60.4% male, 39.6% female) with a median age at diagnosis of 59 years (range 9.0-89.0). Ethnicities included were 121 white (84%), 15 black (10.4%), and 8 (5.6%) other. Types of cancer included papillary thyroid in 105 patients (75.6%), follicular thyroid in 30 (21.5%), and Hürthle cell in 4 (2.9%). Median MACIS score was 8.8 (from 4.5 to 12.1), and median length of follow-up from diagnosis to mortality was 70.5 months (from 1.0 to 564.0). The 15-year mortality rate was 26.6% (37 patients) and cancer-specific mortality was 23.0% (32 patients), with OS and CSS having the same risk factors with similar hazard ratios.

Risk factors for a decreased CSS included: older age upon diagnosis (> 45 years, HR=3.62, CI=1.21-10.85, p=0.021), multiple metastatic locations (HR=3.80, CI=1.55-9.31, p=0.003), incomplete/unknown tumor resection (HR=2.47, CI=1.19-5.10, p=0.015), bone metastases on follow-up (HR=2.29, CI=1.31-5.97, p=0.008), other metastases on follow-up (HR=3.19, CI=1.49-6.82, p=0.003), and higher MACIS scores (HR=1.91, CI=1.39-2.62, p=0.001). Lung was the most common site of metastases in 54 patients (37.5%), and within this group, a pleural effusion had a significant association with CSS mortality (HR=6.02, CI=1.97-18.37, p=0.002).

Discussion: Significant risk factors for a decreased OS and CSS were age > 45, multiple metastatic locations, incomplete/unknown tumor resection, development of bone metastases, development of other metastases and a higher MACIS score. Interestingly, this is the first time that development of a pleural effusion was identified as a significant risk factor for decreased OS and CSS.

Conclusion: The development of a pleural effusion and its significant association with a decrease in OS and CSS represents a novel prognostic finding in patients with well-differentiated thyroid carcinoma with lung metastases.

Abstract #1060

THE PREVALENCE OF SUBCLINICAL HYPOTHYROIDISM AND ITS ASSOCIATION WITH CARDIO METABOLIC RISK FACTORS IN NORTH-WESTERN NIGERIA. A POPULATION-BASED STUDY.

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Objective: Subclinical Hypothyroidism (SCH) is a clinical condition characterised by raised thyroid stimulating hormone (TSH) and normal thyroxine levels. Overt hypothyroidism has been positively associated with cardio metabolic risk factors and the influence of SCH to that effect is not known.

The study is aimed to find the association between SCH and MS and its individual components in a population based study.

Methods: A cross sectional study comprising of healthy 247 participants aged 18-62 years and, 188 males and 59 females. Consent of the subjects was sought and study protocols approved. Physicals include anthropometry and blood pressure readings. A fasting blood glucose, lipids and thyroid function test (TSH, T4, T3) using standardised enzymatic and ELISA assays were determined. The IDF criteria for the diagnosis of metabolic syndrome was used. The SPSS version 23 software was used to analyse the data with p<0.05 as significant.

Results: Subclinical hypothyroidism was 17.0% (42/247) and overt hypothyroidism 4.8% (12/247). Metabolic syndrome among the SCH group was 21.4% (9/42) and
Euthyroid (control) group 5.2% (10/193), p < 0.05. The SCH is common in females with 28.8% (17/59) and 13.3% (25/188) in males. Chi sq = 4.0, p = 0.035.

The means of BMI 23.9(4.7)kg/m2, SBP 118(18)mmHg, TC 3.94(1.1)mmol/L, TG 1.01(0.53)mmol/L and HDL 1.45(0.40)mmol/L in SCH group were significantly high than in Euthyroid group. p < 0.05.

Logistic regression showed positive association between SCH and the BMI, TC, TG, and SBP p < 0.05.

**Discussion:** A prevalence of SCH of 17% was recorded and of this, 21.4% have metabolic syndrome. The finding is in concordance with a similar survey among the Caucasians (18%) and a lower rate of (3.4%) among Chinese. Among the SCH subjects, 1 out of 5 has metabolic syndrome which is similar to that Ogbera et al. There were more females with SCH in this study as with many others.

Subclinical hypothyroidism was found to be positively associated with all the cardio metabolic risk factors. The implication of this finding is that SCH may be considered as a cardio metabolic risk factor among this population group. Previous studies have shown a link between SCH and CV risk factors such as alterations in blood pressure, lipid levels, atherosclerosis and like overt hypothyroidism, is associated with metabolic syndrome and heart failure. In other words the serum TSH is associated with cardiovascular diseases, thus using levothyroxine therapy in SCH may be beneficial.

**Conclusion:** This study found a positive relationship between SCH and metabolic syndrome and also a predictor of cardiovascular risk factors.

**Abstract #1061**

**GRAVELY PARALYZED: A CASE OF HYPOKALEMIC PERIODIC PARALYSIS IN A PATIENT WITH GRAVES’ DISEASE**

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**Case Presentation:** A 37-year-old Cambodian male with history of untreated Graves’ disease (TSI 2.26) presented with lower extremity paralysis. He was recently diagnosed with hyperthyroidism after his primary care physician obtained labs to evaluate his symptoms of weight loss, heat intolerance, diarrhea and tremulousness. Treatment had not been initiated because his appointment with the endocrinologist wasn’t until the following week. In the emergency room, he was found to have decreased muscle strength in his lower extremities and had a potassium level of 1.9. Following administration of potassium chloride 100 mEq, labetalol 20 mg, intravenous fluids and atenolol the patient developed upper extremity paralysis. Repeat potassium was <1.5 so an additional potassium 40 mEq was administered. The patient was diagnosed with hypokalemic periodic paralysis. With discontinuation of atenolol and initiation of propranolol and methimazole, his potassium level overcorrected to 6.8. His potassium level normalized with administration of furosemide and intravenous fluids. He was discharged with symptom resolution.

**Discussion:** Thyrotoxic periodic paralysis (TPP) is a rare presentation of hyperthyroidism. It is more common in Asians versus Caucasians and males versus females. Patients present with severe hypokalemia and differing severities of weakness ranging from mild weakness to total paralysis but intact cognition and sensation. Symptoms appear after heavy exertion or eating a carbohydrate heavy meal. Our patient had steak, corn and bread pudding the night before symptom onset. Any type of thyrotoxicosis can cause TPP but Graves disease is the most common. The proposed mechanism is the T4 directly stimulates the Na-K-ATPase dependent potassium channel resulting in intracellular potassium shift. Treatment includes potassium, preventing intracellular shift of potassium with nonselective beta blockers and treating the thyroid disorder. Our patient was initially treated with a beta 1 receptor antagonist which contributed to worsening hypokalemia. It is important to avoid rebound hyperkalemia which is caused when too much potassium is given. Approximately half of patients with TPP develop rebound hyperkalemia after receiving >90 mEq of potassium chloride.

**Conclusion:** It is important to recognize patients with hypokalemia and paralysis as this can be a life threatening condition if untreated. Ultimately, this syndrome will be cured when the patient becomes euthyroid.

**Abstract #1062**

**A CASE OF AMIODARONE INDUCED HYPOTHYROIDISM THROUGH INHIBITING PERIPHERAL CONVERSION OF T4 TO T3**

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**Objective:** Amiodarone is a class III antiarrhythmic agent which inhibits adrenergic stimulation, affects sodium, potassium and calcium channels, markedly prolongs action potential and repolarization; decreases AV conduction and sinus node function; amiodarone has a long half-life reaching 107 days. It is widely used for ventricular and supra-ventricular arrhythmias. Amiodarone is well known to cause hyperthyroidism, both through thyroiditis and non-thyroiditis related mechanisms, in up to 10% of patients; it can also cause hypothyroidism in up to
22% of patients mostly through suppressed uptake and organification of iodine in the thyroid gland.

Case Presentation: This is a case of a 56-year-old female with history of recurrent ventricular tachycardia who failed multiple therapies and was started on amiodarone. She was admitted to the hospital, about two weeks after initiation of amiodarone, with bradycardia, fatigue, worsening constipation and was found to have TSH of 26 and fT4 of 1.0; she was started on levothyroxine 150 mcg daily and amiodarone was stopped. Few days into her admission, she was still having systemic fatigue with myalgia, repeat TSH was up to 32, fT4 up to 1.5 while T3 was low at 25 with fT3 low at 0.6 and high rT3 at 86.1. We started the patient on liothyronine 5 mcg daily and increased the dose up to 60 mcg total daily dose. Throughout this process, the patient started to retain her energy, she was ambulating at her baseline and her mental status improved, her heart rate was within normal limits. Her T3 was up to 67, fT3 up to 1.0 and TSH down to 1.7.

Discussion: Amiodarone has been found to decrease serum T3 by blocking peripheral T4 5'-deiodinase. Specifically, amiodarone and its main metabolite, desethylamiodarone (DEA), are noncompetitive inhibitors of the type 2 deiodinase (D2), which is thought to be the major source of plasma T3 in humans and also plays a critical role as a source of intracellular T3 in a number of cell types. This inhibition at the level of the pituitary gland contributes to the rise in TSH seen in patients taking amiodarone. The reduction in T3 levels may contribute to the effectiveness of this drug in moderating cardiac arrhythmias.

Conclusion: It is crucial to keep in mind the various effects of amiodarone on thyroid function including the inhibition of T4 to T3 conversion and the side effects which might be seen with low T3 that might be life threatening; and, therefore, replacement with T3 hormone can be invaluable, in such circumstances, to ameliorate the symptoms of hypothyroidism which can be persistent for up to several months.

Abstract #1063

METHIMAZOLE INDUCED HEPATOTOXITY IN PATIENT WITH HYPERTHYROIDISM AND PAPILLARY THYROID CANCER

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Objective: To present a case of methimizole (MMI) induced cholestatic hepatitis in hyperthyroid patient who was concurrently found to have papillary thyroid cancer.

Case Presentation: 71 years old female presented with 6 month history of tremors, feeling jittery and increased frequency of bowel movements. She denied increased sweating, weight loss or heat intolerance. Labs revealed: TSH 0.03 (normal 0.3-4.2 mIU/L), free T4 2.1 (normal 0.9-1.7 ng/dL) and total T3 231 (normal 80 - 213). TSI was less than 1. She denied over-the-counter iodine supplement, amiodarone use, excessive seafood or IV contrast. TSH remained persistently suppressed over few months. Radioactive iodine uptake and scan reported heterogenous appearance without focal increased activity to suggest hyperfunctioning nodule. 24 hour uptake was 27.6% (normal 10-35%). Thyroid ultrasound reported 1.3 cm right lower nodule with micro-calcification, 1.7 cm right upper nodule and 2.3 cm left lower nodule. Based on fact that these were warm and not hot nodules, thyroid FNA biopsy was performed of right nodule with micro-calcifications and left-sided nodule. Cytology of right thyroid nodule was reported as papillary thyroid cancer. Total thyroidectomy was planned. To achieve euthyroidism before total thyroidectomy, she was started on MMI. Baseline liver function test was normal. MMI dose was increase every 2 weeks as thyroid level continued to remain elevated depite of MMI. She was ultimately on 40 MG per day dose. After 2 weeks on this dose, bilirubin, AST, ALT and alkaline phosphatase increased significantly. Patient remained asymptomatic other than mild icterus. Methimazole was stopped. Liver ultrasound did not report any abnormality. Serial liver function improved over next weeks. She was not started on glucocorticoid. Later she underwent total thyroidectomy successfully. Final pathology reported unifocal right 1.4 cm papillary thyroid cancer surgical margins positive with minimal extrathyroidal extension present. AJCC stage T3 NX.

Discussion: MMI can cause hepatotoxicity. The underlying mechanism is believed to be idiosyncratic or immunologic. Hepatotoxicity is rare with frequency of 0.1-0.2%. It has been reported in both sexes, increased incidence with advancing age, presents anywhere from 3 days to 5 months after drug initiation and with doses more than 30 MG daily. MMI-induced cholestasis generally resolves within 5 days to 6 months after stopping drug and rarely results in death.

Conclusion: Care must be taken when prescribing MMI in elderly and note that higher dose is associated with increased risk of hepatotoxicity.
**Abstract #1064**

**BIOTIN SUPPLEMENTATION MIMICKING GRAVES’ DISEASE**

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**Objective:** To present a case of abnormal thyroid function tests suggesting Graves’ disease in a patient taking mega doses of biotin.

**Case Presentation:** A 53-year-old healthy female presented for abnormal thyroid function tests. For the past 2 years she had been seeing a holistic medicine practitioner. She had been placed on a number of vitamins and supplements, including high-dose biotin 100 mg (100,000 mcg). She was taking all of these daily, and reported taking the biotin for the past 8 months. At a routine office visit, the patient endorsed a few nonspecific symptoms that prompted thyroid function testing. Labs revealed a TSH of 0.008 uIU/ml, Free T4 >7.77 ng/dl, and Free T3 of 9.6 pg/ml. Thyrotropin receptor antibodies (TRAb) came back elevated at 6.99 IU/L (reference range 0.0-1.75). In addition to thyroid labs, DHEAS was significantly elevated at 939.1 ug/dl. A thyroid US was obtained which showed a normal sized gland with normal blood flow on Doppler. Endocrinology evaluation revealed no clinical symptoms consistent with Graves’ thyrotoxicosis. The patient was instructed to hold all supplements and repeat labs. Two weeks after discontinuing her supplements, her thyroid function tests all returned to normal, including TRAbs.

**Discussion:** Biotin supplements are very common. Also common are biotin-streptavidin based immunoassays. This is especially important in endocrinology, as many assays utilize the biotin-streptavidin bond to measure hormones. These include LH, FSH, prolactin, estradiol, testosterone, progesterone, DHEAS, cortisol, PTH, and most importantly for this patient, TSH, FT4, FT3, and TRAbs. Depending on the type of immunoassay (sandwich or competitive), biotin interference can either falsely decrease or increase the result. In the case of thyroid function testing, biotin interference can paint a biochemical picture indistinguishable from Graves’ disease. Biotin can also falsely decrease thyroglobulin levels, potentially masking thyroid cancer recurrence. If taking mega doses, it may take a week or more for the biotin to be cleared below the level of interference. However, smaller doses of biotin should be cleared within a few days, and holding the biotin for 48 hours may be adequate for most doses.

**Conclusion:** Biotin can interfere with many common endocrine hormone assays. Laboratories should consider including a biotin interference warning when reporting results of these assays.

**Abstract #1065**

**THYROID MASS PROGRESSED TO ANAPLASTIC THYROID CANCER FIVE YEARS AFTER AN INCIDENTAL FINDING OF TRACHEAL DEVIATION ON CXR**

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UMKC

**Objective:** Tracheal deviation on CXR is nonspecific and with normal lung parenchyma can be an incidental finding for thyroid mass.

**Case Presentation:** 64-year-old male presented with two days symptoms suggestive of upper airway compromise and right neck swelling. He also had 40 pounds weight loss over the last few months. Physical exam confirmed right thyroid mass with ipsilateral neck adenopathy. Patient reported that his symptoms included stridor and shortness of breath which along with the neck mass have progressed over the last two days. CXR showed tracheal deviation and right neck fullness, records review showed that this finding was reported five years prior to current presentation with no further follow up. CT neck confirmed 6.1 x 4.4 cm right thyroid mass with extensive bilateral cervical and superior mediastinal lymphadenopathy. Laryngoscopic exam by ENT showed mild vocal cord paresis. FNA was performed and resulted as papillary thyroid cancer. Patient was transferred to another facility for further consultation and work up given the mismatch between the pathology results and the clinical course. Clinical impression was anaplastic thyroid cancer and patient was told that he is not a candidate for any intervention and hospice was recommended. Patient refused hospice and presented to our hospital two weeks later with worsening respiratory symptoms, neck mass size, lymphadenopathy and new internal jugular and right subclavian vein thrombosis. He also had vocal cord paralysis that necessitated emergent tracheostomy with isthmus resection for pathology. Pathology report this time was consistent with anaplastic thyroid cancer. Patient refused hospice again and was offered palliative radiation therapy, of which he received two sessions before his condition deteriorated and finally agreed to hospice.

**Conclusion:** Neck mass could have been detected years earlier should there have been follow up on the CXR incidental finding of tracheal deviation. Anaplastic thyroid cancer in this case might have been preceded by papillary thyroid cancer. Second biopsy is recommended when pathology results don’t match the clinical course.
Abstract #1066

COMPARATIVE EFFECTIVENESS OF SYNTHROID® VERSUS GENERIC LEVOTHYROXINES ON TSH LAB OUTCOMES: A CONFIRMATORY ANALYSIS OF US MEDICARE CLAIMS DATA

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AbbVie

Objective: Previously published real world evidence has shown potentially better TSH outcomes among Synthroid versus generic levothyroxine treated hypothyroid patients. This study aims to confirm these findings by replicating the analysis in another real world database.

Methods: Retrospective observational study was conducted using Humana claims database, which includes medical and pharmacy claims for US Medicare patients. We identified patients who had at least one hypothyroidism diagnosis code between 2011 and 2015, and initiated treatment with either Synthroid® or generic levothyroxine within 365 days of that diagnosis. Patients below 18 years old, with diagnosis of thyroid cancer, on combination T3/T4, invalid or missing lab data, were excluded. Patients were required to have continuous enrollment and stay persistent to whichever therapy was initiated during the one year follow-up period. Generic levothyroxine patients were matched 2:1 with Synthroid patients based on age, gender, and region. Primary outcome was proportion of patients for whom the last TSH lab during the 1 year follow-up period was outside of the reference range (defined as <0.3 or >4.12 mIU/L). Odds of having TSH labs out of range was calculated using logistic regression controlling for Charlson comorbidity index score, year of index date, gender, and region. Various sensitivity analyses were conducted to ensure robustness of findings.

Results: The final matched cohorts included 3,190 levothyroxine patients and 1,595 Synthroid® patients. Most patients (85%) were female and the average age was 74 (range 35-104) years. The last TSH lab during follow-up were out of range for 21.4% of patients in the generic levothyroxine cohort vs 19.4% in the Synthroid® cohort (difference of 2.0%, p<0.0457). Adjusted odds of a patient having a TSH labs out of range was 0.90 (95% CI 0.78 – 1.05) for Synthroid® vs. generic levothyroxine. Sensitivity analyses were generally aligned with findings in the base case. (Table 1)

Discussion: In our study, we found that significantly less patients on Synthroid® had TSH labs out of range when compared with similar patients taking generic levothyroxine. Findings were in line with previous study findings. Some limitations to the data should be considered when interpreting results; for example, unmeasured factors may be driving the differences seen between Synthroid and generic levothyroxine, such as the number of switches among the generic manufacturers and the potential number of dose changes associated with switching.

Conclusion: Synthroid® was associated with better TSH lab outcomes compared to generic levothyroxine among a US Medicare insured population.

Abstract #1067

UNUSUAL THYROID CANCER PATIENT WITH UNIQUE DIAGNOSTIC & THERAPEUTIC CHALLENGES

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Case Presentation: 60 year-old lady with a 20-year history of stable moderate goiter, noticed rapid enlargement (to 2x2 inches) in last 1 year. And since 1 month she noted (warm and pulsatile) scalp & chest swellings, along with backache. Clinical impression was Follicular Thyroid Cancer (FTC) with bone metastases (mets). TSH was normal. Thyroglobulin levels were immeasurably high. CT scans showed lytic parietal skull lesions, a 5x4 cm destructive sternal mass, bilateral adrenal masses, a colonic mass, T11 vertebral involvement, multiple bilateral lung mets & right hilar lymphadenopathy. Differential diagnoses comprised of Multiple Endocrine Neoplasia (MEN) 2 syndromes versus FTC with distant mets. However, a Fine Needle Aspiration Biopsy suggested Papillary Thyroid Cancer (PTC). There was no biochemical evidence of MEN2 or hyper/hypo-cortisolism. Total Thyroidectomy with Central Compartment Lymph Node Dissection was notably difficult owing to dense strap muscle adhesions. Histo-Pathological Examination demonstrated invasive FTC. Immuno Histo Chemistry (IHC) was HBME1 positive & CK19 negative, favoring follicular variant of PTC. Colonic mass biopsy confirmed metastatic thyroid carcinoma with follicular pattern, & IHC read TTF1, TG and CK7 positive while CK20 was negative. Whole Body Radio Active Iodine (RAI) 131 Scan & FDG18 PET confirmed widespread disease in above mentioned sites plus L3 vertebra & other pelvic bones. We gave 217 mCi RAI 131 & 5 sessions of local spinal bone irradiation followed by monthly Zoledronic acid infusions. Six months later, mets stabilized & a similar dose of RAI 131 was repeated. Future management plan includes annual adjuvant RAI 131 therapy & consideration for Tyrosine Kinase Inhibitors.

Discussion: This represents an anomalous case because intestinal & adrenal mets are rarely reported with
Differentiated Thyroid Cancer (DTC). Hitherto, only one case of PTC with diffuse multi-system spread has been recorded from this country (India, 2010).

**Conclusion:** This patient is doing fairly well as of 2017. Rare possibility of DTC should be considered even in the setting of thyroid mass with bilateral adrenal masses and/or visceral mets.

**Abstract #1068**

PREVALENCE OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH HYPOTHYROIDISM: DATA FROM NATIONAL INPATIENT SAMPLE

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**Objective:** Although the relation between thyroid function and kidney has been known for years, it has been evaluated more comprehensively only in the last few years. Thyroid dysfunction is highly prevalent in chronic kidney disease (CKD) and end stage renal disease (ESRD), including those treated by peritoneal or hemodialysis and renal transplants. Hypothyroidism and subclinical hypothyroidism are the most commonly observed alterations.

**Methods:** We utilized a large inpatient database in the US called National Inpatient Sample (NIS) from the years 2009-2011 to study CKD prevalence in relation to hypothyroidism and used ICD-9 codes to identify patients with CKD (585.x) and thyroid disorders. We performed univariate as well as multivariate analyses to estimate odd ratio of association of CKD with hypothyroid patients compared to those without documented abnormal thyroid profile. All patients with hyperthyroidism and euthyroid sick syndrome were excluded from the final analysis. P <0.05 was considered statistically significant.

**Results:** We found that CKD was more prevalent in the hypothyroid group (18.45%) compared to euthyroid group (13.10%), p<0.0001. Hypothyroidism was associated with increased odds of CKD in univariate [OR 1.50 (95% CI 1.48-1.52), p<0.0001] and multivariate [1.25 (95% CI 1.23-1.26), p< 0.0001] analyses. Although most of the hypothyroid patients were females (75.22%), stratified analyses showed similarly increased odds of CKD prevalence among males [OR 1.63 (95% CI 1.60-1.65), p=0.0001] and females [OR 1.22 (95% CI 1.20-1.24), p=0.0001] (Table 1). Other factors associated with increased odds of CKD in multivariate analysis were increased age, DM, HTN, Obesity and CAD.

**Discussion:** Our study is in line with several prior studies which have shown increased CKD prevalence in hypothyroid patients. Impaired renal function in hypothyroidism may occur as a result of Direct effect on i. Glomerular functions - ↓ Renal Plasma Flow (RPF) and Glomerular Filtration Rate (GFR) and ii. Tubular functions -↓ free water excretion and ↓ activity of Na/K ATPase and Na-H exchanger with resultant urinary Na loss or iii. Indirectly due to hemodynamic changes- ↓cardiac contractility and output, ↑ arterial stiffness, ↑ intra-renal vasoconstriction, ↓ renin release and RAAS activity causing impaired renal auto-regulation. The GFR has been reported to decrease by about 40% in hypothyroidism.

**Conclusion:** Hypothyroidism may be an under recognized CKD risk factor. Further studies will help confirm association and formulation of screening guidelines. Early detection and treatment of hypothyroidism, especially in patients with other CKD risk factors, may help to decrease CKD onset and progression.

**Abstract #1069**

HEMIAGENESIS OF THE THYROID WITH GRAVES’ HYPERTHYROIDISM: THE DIAGNOSTIC UTILITY OF THYROID ULTRASOUND

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**Objective:** Hemiagenesis of the thyroid is a rare congenital anomaly, present in only 0.02%-0.05% of the general population. Thyroid hemiagenesis is more common in women than in men (3:1) with left sided hemiagenesis in approximately 80% of patients. Although it is usually associated with normal thyroid function, 10% of cases are associated with hyperthyroidism. Here we present a patient whose Graves’ disease and left thyroid hemiagenesis were diagnosed with thyroid ultrasound (US).

**Methods:** A 33 year old male presented with classic symptoms of hyperthyroidism and right-sided neck swelling. His physical exam was significant for no ophthalmopathy and a 6 cm right thyroid mass without bruit. Thyroid function testing showed free T4 5.19 ng/dl (0.76-1.46) TSH <0.005 mIU/ml (0.36-3.74). Due to asymmetric neck swelling, a thyroid US was performed.

**Case Presentation:** Thyroid US demonstrated an enlarged 6.3x3.3x2.9 cm heterogeneous iso-hypoechoic right thyroid lobe with diffusely increased vascularity (“thyroid inferno” pattern), a 0.3 cm thick isthmus and an absent left thyroid lobe. The diffusely increased vascularity was consistent with Graves’ disease. He was treated with methimazole and propranolol. Subsequent measurement of Thyroid Stimulating Immunoglobulin 435 (normal<140%) confirmed Graves’ disease.

**Discussion:** Hemiagenesis of the thyroid is a rare finding and the etiology of embryological development...
of agenesis of one thyroid lobe is unclear. Most patients are asymptomatic and are discovered incidentally as in our patient. However, patients with this condition have increased risk of concomitant thyroid disease. In active Graves’ disease, the US imaging can show extensive diffuse small areas of increased color flow doppler vascularity and arteriovenous shunting, termed “thyroid inferno,” which was seen in this patient. This was strongly suggestive of Graves’ hyperthyroidism and later confirmed by immunologic testing.

**Conclusion:** Evaluation of symptomatic patients who have unilateral thyroid enlargement with US of the thyroid can establish the diagnosis of thyroid hemiagenesis, and also has valuable utility in determining the most likely diagnosis for hyperthyroidism. Graves’ disease, toxic nodule or multinodular goiter are best differentiated by thyroid US with color flow doppler.

**Abstract #1070**

**AN UNUSUAL CASE OF METASTATIC FOLLICULAR THYROID CANCER 40 YEARS AFTER INITIAL DIAGNOSIS**

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University of Arkansas for Medical Sciences

**Case Presentation:** A 63 year old man with history of follicular thyroid cancer (Ca) treated with total thyroidectomy in 1977 and 30 mCi of radioactive iodine in 1978 presented in 2017 with new onset of wheezing on exertion. He was discharged by Endocrinology in 2014 after 37 years of follow up indicating excellent response to therapy given normal neck US, undetectable thyroglobulin (Tg) levels, negative Tg antibodies and absence of symptoms. Routine follow-up with thyroxine withdrawal 131I whole body scan (WBS) in 1984 and 2002 and thyrogen-stimulated WBS in 2010 showed no evidence of recurrent or metastatic disease. A chest x-ray for evaluation of his wheezing showed an indeterminate left paraspinal/periaortic mass. CT chest showed a 5.3 cm x 3.7 cm x 5.4 cm left hilar and infrahilar mass occluding the left lower lobe bronchus. He underwent bronchoscopy with endo-bronchial ultrasound and transbronchial lymph node aspiration. Cytology revealed metastatic follicular thyroid Ca. The tumor cells were positive for thyroid transcription factor-1, cytokeratin 7 and focally positive for Tg. Neck ultrasound revealed no evidence of local recurrence. PET/CT showed a 3.9 cm x 3.7 cm x 5.2 cm FDG avid left lower lobe mass and subcentimeter, non FDG avid bibasilar parenchymal nodules. Tg level remained undetectable. Left pneumonectomy and mediastinal lymphadenectomy was performed. Final pathology revealed metastatic thyroid Ca consisting of a mixture of well-differentiated follicular Ca (70%) and anaplastic Ca component (30%). The tumor showed perineural/angiolympathic invasion and the anaplastic component was associated with extensive intra-tumoral necrosis. Nine lymph nodes were sampled; all were negative for malignancy. He was referred to oncology for further management.

**Discussion:** This case of metastatic follicular thyroid Ca 40 years after initial diagnosis highlights the importance of counseling patients of the unlikely situation of late recurrence and identification of potential red flags prompting early follow up (e.g. dyspnea). This case also demonstrates the limitations of Tg levels in following thyroid Ca. It is unusual that the Tg levels were undetectable despite the tumor staining positive for Tg. Our hypothesis is that the metastatic follicular Ca was present in the lung for a long time before undergoing anaplastic transformation. It is unknown if the metastasis was present but not found at the WBS in 2010.

**Conclusion:** The ideal time period for which patients with differentiated thyroid Ca should be followed for recurrence is unknown; metastasis may occur decades from the initial presentation. Physicians should be aware of the limitations of Tg levels in evaluating for recurrence/metastasis.

**Abstract #1071**

**GIANT POSTERIOR MEDIASTINAL GOITER: A CASE REPORT AND LITERATURE REVIEW**

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**Objective:** 1. To report a rare case of posterior mediastinal mass that was found to be a giant retrosternal goiter. 2. To review the existing literature related to the diagnostic work up and feasible surgical approach to manage the goiter. 3. To emphasize on the importance of multidisciplinary approach to a such case.

**Methods:** A case is evaluated and managed with appropriate history, physical examination, laboratory and radiological investigations, then she was managed successfully with surgical resection. Moreover, the literature on the topic of posterior mediastinal goiter is systematically reviewed.

**Case Presentation:** Here, we report a 47-year-old Saudi lady who presented with a progressive shortness of breath and found to have a giant posterior mediastinal goiter that was successfully resected through a classical transverse cervical incision, lateral right thoracotomy and median sternotomy. Histopathology report showed multinodular...
goiter with an incidental finding of a micro-papillary thyroid carcinoma of 0.6 cm. The patient had a smooth post-operative recovery and was in a good condition during the follow up period.

**Discussion:** Retrosternal goiter is defined as any goiter that might extend to a level below the subcarinal region or a goiter in which at least 50% of it is retrosternal. It usually has a slow progressive and a longer course of illness. Posterior mediastinal goiters are rare of all intrathoracic goiters and may lead to respiratory symptoms caused by tracheal compression and airway obstruction. Patients might be asymptomatic initially but with time they might progress to obstructive symptoms mimicking bronchial asthma presentation resulting in misdiagnosis of the condition with inappropriate management subsequently. The presence of posterior mediastinal goiter is an indication for a multidisciplinary approach to manage it in a highly specialized center. Earlier surgical intervention is indicated for obstructive symptoms while the observational approach is recommended for asymptomatic older patients who are not fit for the surgical intervention.

**Conclusion:** This is a rare case of retrosternal goiter extending to the posterior mediastinum in a young lady presented with obstructive respiratory symptoms. Because it was compressing major vessels in the mediastinum, a multidisciplinary team approach including the endocrinologist involvement for the work up of the mediastinal mass, Endocrine, Thoracic and cardiothoracic surgeons involvement in a such high risk surgery was a very important step in managing this difficult case.

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**Abstract #1072**

**ENIGMATIC DISCOVERY OF A FOLLICULAR THYROID CANCER IN AN ATOMIC BOMB SURVIVOR**

Saleh Aldasouqi, MD, FACE, ECNU, Zulma Cardona, None, Vengamamba Polu, MD, Fawzi Abu Rous, MD

Michigan State University

**Objective:** To describe a case of thyroid cancer in a Hiroshima Atomic Bomb survivor, diagnosed in a most unusual way.

**Case Presentation:** We present the clinical findings in a Hiroshima Atomic Bomb (A-Bomb) survivor, with an unusual presentation of thyroid cancer, over 6 decades after exposure to ionizing radiation by the A-Bomb.

**Case Presentation:** A 70-year-old Japanese man, a survivor of the Hiroshima A-Bomb presented to our endocrine clinic in 2007, for evaluation of T2DM. He was 8 years old at the time of the A-Bomb detonation, residing within few miles from the A-Bomb impact center. During physical exam, markedly decreased breath sounds on his right lung were noticed upon auscultation. This prompted a CXR and a subsequent chest CT, which both revealed deviation of the trachea to the left side, with a 3 cm soft tissue mass shadow deep in the neck towards the thoracic inlet. Subsequently, the thyroid mass was found on thyroid ultrasound to be located in the most inferior region of the right lobe with inferior/retrosternal extension. The thyroid mass was surgically removed and pathology results confirmed the diagnosis of follicular carcinoma of the thyroid. The mass was encapsulated with no metastasis. He received radioactive iodine ablation. The patient has been clinically and chemically euthyroid, on thyroid hormone replacement. At the time of the writing of this abstract, the patient is 81 years old, and is cancer-free.

**Discussion:** This case describes the unexpected detection of a malignant thyroid mass not by physical exam of the neck, but rather by the appreciation of asymmetric air entry on lung exam. Expecting an abnormality in the lungs or respiratory passages, this incidental finding prompted imaging of the chest. The thyroid mass had eluded physical exam of the neck due to its deep location into the thoracic inlet. Furthermore, the case describes the clinical course of thyroid disease in a very special and unique patient population, one of the survivors of the Hiroshima Atomic Bomb. It had been believed in prior follow up studies that the cancer risk for thyroid cancer decreased sharply with increasing age-at-exposure and with the passage of time since exposure. However, a recent 60-year follow up study of Hiroshima A-Bomb survivors has shown that the increased thyroid cancer risk associated with childhood exposure has persisted for >50 years after exposure. Our patient’s thyroid cancer was diagnosed 62 years after exposure to the Hiroshima A-Bomb.

**Conclusion:** This case illustrates the utmost importance of a thorough history and physical exam. It was only after close examination and a high index of suspicion by the physician, that the follicular thyroid carcinoma was discovered in this patient.

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**Abstract #1073**

**A MYSTIC CYSTIC MASS: A CASE OF A BENIGN THYMIC CYST IN A PATIENT WITH PAPILLARY THYROID CANCER**

Amanda Fernandes, Matthew Gilbert

University of Vermont

**Objective:** Differentiated thyroid cancer is associated with a low risk of morbidity and incidence of distant metastasis. Use of radioactive uptake in cases of distant metastases
ABSTRACTS – Thyroid Disease

raises important questions. Does uptake of radioiodine indicate pathology and what is the differential diagnosis for radioactive uptake outside the thyroid?

Case Presentation: A 61-year-old female with no significant past medical history presented to her primary care doctor after noting a nontender lump in her neck. Physical examination revealed a nontender nodule in the neck which on ultrasound was a 2.1 cm left sided isthmus nodule. She underwent an ultrasound-guided fine-needle aspiration which showed papillary thyroid carcinoma. She had a total thyroidectomy with pathology noting 1.7 x 1.4 x 1.0 cm unifocal papillary carcinoma with classical architecture and cytomorphology. Staging per the American Thyroid Association 2009 guidelines was consistent with T1b N1a MX given surgical margin positivity and focal lympho-vascular invasion in 1 out of 6 dissected lymph nodes. A 24-hr I-123 uptake and scintigraphic scan showed a focus of minimal uptake in the mediastinum and further CT localization showed a large 8.4 x 9.4 x 8.2 cm multi-cystic mass in the anterior mediastinum. A fine-needle biopsy was performed that revealed only hemorrhagic material prior to receiving radioactive iodine. Due to the unclear etiology of this mass and concern for metastatic disease, the patient underwent surgical resection. This showed a multi-loculated mass composed of cystic spaces lined by a variety of epithelial cells consistent with a benign multilocular thymic cyst.

Conclusion: Uptake of radioiodine by non-thyroid structures is not always pathological. It can result from normal expression of the sodium-iodide symporters in the gastrointestinal tract, thymus, and salivary glands and even in inflamed tissues. When considering lesions in the mediastinum and further CT localization showed a large 8.4 x 9.4 x 8.2 cm multi-cystic mass in the anterior mediastinum. A fine-needle biopsy was performed that revealed only hemorrhagic material prior to receiving radioactive iodine. Due to the unclear etiology of this mass and concern for metastatic disease, the patient underwent surgical resection. This showed a multi-loculated mass composed of cystic spaces lined by a variety of epithelial cells consistent with a benign multilocular thymic cyst.

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Abstract #1074

IODINE CONTENT OF THE BEST-SELLING UNITED STATES ADULT AND PRENATAL MULTIVITAMIN PREPARATIONS

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Objective: Iodine is essential for thyroid hormone production and normal fetal development. Even mild maternal iodine deficiency in gestation has been associated with impaired child neurodevelopment. Iodine requirements are higher during pregnancy and lactation because of increased thyroid hormone synthesis and transport into breast milk for neonatal iodine nutrition. Supplements containing 150 µg/day potassium iodide are recommended for all United States (US) women who are pregnant, lactating, or planning pregnancy. Multivitamin supplements may be a significant source of iodine for pregnant and non-pregnant US adults, but this has not been well studied. We aimed to better understand the contribution of the top-selling adult and prenatal multivitamins to iodine nutrition in the US.

Methods: Product names, dollar sales, unit and volume sales, and recommended daily intakes of the top-selling 99 adult multivitamins (AMV) and 60 prenatal multivitamins (PMV) with the largest market share from July 2016 to July 2017 were obtained from Information Resources, Incorporated. Supplements from food, drug, and mass merchandise stores were included, but specialty stores and internet sales were excluded. Iodine content and source were determined from product labels. After excluding ten AMV that represented private-label brands and one PMV with a product label unavailable, we analyzed a final sample of 89 AMV and 59 PMV.

Results: Of the 89 AMV, 74.2% contained iodine. The median (range) iodine content of AMV was 150 µg (38µg – 150µg) per daily dose. Over the study period, 8,924,371,955 AMV doses were sold, of which 84.8% contained iodine. Thirty-four (57.6%) of the 59 PMV contained iodine, with a median (range) iodine content of 150 µg (25µg – 290µg) per daily dose. Over the study period, 466,927,559 PMV doses were sold, of which 76.8% contained iodine. All of the iodine-containing AMV used potassium iodide as an iodine source. Of
iodine-containing PMV, 73.5% used potassium iodide, 23.5% kelp, and 2.9% inactivated S. cerevisiae as an iodine source.

**Conclusion:** During the study period of one year, 84.8% of the top adult vitamin doses sold contained iodine. On the other hand, only 76.8% of the top prenatal vitamins doses sold contain iodine. The median iodine content of the top-selling AMV and PMV was 150 µg per daily dose, as recommended by the American Thyroid Association, but the range remains wide. More effort is needed to ensure adequate iodine content in prenatal vitamins for women who are pregnant, lactating, or planning pregnancy.

**Abstract #1075**

**METASTATIC FOLLICULAR THYROID CANCER WITH HEMORRHAGIC METASTASES TO THE PITUITARY GLAND**

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**Objective:** To present a case of a patient with metastatic follicular thyroid cancer with hemorrhagic metastases to the pituitary gland who presented with diabetes insipidus (DI).

**Case Presentation:** A 56 year-old man with metastatic follicular thyroid cancer presented with failure to thrive. Eight years prior to admission he underwent a left hemi-thyroidectomy for a compressive goiter with pathology noting a follicular adenoma. Four years later while undergoing routine imaging, multiple lung and bone lesions were identified prompting a bone biopsy with pathology of metastatic follicular thyroid cancer. A complete thyroidectomy with lymph node dissection was performed confirming follicular thyroid cancer. Over the next several years, due to persistent disease confirmed both biochemically and with imaging, the patient received external beam radiation followed by 6 doses RAI totaling over 1200 mCi resulting in pancytopenia, thus precluding the use of tyrosine kinase inhibitors. Five months after his last dose of RAI, the patient presented to our hospital with failure to thrive. Labs included TSH 0.021 mcU/mL (on levothyroxine), thyroglobulin > 47000 ng/mL (antibody negative). Palliative care was consulted and dexamethasone was started for appetite stimulation. The following month the patient presented with confusion, blurry vision, polydipsia, polyuria with severe nocturia impacting his quality of life. Labs included sodium 140 mEq/L, serum osmolality 288 mOsm/kg, urine osmolality 192 mOsm/kg and urine sodium 39 mmol/L. Non-contrast MRI head showed a large mushroom appearing sellar lesion with hemorrhagic supra-sellar component compressing the optic chiasm. Dexamethasone was increased and intranasal DDVAP started for symptomatic relief. Patient was discharged on home hospice and passed away 6 weeks later.

**Discussion:** Pituitary metastases, a rare complication of systemic malignancies, most commonly breast and lung cancer, are estimated to be 1-5% of sellar neoplasms, with the most reported presentation being DI (estimated to be 45%). Metastatic thyroid cancers, with an incidence of 10-35%, have a tendency to spread to the lung, followed by bone, brain, liver, and skin with pituitary metastases being extremely rare. In a case series of 22 patients with metastatic thyroid cancer to the pituitary gland, only 5 patients presented with DI out of which only one had follicular thyroid cancer. We present the second case report of a patient with follicular thyroid cancer with metastases to the pituitary who presented with DI.

**Conclusion:** Although rare, thyroid cancer may metastasize to the pituitary gland resulting in DI.

**Abstract #1076**

**DO BIOCHEMICAL PARAMETERS CHARACTERIZE A SUBGROUP WITH HYPOTHYROIDISM AND UNSATISFACTORY CLINICAL RESPONSE TO LEVOTHYROXINE REPLACEMENT?**

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University of Miami

**Objective:** Recent studies point to a variation in thyroid hormone metabolism to explain why a subgroup does not achieve a full clinical remission of symptoms of hypothyroidism while receiving levothyroxine-only therapy. The objective of this observational study is to determine if biochemical differences exist between hypothyroid patients asymptomatic on levothyroxine replacement versus those requiring levothyroxine plus triiodothyronine to achieve euthyroid status.

**Methods:** We evaluated peripheral T4, T3, TSH, and T3 resin uptake levels as well as age, sex and BMI in the following groups; 1.) 65 patients (16.9% male) with hypothyroidism who were clinically euthyroid on levothyroxine replacement 2.) 53 patients (15.1% male) persistently symptomatic on optimized levothyroxine doses subsequently requiring levothyroxine replacement versus those requiring levothyroxine plus triiodothyronine 3.) 60 adults (53% male) without known thyroid disease (Normal). Peripheral thyroid hormone levels were adjusted for binding using the free thyroid hormone index (Thyroid hormone level x T3resin uptake)
Results: Mean free T3 index (fT3In) level in group 1 (0.26 ± 0.052), group 2 (0.27 ± 0.057) and normal (0.27 ± 0.052) were not significantly different. Mean free T4 index (fT4In) in Normal (2.2 ± 0.4) was lower than group 2 (2.7 ± 0.6), p<0.001, and group 1 (2.6 ± 0.5), p<0.001. Mean TSH level in Normal, 1.58 ± 0.73 µIU/mL was higher than group 1, 1.24 ± 0.74 µIU/mL, and group 2, 1.02 µIU/mL, p= 0.013 and p<0.01, respectively. Mean TSH level between groups 1 and 2 was similar. Mean T3/T4 ratio was higher in Normal (0.126) compared to group 1 (0.100, p< 0.01) and group 2 (0.105, p < 0.01). The mean daily levothyroxine dose per kg of group 1 and 2 were similar, 1.31 ± 0.40 mcg/Kg/day for group 1 and 1.41 ± 0.49 mcg/Kg/day for group 2. FT3In and fT4In correlated positively with levothyroxine dose in group 1, p=0.015 and p=0.005, respectively but neither of these correlations were found for group 2. The normal inverse relationship of FT3In with age was preserved in group 1 but not group 2, p=0.03.

Discussion: Although the mg/Kg/day dose of levothyroxine was similar in the two treatment groups, free hormone indices correlated with the treatment dose only in group 1 but not group 2. Also, a difference in the manner in which T3 levels varied with age was detected between the treatment groups.

Conclusion: These findings suggest differences in peripheral thyroid hormone metabolism exist between those with satisfactory clinical response to levothyroxine-only replacement versus those with persistent symptomatology. Comparing peripheral thyroid hormone levels alone however, does not appear to provide a simple way to differentiate these two groups.

Abstract #1077

EVALUATION OF CARDIOVASCULAR STATUS IN THYROID DISORDERS

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Objective: Thyroid disorders (hypothyroidism and hyperthyroidism) are associated with clinically significant cardiovascular changes. In our study, patients with various types of thyroid disorders are examined clinically and biochemically. Their cardiovascular status assessed by electrocardiography, radiologically and echocardiographically, and compared with controls with an aim to determine the effect of thyroid disease on the cardiac status.

Methods: This is a case control study, conducted at a tertiary care centre for 2 years. This study included 80 cases, comprised of 40 cases of hyperthyroidism and 40 of hypothyroidism. 40 healthy age and sex matched subjects were included as a control for comparison.

The mean age for the patients with hyper/hypothyroidism was 36.38±7.90 and 37.73±9.13 years respectively while for control subjects it was 36.33±9.97 years. With 65%, 70% and 57.5% females were seen in group of hyperthyroidism, hypothyroidism and controls respectively.

Pearson's Chi Square test was used for qualitative data to observe the association of the thyroid diseases with cardiovascular abnormalities in hyperthyroid, hypothyroid patients and control subjects.

Case Presentation: Among hyperthyroid patients, sinus tachycardia 35 (87.5%) cases was the predominant ECG abnormality while, sinus bradycardia in 32 (80.0%) seen in hypothyroid cases. Diastolic dysfunction seen in 10% hyperthyroid subjects and 5% of hypothyroid ones. Systolic dysfunction seen in 14% of hyperthyroid subjects and 17% hypothyroid. Interventricular septum thickness was increased in 17.5% of hypothyroid cases. Ser.Ch & TGs were significantly higher in hypothyroidism subjects.

Discussion: The study was undertaken to investigate the left ventricular function by means of echocardiography in thyroid disorder. Cardiomegaly detected in 26 (65.0%) in hyperthyroid group, in another study 13/33 had cardiomegaly on CXR and 6 had pericardial effusion on echo.

In our study, Diastolic dysfunction on Echo was seen in 10% hyperthyroid & 5% hypothyroid subjects. In another study, 27% patients had diastolic dysfunction. Systolic dysfunction was seen in 14% of hyperthyroid subjects and 17% hypothyroid. Other studies showed low systolic function indices in hypothyroid patients. There were 12.5% hypothyroid cases of LVPW thickness,

Conclusion: The cardiovascular signs and symptoms of thyroid disease are some of the most profound and clinically relevant findings that accompany both hyperthyroidism and hypothyroidism. Echocardiography is a very valuable tool in evaluation of the effects of hypothyroidism on heart and can detect earliest changes.
Abstract #1078

IODINE DEFICIENCY GOITER IN A YOUNG MALE IN UNITED STATES

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Objective: Iodine is an essential component of diet and its deficiency leads to impairment of thyroid hormone synthesis with undesirable consequences. Iodine deficiency disorders (IDDs) remain a major public health concern in most parts of the world, but the National Health and Nutrition Examination Surveys (NHANES), determined that iodine nutrition in the U.S. was adequate, thus making IDDs extremely rare in North America. However, certain populations with restricted diets and pregnant and lactating women are at risk for IDDs.

Case Presentation: A 27-year-old Caucasian male was seen in the endocrinology clinic in May 2017 for evaluation of goiter. Ultrasound (US) neck in December 2016 showed enlarged gland with no nodules with elevated TSH (24.350 mIU/L), free T4 <0.4 ng/dl, total T4 1.8 mcg/dl and positive anti-thyroid peroxidase antibody (43 IU/ml). He denied history of upper respiratory tract infection, neck pain, radiation exposure and swallowing difficulty. He reported ongoing gastrointestinal issues for about 2 years and was on a very restricted diet. Physical exam was significant for diffusely enlarged thyroid gland but without nodules and lymphadenopathy. The goiter and abnormal thyroid function tests (TFTs) were attributed to be sequelae of thyroiditis (likely Hashimoto’s). Investigations done in June 2017 showed TFTs still consistent with primary hypothyroidism, US showing enlarged gland and a radioactive iodine (RAI) uptake scan showing increased uptake (91%) suggestive of hyperthyroidism. These findings were presumed to be due to recovering phase of the thyroiditis; however, given his poor diet a 24-hour urinary iodine was ordered. His 24-hour urinary iodine levels were consistent with severe iodine deficiency [3.9 mcg/L and 10.1 mcg/24 hour]. In the interim, he continued to follow up with GI service and was able to tolerate seafood and dairy products. On follow up later with endocrinology, the patient reported a decrease in goiter and improvement in fatigue. Nontoxic goiter with hypothyroidism was attributed to severe iodine deficiency secondary to poor dietary intake. He was started on multivitamins with 150 mcg of iodine.

Conclusion: Rarely, in U.S. a hypothyroid patient with TFTs suggestive of hypothyroidism, low urinary iodine levels and paradoxical finding of diffusely increased RAI uptake strongly suggests that the patient may have IDD in the setting of poor dietary intake. Many cases of IDDs go undiagnosed as RAI study is not routinely indicated for hypothyroidism. It is imperative to timely diagnose IDDs in a patient who is on restricted diets with urinary iodine levels and probably RAI study, as it is a reversible condition with simple dietary iodine supplementation.

Abstract #1079

NIVOLUMAB INDUCED THYROIDITIS

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Objective: Nivolumab is an immune checkpoint blocking antibody used in the treatment of inoperable or metastatic melanoma, squamous non-small cell lung cancer and renal cell carcinoma. It is associated with adverse events defined as immune related adverse events (IrAEs), which can affect numerous systems including the endocrine system.

Case Presentation: A 54 year old Caucasian man with stage 4 high grade carcinoma of the right kidney with metastasis to lung and lymph nodes, coronary artery disease and peripheral vascular disease presented for evaluation of his thyroid function. Patient had been on Nivolumab (2mg/kg every 2 weeks) for 6 weeks after the disease had progressed on Pazopanib. Patient was screened for thyroid function at each of his oncology visits. At the 4 week appointment after starting Nivolumab, the TSH was found to be declining and at 6 weeks was found to be suppressed. At this point the TSH was <0.01 μIU/mL (0.35-4.89), FT4 was 2.6 ng/dL (0.6-1.8), TPO Ab 13.8 IU/mL (<5.0), Tg Ab 10.7 IU/mL (<4.1) and TSI 14% (<140% baseline). He had developed fatigue, loss of appetite ad had experienced weight loss. Physical exam showed a mildly enlarged non-tender and firm thyroid. Thyroid ultrasound showed a diffusely enlarged thyroid gland with heterogenous echo texture and increased vascularity. He was started on low dose beta blockers. At 12 weeks after initiation of Nivolumab his labs revealed primary hypothyroidism with a TSH of 32.5 μIU/mL and a FT4 of 0.8 ng/dL. Levothyroxine was started and showed an improvement in his clinical and laboratory picture.

Discussion: Nivolumab is a IgG4 monoclonal antibody. It acts as an immunomodulator by blocking ligand activation of programmed death receptor 1 on activated T-cells and thus increasing tumor cell destruction. It can affect immune tolerance, enabling pathological T cells to react with native self-antigen. IrAEs affecting the endocrine system are common but usually not severe and often reversible. Endocrinopathies can include thyroiditis, hypophysitis, adrenalitis and autoimmune diabetes. Thyroid dysfunction
can present as hypo or hyperthyroidism. If this is mild it
does not require discontinuation of the drug.

**Conclusion:** Nivolumab and other check point inhibitors
are promising drugs in patients with various malignancies.
IrAEs are common. Early recognition and intervention are
essential because symptoms of thyroid dysfunction can
often mimic cancer progression. Appropriate treatment
can ameliorate the symptoms. Our patients had an elevated
levels of TPO Ab, but a pre-treatment baseline was not
available. Because of the high prevalence of Hashimoto’s
thyroiditis, we believe TPO antibody levels should be
included in the initial assessment.

**Abstract #1080**

**PATTERN OF THYROID CARCINOMA IN GIZAN
REGION OF SAUDI ARABIA**

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1. SAIMS Medical college, 2. MGM Medical College

**Objective:** To study the frequency, clinical features, and
histopathology of thyroid carcinoma (TC) in Gizan,
Saudi Arabia (KSA). TC accounts for nearly 1% of all
malignancies and around 10% in KSA. It is the second
most common carcinoma in Saudi women, peak incidence
is in the 3rd and 4th decades.

TC is divided into papillary (PTCs), follicular (FTCs),
medullary, anaplastic carcinomas, primary thyroid
lymphomas and sarcomas.

**Methods:** Over a span of 6 years, 231 patients underwent
thyroidectomy at King Fahd Central Hospital (KFCH),
aTertiary Care Centre in Gizan, of these 32 had TC. The
clinical features, histopathology and lab data was analysed.
USG and CT was used to evaluate the soft tissue extension
and metastasis. Qualitative variables were analysed using Chi
square test and p value was calculated between the 2 groups.

**Case Presentation:** Out of 32 (13.6%), 7 were Males and
25 Females (18-90 yrs), mean age (±SD) of 49.6 (±15.8).
PTC seen in 25 (18 F, 7 M), FTC in 5, Anaplastic in 2.
Mean age for PTC (43.1 ± 12.7) and FTC (61.3 ± 15.4)
was significantly different (p-0.015). FTC and anaplastic
type were diagnosed exclusively in women. FNAC done
in all, it was negative in 11, PTC in 12, FTC in 8 and
anaplastic in 1 case. Patients presented with thyroid
masses or Nodules (32), pain (6), dysphagia (3), and
hoarseness in 3.

**Discussion:** TC is the most common endocrine malignancy.
Radiation exposure significantly increases the risk for
thyroid malignancies, particularly PTC. Populations with
low dietary iodine have a high proportion of follicular and
anaplastic carcinomas.

PTC causes more pressure effects like stridor, hoarseness,
dysphagia, and weight loss. While FTC presented with
neck mass and neck pain.

**Conclusion:** In Gizan region, incidence of TC is around
14% among patients undergoing thyroidectomy. Painless
thyroid nodule is the most common clinical feature. PTC
is the most common variant. FNAC is useful for diagnosis
but it can be false negative in some cases.

**Abstract #1081**

**PRIMARY HYPERTHYROIDISM WITH AN ELEV-
ATED THYROID STIMULATING HORMONE – A
DIAGNOSTIC CHALLENGE**

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**Objective:** Thyroid hormone measurement using
immunoassay is an important diagnostic tool for thyroid
diseases. Primary hyperthyroidism is diagnosed by
elevated thyroxine (FT4) and triiodothyronine (T3) with
suppressed thyroid-stimulating hormone (TSH). Elevated
FT4 and T3 with an increased TSH in a patient with
clinical hyperthyroidism poses a diagnostic challenge.

**Case Presentation:** A 22-year-old female presented
with signs and symptoms of hyperthyroidism. Initial
thyroid function test showed an FT4 of 3.93 (ref: 0.58-
1.64) ng/dl with a serum TSH of 3.543 (ref 0.3-5.0)
mIU/L. Repeated tests revealed persistently elevated
FT4 and total-T3 at 3.35-4.29 ng/dL and 3.1-4.7 ng/ml,
respectively, with normal/high TSH of 3.19-5.50 uIU/mL.
FT4 by equilibrium dialysis (the most accurate test for
FT4) again demonstrated an elevated FT4 at 5.3 (ref 0.8-
2.0) ng/dl. Her thyroid stimulating immunoglobulin index
(TSI) was elevated at 4.3 (ref ≤1.3). Subsequent tests of
pituitary function to suggest secondary hyperthyroidism
were normal: prolactin at 7.5 ng/ml and IGF-1 at 229
ng/ml. Sex-hormone-binding globulin (SHBG), a useful adjunct for thyrotoxicosis diagnosis, was raised to 325 (ref 18-144) nmol/l. MRI-pituitary was refused by the patient. Resistance-to-thyroid-hormone (RTH) mutation analysis, done in the light of elevated TSH even with elevated fT3 and fT4, was negative. Thyroid ultrasound showed increased vascularity and diffuse enlargement, consistent with Grave’s disease. This prompted us to finally exclude falsely elevated TSH due to presence of human anti-mouse-monoclonal antibody (HAMA) by pre-treating the patient’s serum with mouse-IgG. This resulted in a suppressed TSH (≤0.01 mIU/l), confirming primary hyperthyroidism with erroneous TSH. She was treated with methimazole and beta-blocker with gradual improvement in symptoms, while awaiting definitive treatment with radioactive ablation.

Discussion: Although most thyroid function tests correlate with the clinical picture, a discordance may exist in a subset of patients. Immunoassay interference may alter the measured hormone levels. Heterophile antibodies may be present in the serum of 0.2-15% of general population. HAMA, one of the commonest heterophile antibodies affecting thyroid immunoassay, interferes 0.05-6% of immunoassays. When interference is suspected, measurement can be repeated after dilution; by using an alternate technique or after addition of a blocking agent such as mouse IgG, as was done in our patient.

Conclusion: HAMA interference should be suspected in patients with clinical hyperthyroidism associated with normal/elevated TSH. A high suspicion for, and early assessment of HAMA will reduce unnecessary and expensive investigations.

Abstract #1082

ULTRASOUND-GUIDED LASER TREATMENT FOR LOCAL CONTROL OF NECK RECURRENCES OF MEDULLARY THYROID CANCER

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Objective: Medullary thyroid cancer (MTC) is frequently associated with cervical persistence or recurrence of disease after initial treatment. Surgery is the standard treatment of neck nodal metastasis but repeat surgical dissections carry the risk of complications, have an unfavorable impact on the quality of life and may not attain a complete cure of the disease.

On the basis of previous feasibility study we evaluated the clinical outcomes and the tolerability of ultrasound (US)-guided percutaneous laser ablation (PLA) for local control of neck recurrences of MTC.

Methods: From October 2012 to October 2017, 7 lesions in 4 patients (2 male and 2 female, mean age 74 yrs, range 72-82) were treated with PLA for cervical recurrence of MTC. All patients had a previous total thyroidectomy followed by cervical lymphadenectomy and showed a further local recurrence. Two cases had also distant metastasis with level of Calcitonin (CT) mean 2000 pg/mL. All patients had contraindications or refused additional surgery. Treatments were carried out under US-guidance in an outpatient setting, followed by a 2-hour observation. The procedure was performed after local anesthesia with 1 or 2 optical fibers and a Nd:YAG laser source (Echolaser, Elesta, Florence, Italy) as previously described (2). The energy delivered ranged from 250 to 3500 (mean 1760) Joules according to the volume of cancer recurrence. Evaluation of neck US examination (Twin, Esaote, Genoa, Italy) and serum CT were scheduled at 1, 6 and 12 months.

Results: The procedure was well tolerated and required analgesics only for 1 or 2 days. No complication or hospitalization was registered. In 2 out of 7 lesions a second treatment was requested. After 24 hours, color Doppler and contrast-enhanced US examination showed marked decrease of vascular signals within the treated area. Follow-up was performed with neck ultrasound and calcitonin measurement for a period ranging from 6 months to 5 years (median months). The mean volume of the lesions decreased from 12±2.1 at baseline to 8±2 (50 %) at 1 month, and to 4±1.7 mL (67 %) at 6 months. No re-growth was observed during follow-up. Serum CT level in patients without distant metastasis decreased from 247 pg/ml at baseline to 48,1 pg/mL at 3 months and 21 pg/mL at 6 months.

Discussion: Surgery is the standard treatment for local recurrence or persistence of MTC but PLA appears as a safe, well-tolerated and effective tool for the management of local recurrence or persistence of disease.

Conclusion: Relevant advantages of PLA are the treatment in an outpatient setting, without general anesthesia, together with the safety and tolerability of the procedure.
ABSTRACTS –Thyroid Disease

Abstract #1083

UTILIZATION OF DENOSUMAB FOR MANAGEMENT OF METASTATIC BONE DISEASE SECONDARY TO FOLLICULAR THYROID CARCINOMA

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Case Presentation: An 84 year-old female with chronic back pain previously treated with lumbar laminectomy developed T6 and T7 fractures. Imaging studies showed destruction of T6, T7 and T8 vertebrae and severe spinal cord compression along with a peripheral calcified left thyroid lobe nodule causing tracheal displacement to the right. Biopsy from T7 vertebral body revealed metastatic thyroid carcinoma with immunostaining positive for TTF1, PAX8, ER and thyroglobulin. Spinal cord biopsy was positive for adenocarcinoma. Neck ultrasound revealed 2.9 cm left thyroid lobe nodule without pathological lymphadenopathy. Fine needle aspiration cytology revealed changes suspicious for follicular neoplasms. Thyroglobulin was elevated at 985 ng/mL without Anti-thyroglobulin antibody. Her metastatic bone disease was initially managed with radiation therapy along with Zolendronic acid 4mg IV infusion. Surgical pathology following complete thyroidectomy revealed stage pT3NXM1 follicular thyroid carcinoma involving the left lobe. Cervical lymph node mapping was negative and radioactive iodine (RAI) whole body scan showed focal abnormal uptake in mid-thoracic spine consistent with her known metastasis. Follow up CT chest and neck and whole body bone scan didn’t reveal any other focus of metastasis. Monthly Denosumab 120mg (Xgeva) injections was initiated for one year followed by injections every 3 months that led to an excellent response noted with decrease in her thoracic pain from 10/10 to 2/10. She has been able to do her activities of daily living independently. She hasn’t had any new fractures or dental problems. Her metastatic bone disease has been tolerating it without any skeletal-related events or side effects for the past 26 months.

Conclusion: Xgeva can be successfully used to treat osseous metastasis from thyroid carcinoma.

Abstract #1084

PREVALENCE OF THYROID CANCER IN NODES EQUAL TO OR GREATER THAN 3 CM IN THE VETERAN POPULATION

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Objective: Thyroid nodules are incidentally identified in 4%-10% of the general population in the United States, and possible malignancy is a major concern. This study examined malignancy rates in patients with nodules equal to or greater than 3 cm compared to patients with smaller nodules.

Methods: A retrospective chart review of 450 patients presenting for thyroid nodule evaluation at the Dayton Veterans Affairs Medical Center (VAMC) was conducted. All patients had fine needle aspiration (FNA) between January 2000 and May 2016. Data collected included demographics, selected clinical variables, nodule size, FNA results, and surgical pathology (when available).

Results: A total of 329 patients with thyroid nodules were eligible for the study, 236 were less than 3 cm and 93 were ≥3 cm. Prevalence of cancer based on FNA for nodules less than 3 cm was 6.4% and for nodules ≥3 cm was 8.6% (p=0.23). When divided into four subgroups, prevalence of malignancy was 6.7% in nodules <2 cm, 5.5% in nodules 2 cm to <3 cm, 9.1% in nodules 3 cm to 4 cm, and 7.9% in nodules >4 cm (p=0.32).

Discussion: Studies of the relationship between thyroid nodule size and malignancy have produced conflicting results. Our study, the first to examine this relationship in the Veteran population, found no association between nodule size and malignancy using either FNA or surgical pathology. Current clinical practice is to refer patients with
larger nodules for surgical evaluation. Given our findings and prior conflicting results, the decision for surgical intervention must be individualized and not solely based on nodule size.

Conclusion: In conclusion, there is no increased or decreased risk of cancer for nodules equal to or greater than 3 cm when compared to nodules less than 3 cm. Current clinical practice is to refer patients with larger nodules for surgical evaluation. Given our findings and prior conflicting results, the decision for surgical intervention cannot be made solely on nodule size and requires consideration of other factors.

Abstract #1085

CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS ASSOCIATED WITH METHIMAZOLE

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Case Presentation: Anti-thyroid Drugs (ATD) such as propilthiourcil (PTU) and methimazole (MTM) can cause a number of systemic changes such as fever, rash, and respiratory symptoms (from epistaxis to diffuse alveolar hemorrhage). Guidelines almost always recommend MTM over PTU because it has fewer side effects. We present a patient diagnosed with Grave’s Disease who developed vasculitis shortly after the initiation of MTM. Interestingly, after suspension of MTM and without use of any immunosuppressive medication cutaneous lesions started to involute.

64 year old Caucasian female with hypertension and recently diagnosed Graves disease was started on metoprolol and MTM. Approximately 10 days after starting the MTM, she developed small red pruritic spots on her forearms, hands, and ankles, which had been relatively stable. Denies other drug use or family history of similar rash or autoimmune conditions. Physical exam: multiple scattered non-blanching red-purple macules bilaterally in upper and lower distal extremities. On ankles lesions have horizontal linear cut-off which appears to present at a previous sock line. Labs: immunological that was mildly positive for ANA 1:160 with homogeneous pattern. C-ANCA and P-ANCA, RF, Histone Ab were negative. C3 and C4 levels were within normal limits. Skin punch biopsy showed prominent superficial perivascular neutrophilic leukocytoclasia and purpura with eosinophils. Correlation of the morphology with the positive direct immunofluorescence showing granular staining of superficial dermal vessels for IgG and C3 diagnostic of drug associated leukocytoclastic vasculitis. We decided to discontinue MTM and her rash was resolved in the next seven days.

Discussion: Clinical recognition of drug-induced vasculitis is very important because continued use of the offending drug can lead to irreversible and life threatening vasculitic organ damage. Vasculitis is the third main cause of toxic reaction observed by ATD classically associated with PTU. In our case, we observed unique features such as positive ANA, negative ANCA, and Histone AB, absence of systemic disorder and the quick resolution of the symptoms by stopping the offending agent without use of immunosuppressive medication. This suggests that ATD associated vasculitis has possibility of clinical spectrum.

Conclusion: In conclusion, MTM vasculitis is a rare complication with few case studies described it in medical literature. An early diagnosis of ATD vasculitis is crucial to prevent progression of the disease and systemic complications. In addition, this raises questions about preference of MTM over PTU and that clinician may need to closely monitor the patients for sign ATD induced vasculitis.

Abstract #1086

A RARE CAUSE OF GRAVES DISEASE IN HIV INFECTION

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Objective: Immune reconstitution inflammatory syndrome (IRIS) refers to a clinical phenomenon of immune-mediated inflammation against various antigens during recovery from immunosuppressed state. IRIS is a rare cause of Graves’ disease in Human Immunodeficiency virus (HIV) infection after initiation of highly active antiretroviral therapy (HAART) leading to immune recovery and elevated CD4 T-cell counts. Relatively few cases of Graves’ IRIS have been reported in literature to date. A similar case is described here.

Case Presentation: A 42-year-old male with HIV-1 infection had a nadir CD4 T-cell count of 23 cells/µL and viral load >49,000 copies/mL at initial diagnosis. He was started on HAART (Efavirenz, Emtricitabine and Tenofovir). One-year later, viral load was undetectable and CD4 T-cell count increased to >500 cells/µL, remaining stable at 500-700 cells/µL for next 3 years. After 3 years of well controlled HIV infection, he developed hyperthyroid symptoms including 15lb. weight loss, anxiety, tremors, heat intolerance, palpitations, and insomnia. Physical exam revealed enlarged thyroid gland with bruit, exophthalmos, and lid lag. He had no personal or family history of thyroid
or autoimmune disease and had a normal TSH, 3.4 mIU/mL prior to diagnosis of HIV. Laboratory results revealed suppressed TSH, <0.01 mIU/mL (0.3-5.3), elevated FT4, 2.9 ng/dL (0.7-1.4), Thyroid Peroxidase antibodies, 290 IU/mL (0-9), and Thyroid Stimulating Immunoglobulin antibodies, 195% (<122%). Thyroid ultrasound showed diffuse thyroid gland enlargement with hypervascularity. He was diagnosed with IRIS Graves’ disease and started on Methimazole with complete clinical response. Steroid treatment caused remission of ophthalmopathy as well.

**Conclusion:** About one to two percent of HIV patients present with clinically apparent, overt thyroid disease. IRIS Graves’ disease has been reported as a rare occurrence in immunocompromised patients after recovery of low CD4 counts. It usually presents 1-3 years post HAART initiation. Graves ophthalmopathy in this setting is extremely rare. IRIS Graves’ should be suspected in well-controlled HIV infected patients, if they present with signs and symptoms suggestive of hyperthyroidism along with clinical deterioration despite good virologic and immunologic response to HAART. Patients who start HAART on a very low CD4 count and subsequently experience a rapid increase in CD4 counts associated with drastically reduced or undetectable viral loads, are more susceptible and should be monitored for onset of Graves’ disease. HAART should be discontinued temporarily. Hospitalization may be needed in patients who experience life-threatening IRIS or enlarging goiter with airway obstruction.

**Abstract #1087**

A CASE OF GRAVES’ DISEASE WITH HYPERCALCEMIA IN THE SETTING OF GRAVES’ DISEASE

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**Objective:** Hypercalcemia may occur due to hyperparathyroidism, thyrotoxicosis, immobilization, Paget’s disease of bone and malignancy. Hyperthyroidism itself is one of the etiologies of hypercalcemia which can be either primary, autoimmune versus inflammatory thyroiditis, toxic multinodular goiter, solitary adenoma, or rarely a TSH-secreting pituitary adenoma. It is important to consider hyperthyroidism during the initial work up of hypercalcemia. **Case Presentation:** A 49 year-old male with secondary hyperparathyroidism, chronic kidney disease due to FSGS and hypertension presented with headaches, abdominal cramping, vomiting, and weakness. He complained of lightheadedness, polyuria, polydipsia, weight loss of 150 pounds within the last three years and 30 pounds in the last month. He had palpitations, tremors, anxiety and felt a gritty sensation in his eyes with no visual changes. He was on Calcitriol 0.25 mcg daily at home. Outpatient lab testing, 4 months prior, showed Intact PTH 120 pg/mL and Ca of 9.5 mg/dL. On admission, corrected calcium level was 13.6 mg/dL, phosphorus 5.3 mg/dL, normal magnesium and alkaline phosphatase levels, 1,25 OH Vitamin D 15.5 pg/mL, 25OH vitamin D 36 pg/mL, inappropriately normal PTH 19.7 pg/mL, creatinine 2.86 mg/dL, TSH 0.03 mU/L, and free T3 9.8 pg/mL. Urine Ca was 157 mg/day, phosphorus was 476 mg/day. Physical examination revealed BP 160/80, tachycardia, bounding pulse, excessive blinking, lid lag, scleral injection, and coarse tremor in both hands and goiter with a palpable nodule but no bruit. Pemberton’s sign was negative. Calcitriol was stopped. IV fluids and furosemide was started without improvement. Therefore, he underwent hemodialysis due to persistent hypercalcemia. TSI level was > 400. Thyroid ultrasound showed multinodular goiter. Methimazole 20 mg daily, propranolol and lubricating eye drops were started. Despite the therapy, he continued to have persistent hypercalcemia. Saturated potassium iodide solution was started without improvement in calcium levels. One month follow up showed calcium 9.5 mg/dL, free T3 1.67 pg/mL and PTH 120 pg/mL, still on hemodialysis and methimazole. Symptoms have now resolved.

**Conclusion:** We describe a case of hypercalcemia in the setting of Graves’ disease. This case marks the importance of a thorough physical exam, which included observation of excessive blinking, palpation of a bounding pulse, tachycardia and the findings of tremor on exam. It is important to consider hyperthyroidism as a contributing cause in patients who present with hypercalcemia. While it was not the only etiology of this patient’s hypercalcemia, severe hyperthyroidism should be considered as a contributing factor to his hypercalcemia.

**Abstract #1088**

RARE SITE OF PRESENTATION OF A RARE MANIFESTATION OF GRAVES’ DISEASE

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**Objective:** Infiltrative dermopathy is an uncommon manifestation of Graves’ disease. The pretibial area is the most commonly involved (99.4%) region. Rarely it affects the hand, elbow, arm, and forearm. We report a case who presented with thyroid associated orbitopathy and localized myxoedema over both the shoulders. The literature on Graves’ dermopathy indicates that this form
of dermopathy, is unusual.

**Case Presentation:** A 45 year old fisherman, presented to our outpatient department with features of thyrotoxicosis and thyroid associated orbitopathy of nine years duration. He had exophthalmos, and diffuse thyroid enlargement, with a firm texture but no nodule. Pretibial areas and feet were normal. Localized non tender swelling was noted over both his shoulders (Fig. 1). On further enquiry he revealed the history of carrying fish baskets over his shoulders. Skin biopsy showed deposits of eosinophilic hyaline material and mild perivascular inflammatory cell infiltration in dermis suggestive of myxedema.

**Discussion:** This patient had the unusual presentation of localized myxedema involving both suprascapular areas. It is the least common (4 to 5%) manifestation of Graves’ disease. Skin thickening is the characteristic abnormality and is usually limited to the pretibial area (99.4%). Hence it has been called pretibial myxedema. Localized myxedema is a more appropriate term as it involves other areas also occasionally.

Localized myxedema is an autoimmune manifestation of Graves’ disease and the usual pretibial localization relates to mechanical factors and dependent position. Rarely the fingers, hands, elbows, arms, or face are affected. The TSH receptor is the antigen for T-cell reaction, and TSH receptor antibodies are important in the pathogenesis of Graves’ dermopathy, similar to that of Graves’ orbitopathy. This also explains the occasional worsening of dermopathy after trauma, surgery, and radiiodine therapy for hyperthyroidism.

Clinical features of infiltrative dermopathy are nonpitting scaly thickening and induration of the skin, papules, nodules, pigmentation, plaque, and rarely elephantiasic form. Hyaluronic acid and chondroitin sulfate content in the dermis is increased, leading to compression of the dermal lymphatics and nonpitting edema. Differential diagnoses of infiltrative dermopathy are chronic lymphatic and venous obstruction of the lower extremities, chronic dermatitis, and cutaneous mucinosis. To establish the correct diagnosis skin biopsy may be necessary.

**Conclusion:** Localized myxedema is a rare clinical manifestation of Graves’ disease. Localized myxedema in shoulder area is even rarer. Trauma may be a precipitating factor for localized myxedema.

**Abstract #1089**

**MANAGEMENT OF GRAVES’ HYPERTHYROIDISM IN A PREGNANT WOMAN WITH ACUTE HEPATITIS**

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**Objective:** Liver disease (LD) can be seen in patients with hyperthyroidism and complicates management when present. There are limited data regarding treatment of Graves’ disease in pregnant females with LD.

**Case Presentation:** A 21 year-old female, G3P2 at 19 weeks of gestation was hospitalized for hyperthyroidism and acute hepatitis. No medical therapy for her hyperthyroidism had been initiated due to her LD. She was diagnosed with a goiter and Graves’ disease during her first pregnancy in 2013 that was not treated due to her LD. Her first son was born with Hirschprung disease and intestinal malrotation and passed away from infectious complications. She had a second unplanned pregnancy in 2014 that was also complicated by hyperthyroidism and LD. She did not seek medical care during that pregnancy and her daughter was born with a trachea-esophageal fistula. She received a dose of I-131 in October, 2015 but was lost to follow up. Physical exam revealed a significantly enlarged thyroid gland with a bruit. There was no evidence of ascites or encephalopathy. Lab work showed the following (normal range): creatinine 0.21 mg/dl (0.51 – 0.95), AST 850 U/L (9-37), ALT 374 U/L (12-78), alkaline phosphatase 198 U/L (46-116), total bilirubin 14.1 mg/dl (0.2-1), ammonia 131 umol/L (11-38), TSH < 0.005 uIU/ml (0.358-0.374), free T4 3.78 ng/dl (0.76-1.46), free T3 12.7 pg/ml (2.2-4), TSH receptor immunoglobulin 1453 % (<150) and TSH receptor binding inhibitor immunoglobulin 13.2 U/L (<1). Liver ultrasound (US) and Fetal US at 19 weeks were unremarkable. A large hypervascular goiter without discrete nodules was seen on thyroid US. Echocardiogram was within normal limits. She underwent extensive work up for her LD with the underlying etiology being contributed to seronegative autoimmune hepatitis. She was evaluated for liver transplant and thyroidectomy. Given her high operative risk, medical management was preferred. She was started on methimazole 10 mg daily and prednisone. She tolerated medical therapy well without discrete nodules was seen on thyroid US. Echocardiogram was within normal limits. She underwent extensive work up for her LD with the underlying etiology being contributed to seronegative autoimmune hepatitis. She was evaluated for liver transplant and thyroidectomy. Given her high operative risk, medical management was preferred. She was started on methimazole 10 mg daily and prednisone. She tolerated medical therapy well with significant improvement in liver enzymes and was euthyroid at time of discharge. She delivered a healthy baby with no complications but was unfortunately lost to follow up thereafter.

**Conclusion:** It is difficult to determine if the underlying
LD is secondary to hyperthyroidism or not. Management is complex as antithyroid drugs have also been associated with LD. It is preferable to avoid surgery in pregnant women due to the increased risk of pre-term labor and surgical complications. We present a complex case of Graves’ disease in the second trimester of pregnancy with acute LD who was successfully treated with methimazole and prednisone, avoiding surgical intervention during her pregnancy.

Abstract #1090

TWO CASES OF AMIODARONE INDUCED THYROID STORM

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Objective: Thyroid Storm (TS) is a rare manifestation of severe thyrotoxicosis. TS can result in cardiovascular dysfunction, hyperpyrexia, respiratory failure, arrhythmias, and death. Amiodarone induced thyrotoxicosis (AIT) is a well-established diagnosis, but TS secondary to amiodarone has been described in very few case reports. We describe two cases of amiodarone-induced TS.

Methods: A description of two cases of amiodarone-induced thyroid storm.

Case Presentation: Patient 1:
A 61-year-old man with a history of non-ischemic cardiomyopathy, on amiodarone, was admitted with a left ventricular assist device (LVAD) thrombus and urinary tract infection with bacteremia. LVAD replacement was required and a complicated post-operative course with acute kidney failure and stroke ensued. Ventricular tachycardia (VT) with tachypnea was noted. Amiodarone therapy had been continued during the hospital stay. Labs revealed: TSH < 0.01 miU/l, free T4 > 7.0 ng/dl, free T3 6.7 pg/ml. Ultrasound showed a heterogeneous thyroid, with small nodules and decreased vascular flow. Methimazole and hydrocortisone were initiated. Mentation deteriorated over the ensuing days and VT persisted, resulting in eventual withdrawal of care and patient expired.

Patient 2:
A 67-year-old man with ischemic cardiomyopathy, on amiodarone, was admitted with shortness of breath and non-sustained VT. Hospital course was complicated by gastrointestinal bleed, acute renal failure, and right lung abscess. Mental status slowly worsened and labs showed TSH < 0.01 miU/l, free T4 > 7.0 ng/dl, free T3 6.3 pg/ml. Ultrasound showed multinodular goiter and low vascular flow. Prednisone had been previously initiated for underlying lung disease and PTU was added for thyroid storm. Eventually PTU was changed to methimazole which was continued upon discharge from hospital.

Discussion: Amiodarone has long been known to cause thyrotoxicosis, but reports of amiodarone induced TS are very rare. We report two cases of amiodarone induced TS. Amiodarone had been used to treat potential ventricular arrhythmias, but may have paradoxically increased risk due to inducing TS. Aggressive treatment with thionamides and glucocorticoids is recommended to treat both type 1 and type 2 AIT, but mortality is likely high in patients with poor cardiac status.

Conclusion: Patients with severe cardiomyopathy on amiodarone should have close monitoring of thyroid function. Severe thyrotoxicosis and potentially TS may worsen ventricular arrhythmias and should be treated aggressively with anti-thyroid medication, glucocorticoids, and supportive care.

Abstract #1091

HYPERTHYROIDISM IN MOLAR PREGNANCY: CASE PRESENTATION AND LITERATURE REVIEW

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Objective: Molar pregnancy, also known as “dropsy of the uterus”, is part of a spectrum of diseases known as gestational trophoblastic diseases which originate in the placenta and have the potential to metastasize. It is of uncommon occurrence and can be at times associated with hyperthyroidism.

The aim of the author is to present the case of a patient with molar pregnancy complicated by hyperthyroidism, and review the relevant literature discussing this entity.

Case Presentation: 30 year old previously healthy female patient, pregnant by IVF, presented at 19 weeks of gestation to the outpatient clinic for fatigue, profuse sweating and disturbed thyroid function tests: TSH: <0.01 microU/mL (0.35-4.94 microU/mL), Ft3: 6 pg/ml (1.71-3.71 pg/mL), Ft4: 2.94 ng/dL (0.70-1.48 ng/dL). BHCG: 1 953 000 mIU/mL. TSHR<0.3

Blood pressure repeated twice was 170/80 mmHg with a heart rate of 110 bpm. No exophthalmos or palpable goiter, but she had sweaty palms, hyperreflexia and tremors of the outstretched fingers.

She was diagnosed with hyperthyroidism and started on Methimazole 10mg bid and Propranolol 40mg bid, then admitted for investigation.

Labs ordered showed the following: Hemoglobin: 9.3, Platelets: 296 000, WBC: 11 000, Creatinine: 0.62, PT INR: 1, SGOT: 24, SGPT: 12. BHCG: 1 953 000 mIU/mL. TSHR<0.3

Urinalysis: Proteins: +2, Ketones: +1, no glucose.
ABSTRACTS – Thyroid Disease

24 h urine collection for protein and creatinine: 683 mg/24h and 767mg/24h respectively. Patient was diagnosed with preeclampsia and started on Nicardpine, and Methyldopa. Ultrasound showed findings of molar pregnancy, so she was transferred to another facility for mole evacuation.

After termination of pregnancy, patient was normotensive again, and her thyroid function tests slowly normalized with the decrease in BHCG levels.

Discussion: HCG levels correlate well with many of the clinical features of molar pregnancy, in particular, hyperthyroidism. It has been shown to mimic the thyrotropic activity of TSH, leading to hyperthyroidism ranging from clinically subtle to overt thyrotoxicosis. Some studies described isoforms of HCG affecting its thyrotropic activity and affinity for the TSH receptor. In all the reviewed articles, mole evacuation led to rapid resolution of the hyperthyroidism, and treatment with antithyroid medications and beta-blockers was necessary to prevent thyroid storm, prior to surgical termination.

Conclusion: HCG has been the most prominent culprit in the hyperthyroidism of molar pregnancy. However, some studies failed to support this premise, suggesting a different substance produced by the molar tumor was to blame for this hyperthyroidism. Further research should be undertaken to elucidate such a controversial hypothesis.

Abstract #1092

A CASE OF METHIMAZOLE RESISTANT THYROID STORM RESPONDING TO RADIOACTIVE IODINE ABLATION

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Case Presentation: A 35 year old female with history of Graves’ disease previously controlled on methimazole (MMI) who presents to our hospital with complaints of cough, shortness of breath and lower extremity edema that started 6 weeks prior to presentation after she self discontinued MMI. Past medical history was significant for Graves’ disease that was complicated by thyroid storm in 2012. Family history was positive for thyroid disease in mother. Vital signs: BP 114/49mmHg, pulse 113/min irregular, Temp 35.2 °C, RR 20/min, SpO2 98%. Physical examination revealed agitation, jaundice, no exophthalmos. Thyroid exam revealed a diffuse goiter without bruit, cardiac exam revealed elevated JVP, bilateral LE edema and bilateral crackles. Investigations: TSH <0.01mclU/mL(normal range 0.40-4.5), Free T4 4.6(normal range 0.8-1.8 ng/dL), Free T3 10.9(normal range 2.0 - 4.4 pg/mL), AST 58(10-35 Units/L), ALT 28(10-35 Units/L), Total bilirubin 6.0(0.2-1.3 mg/dL), direct bilirubin 3.5 (0.0-0.3 mg/dL). TSI antibody was positive. EKG showed controlled atrial fibrillation, chest x ray: cardiomegaly with pulmonary edema. Echocardiogram: moderate mitral and tricuspid regurgitation, with LVEF of 45%

Patient was diagnosed with thyroid storm based on the Burch–Wartofsky score>45. She was started on high dose MMI 80mg/day, potassium iodide, steroids and beta blockers. Patient remained hyperthyroid and in heart failure despite treatment with high dose MMI for 5 weeks, free T4 increased to >7.8. Surgical team was consulted for thyroidectomy, but was deemed high risk for surgery given deconditioned status. 24 hour I-123 scan showed an uptake of 58.6% despite being on high dose MMI, so ablation with I-131 was performed without holding MMI. Patient improved 1 week after ablation with interval decrease in her Free T4 levels so she was discharged on MMI. At 6 months was given another treatment dose of I-131 after which she became hypothyroid, and started levothyroxine treatment

Discussion: Thyroid storm is a rare condition that is associated with a high mortality rate. Methimazole is potent thionamide and is considered an effective treatment in most patients with Graves’ disease, but doses > 60-80 mg/day are seldom needed. Very few patient have been reported in literature to have hyperthyroidism resistant to the action of thionamides. Possible mechanisms of MMI resistance include drug malabsorption, rapid drug metabolism, or impairment of thyroid uptake of MMI.

Conclusion: This case demonstrates an important yet rare clinical entity of resistant thyrotoxicosis. Our patient was resistant to standard therapy with high dose methimazole, potassium iodide, steroids and beta blockers but responded after radioactive I-131 ablation while being on methimazole.

Abstract #1093

A PROSPECTIVE OBSERVATIONAL LONG-TERM STUDY ON EFFICACY AND SAFETY OF L-THYROXINE IN A WEEKLY DOSE.

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Objective: To assess the long-term efficacy and safety of L-thyroxine in the treatment of Hypothyroidism in a weekly dose of 7 fold in young and middle aged females.

Methods: A prospective observational study on 40 females aged between 18 to 55 years with an established
diagnosis of hypothyroidism with TSH value of more than 4.2 mIU/L. The cohort was assigned a weekly dose of 7 fold of normal dose, which was individualized as per the body weight and TSH value. The cohort was observed for a period of 24 months. The primary end points of this study were the proportion of patients maintaining euthyroid status and evaluation of other clinical endpoints like arrhythmias, palpitations, menstrual irregularities, excessive sweating and weight loss/gain. The secondary endpoints were evaluated on variety of other metabolic endpoints like total cholesterol, triglycerides, low density lipoprotein, high density lipoprotein, aspartate aminotransferase, alanine transaminase and alkaline phosphatase. The patients were screened at 3, 6, 9, 12, 15, 18, 21 and 24 months. All patients in this cohort were screened for malabsorption and were not receiving any drugs which interfere with the absorption of L-thyroxine. The minimum to maximum dose used in this study was 175 mcg to 1050 mcg. Euthyroid status was assessed using TSH values ≤ 4.2 mIU/L.

Results: Out of 40 patients, 38 completed the study. 2 patients opted out as they had to relocate. 32 patients maintained euthyroidism throughout the study period of 24 months. We had to withdraw weekly L-thyroxine in two patients, a 42 year female for menstrual irregularities and a 20 year female for weight loss. We could not sustain euthyroidism in 2 patients and could not achieve euthyroidism in 2 patients at 24 months which may be attributed to other metabolic disorders like diabetes, hypertenion and obesity.

Conclusion: Long term use of once weekly 7 fold dose of L-thyroxine was efficacious and safe as an alternative to daily dosing regimen. Long term use of once weekly L-thyroxine did not cause any significant alteration or acute changes in heart function (arrhythmias and palpitations) and there was no indication of acute treatment toxicity or hyperthyroidism symptoms and showed improvement in social functioning, lesser bodily pains and advantage of maintaining weight. For patients who find it difficult to adhere to a rigorous treatment regime it is a valid therapeutic option for sustained long term use. It can also be considered as a first line therapy in young and middle aged non-compliant working females.

Abstract #1094

PAPILLARY CANCER OF THYROID IN A PATIENT WITH PRIMARY HYPERPARATHYROIDISM

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Objective: To present a clinical case of papillary thyroid cancer (PTC) associated with primary hyperparathyroidism (PHPT).

Methods: The clinical and paraclinical findings of the patient are presented.

Case Presentation: A 68-year-old woman with a history of renal, ureteral and bladder lithiasis and recurrent urinary tract infections for 15 years, with multiple previous hospitalizations and multiple surgical interventions with findings of calcium oxalate stones. She was referred to Endocrinology due to hypercalcemia (corrected serum Ca: 11.7mg/dl) Physical examination: grade Ib goiter, no nodules or lymph nodes were palpated, bilateral lumbar percussion pain was presented. Analytical: iPTH: 236pg/ml, TFT and cortisol: normal, phosphorus: 2.6mg/dl, Cr: 0.84mg/dl, Calcium in urine of 24 hours: 300mg/24hours, BMD: L4 and Neck of femur: Score T: -3.7 and -3.4 respectively. Scan Tc-MIBI: hypercaptant focus at the lower third of the LTI, comparable with parathyroid adenoma. The thyroid USG showed hypoecogenic nodules of 12x10x11mm in the lower third and 8x7x6mm in the upper third of RTL.In the LTL hypoecogenic nodule of 9x5x7mm, TIRADS 3. In the cytological study of the RTL reported Bethesda II, she underwent to parathyroidectomy and during surgery the surgeon decided to perform total thyroidectomy without lymph node resection, the pathology reported PTC var follicular 100%, not encap of 10x8mm in LTL with lymphatic tumor microembolism that infiltrates focally the thyroid capsule plus upper left parathyroid adenoma. Treatment with calcium carbonate and calcitriol and ablative therapy with radioiodine was indicated.

Discussion: The association between HPTP and PTC is not infrequent given the increase in both pathologies and risk factors in common. Patients with HPTP in those that detect thyroid nodules ≈ 1 cm or with echographic characteristics suspect should be studied to rule out DTC.

Conclusion: The treatment of both pathologies can be performed in the same surgical act without increasing morbidity.
Abstract #1095

GRAVES OPTHALMOPATHY - WHAT TO DO WHEN STEROIDS IS NOT AN OPTION?

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Objective: Graves ophthalmopathy (GO) is an autoimmune disorder occurring in 25-50% of patients with Graves’ disease.1 GO management is challenging as it is rarely cured. Current medical management is inconsistent which leads to further procedures causing side effects. Poor results are due to the failure to comprehend the pathogenesis of GO and to the delay in diagnosing this disease. We describe a case of minimally improved GO with medical management.

Case Presentation: 60 y/o man with no medical history c/o double vision, pain, redness and swelling for 1 year. He was diagnosed with GO and started on prednisone which provided no improvement. Patent refused further steroid treatments. He was started on methotrexate 15 mg with folic acid for 7 weeks with no relief. He pursued orbital radiation, which resulted in slight improvement but continued to have symptoms. He was seen by endocrinology due to heat intolerance and weight loss of 30 lbs. in 3 months. On exam, he was found to have conjunctival injection, periorbital edema, and inability to achieve convergence. Thyroid workup revealed: TSH < 0.005, FT4 - 1.86, TT3 - 137, TSI - 5.93. He was started on MMI 5 mg daily and a month later found to be biochemically euthyroid. Weight stabilized and heat intolerance improved but vision did not. Selenium 100 mcg bid initiated and swelling decreased. Patient is scheduled for total thyroidectomy.

Discussion: Thyrotropin receptor is targeted in Graves’ disease by pathogenic autoantibodies (TSI).2 Expression of these receptors in orbital tissues and by orbital infiltration fibrocytes propose that it is involved with causing ophthalmopathy. Yet not all affected by this disease have detectable TSI meaning that there are likely other autoantibodies involved. The ambiguity in the pathogenesis of this phenomenon leads to challenges in treatment as it is difficult to develop successful treatment plan.

In most autoimmune diseases, steroids are used and this is the accepted 1st line therapy for GO. If the patient fails this then total thyroidectomy is recommended to help remove the presumed cause of the inciting factor. This will hopefully provide definite relief of the symptoms of severe GO in this patient.

Conclusion: It is imperative to diagnose GO immediately and to establish euthyroidism. This care illustrates the variable response to steroids and the labile nature of this complication. In this patient, who was unable to tolerate steroid therapy and was refractory to other treatments, total thyroidectomy should have been pursued initially. When severe debilitating GO that is not responsive to initial medical therapy it is best to pursue surgery rather than repeat a therapy that had suboptimal response.

Abstract #1096

GRAVES DISEASE AS MANIFESTATION OF IMMUNE RECONSTITUTION SYNDROME IN A PREGNANT PATIENT WITH HIV/AIDS RECEIVING ANTIRETROVIRAL THERAPY

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Objective: To present a case of Graves disease as manifestation of immune reconstitution syndrome in a pregnant patient with HIV/AIDS receiving antiretroviral (ARV) therapy in Indonesia.

Case Presentation: A 36-year old female presented with palpitations, excessive perspiration, heat intolerance and frequent defecation since 1 month prior to consultation on her third trimester of pregnancy.

Five years prior to this episode, she was found to be HIV positive (CD4 count 5 cells/mm3). ARV therapy (Zidovudine/Lamivudine/Efavirenz) was then initiated. Her clinical conditions remarkably improved with the treatment and regimen was changed to Efavirenz/Emtricitabine/Tenofovir 3 years later. During these treatment, she had no episodes of palpitations, weight loss, or heat intolerance. Her CD4 has steadily increased from her nadir at the time of diagnosis. On examination, she was tachycardia, thyroid was palpable diffuse and fine tremor was observed. Laboratory result showed abnormal thyroid function test (TSHs 0.01 mIU/L,FT4 2.38 ng/dL), Thyroid Receptor Antibody (TRAb) 9.9 IU/L and CD4 count was 638 cells/mm3. Anti thyroid drug was promptly started and her symptoms alleviated. She underwent caesarian section and delivered a healthy baby. Her thyroid function is now under controlled with 20 mg of methimazole.

Discussion: Development of Graves disease in this patient occurred as previously depleted T cells recovered due to ARV. Although similar phenomena have been reported but this is the first case to be observed, to our knowledge, in Indonesia and in a pregnant patient. Although pathogenicity of Graves following recovery of severe T cell depletion is unknown, autoimmunity is presumed to develop in the presence of immune tolerance defect. There is evidence of thymus dysfunction in HIV patients facilitating central T
cell tolerance. T cell tolerance defect is thought to occur as Cytotoxic T Lymphocyte-associated Antigen 4 (CTLA-4) function impairment. Patient with low CD4 nadir below 50 cell/mm3 who experienced a drastically increase in CD4 during HAART had CD4 T cell proportion that produces CTLA-4. This may result in higher CTLA-4 that interfere with interaction between CTLA-4 with CD80/CD86 ligands on the Antigen Presenting Cells (APC). Furthermore, low CD4 nadir followed by a significant increase in CD4 count in patients receiving ARV has been observed in cases with Graves in HIV patients as also seen in this patient.

Conclusion: Graves disease as immune reconstitution syndrome is to be considered in HIV patients with ARV drugs who developed thyrotoxcocity. Patients with low CD4 nadir who underwent drastic increase in CD4 count due to effective treatment may be at risk to develop Graves disease as in this patient.

Abstract #1097
THE SECOND LOOK THAT SAVED A GIRL’S SIGHT-A RARE PRESENTATION OF GRAVES ORBITOPATHY-UNILATERAL PTOSIS IN A EUTHYROID PATIENT

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Objective: Graves orbitopathy or thyroid associated ophthalmopathy (TAO) is a sight threatening condition if left undiagnosed or untreated. We are reporting a very rare and unusual presentation of TAO diagnosed in a euthyroid patient with completely normal imaging findings.

Case Presentation: Our patient is a 20 y.o. female who presented to her primary care physician with complaints of sudden onset left sided ptosis and occasional unilateral tearing in the left eye. She was initially referred to a neuro-ophtalmologist and an extensive work up including MRI of the brain, CT of the Orbits, ANA, SSA/SSB, IgG4, ANCA and Myaesthenia Gravis panel were ordered with unremarkable test results. Her thyroid function tests were normal with a TSH of 0.79 (Normal 0.2-0.4 mIU/L) and Free T4 level of 0.92 (Normal 0.7-1.9 ng/dl). Interestingly, in spite of a normal initial screen, her physician decided to take a second look at her thyroid function & checked her thyroid stimulating immunoglobulin (TSI) levels which were found to be elevated at 287 IU/mL (Normal 0 to 20 IU/mL). She was then referred to the endocrinology clinic. The above history and examination findings were confirmed. Additionally, she attested to experiencing pressure behind her left eye and diplopia intermittently. She denied other complaints. There was no obvious eye swelling, exopthalmos, propidness, redness, lid lag, or visual field defects noted on examination. A diagnosis of euthyroid Graves orbitopathy was made. She was started on prednisone 30 mg daily. Within 48 hours of initiating therapy, the patient showed excellent response with improvement in eye size and ocular symptoms. She was advised to follow up with us in 6 weeks for a bedside clinical assessment and to repeat her TSI levels, in the meantime she was gradually tapered off the steroids. At her follow up visit, she reported complete resolution of symptoms with her TSI levels dropping down to 128 IU/mL.

Conclusion: Clinicians must have a high index of suspicion when evaluating patients with new ocular symptoms for thyroid disorders. Absence of classic symptoms, normal thyroid levels, and normal imaging findings must not deter clinicians from initiating further tests for Graves orbitopathy, especially when other diagnoses have been ruled out. While TSH alone or in combination with free T4 is the preferred initial screening test, TSH receptor assays such as TSI, TRab (TSH Receptor Blocking Antibodies), TBII (TSH Binding Inhibitory Immunoglobulin) and LATS (Long Acting Thyroid Stimulator) must be considered owing to their superior sensitivity and specificity. High dose IV or oral pulsed therapy with corticosteroids such as methylprednisone is the preferred initial line of treatment.

Abstract #1098
A CURIOS CASE OF PERSISTENTLY ELEVATED TSH ASSOCIATED WITH HIGH DOSE OVER THE COUNTER BIOTIN SUPPLEMENTATION

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Objective: The use of biotin as a vitamin supplement has been increasing in recent times. Consuming high doses of biotin can result in abnormal thyroid function tests (TFTs), often mimicking the numbers seen in a patient with Graves’ disease. These abnormal labs generally return to normal shortly after stopping the supplement. We are presenting a patient who had an persistently elevated TSH from high dose biotin consumption in spite of stopping it.

Case Presentation: Our patient is a 67-year-old male with a history of Coronary Artery Disease, Hypertension, Type 2 Diabetes on Metformin and Hypothyroidism from receiving radiation therapy to the neck for tonsillar lymphoma on Levothyroxine since 2 years. He was referred to the endocrinology clinic in view of abnormal
& paradoxical TFT results showing a high TSH of 7.4 mIU/L (Normal range 0.5-3.0 mIU/L) & high free T4 of 3.19 ng/dL (0.8 - 1.8 ng/dL). A significant change from his baseline labs of TSH 4.02 and Free T4 1.1.
His complaints included pervasive fatigue, constipation, & forgetfulness since 4 months. His vitals were stable, he had no neck swelling & his eye & systemic examination findings were normal.
Repeat testing showed TSH of 9.3 mIU/L, Free T4 of 4.04 ng/dL, and a total T3 of 287.8 ng/dL (Normal range 80.0 - 187.0 ng/dL).
Our patient denied taking higher than required doses of Levothyroxine. However, he endorsed to taking over the counter biotin supplements to help with the fatigue, often doses as high as 30 mg per day.
We asked him to stop taking the biotin supplement for at least a week and repeated his TFTs.
Repeat testing revealed a TSH of 7.01 mIU/L, free T4 of 1.35 ng/dL, and a total T3 of 132.2 ng/dL. We attributed the abnormal labs to him taking the high dose of biotin supplements & asked him to continue his current dose of Levothyroxine & follow up with us in 6 months.
Repeat labs after 6 months showed a TSH of 7.43 mIU/L and free T4 of 1.1.
Discussion: Biotin has been shown to interfere with commonly used thyroid assays, and tests for anti-thyrotropin receptor antibodies resulting in abnormal results. Biotin may cause symptoms secondary to autonomic dysfunction, such a tachycardia and fever, which can be misinterpreted as an underlying thyroid disorder.
Conclusion: Clinicians must be cognizant of different patterns of abnormalities seen in TFTs of patients on biotin supplements
There is need to improve awareness in the clinical community about biotin as a potential confounder of thyroid function tests.
Laboratories and test manufacturers must reference this as a potential source of error in reports to prevent unnecessary workup & treatment
Further research is required to see if biotin may interfere with other test results as well.

Abstract #1099
A RARE PRESENTATION OF NON-SEMINOMATOUS GERM CELL TUMOR AND PAPILLARY THYROID CANCER
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Objective: Nonseminomatous Germ Cell Tumors (NSGCTs) are rare aggressive germ cell tumors with poor prognosis. Papillary thyroid cancer (PTC) is the most common thyroid malignancy with an increased recognition of a potential genetic component and associated conditions. Several case reports have described germ cell tumors occurring synchronously with PTC. In majority of these patients the association is related to treatment of NSGCTs with radiation/chemotherapy that significantly increases the risk of PTC and its occurrence. While one case series, described pure seminomas associated with PTC but did not show any association with NSGCTs. Herein, we describe a case where patient developed NSGCTs and PTC without any prior treatment.

Methods: Case Report
Case Presentation: A 21 year old male presented for evaluation of chest pain and dyspnea prompting emergent workup with CT chest/abdomen/pelvis revealing a large right anterior mediastinal mass measuring 6.2x6.7cm with metastatic disease to lungs, liver and spleen. Initial imaging showed a thyroid mass and no brain metastases. Subsequent thyroid ultrasound showed three nodules measuring 2.7x2.7x1.8cm, 4.5x4.4x2.6cm and 2.1x1.7x0.9cm. An FNA of the dominant nodule was consistent with papillary thyroid cancer. Tissue sampling of the mediastinal mass showed nonseminomatous germ cell tumor (choriocarcinoma). Lab results showed beta-hCG levels of 64,521 (ref <5 mIU/mL) consistent with the above diagnosis. Patient was started on etoposide and cisplatin.
His disease course was complicated by development of brain metastasis four months after presentation requiring external beam radiation. Given the extent of his cancer burden with NSGCT, PTC was not treated. Unfortunately, patient expired ten months after initial diagnosis of NSGCT from complications arising from the disease.
Discussion: There are several case reports of synchronous germ cell tumors and other primary neoplasms occurring in literature. These case reports describes either pure seminomas associated with PTC or show PTC consequent of underlying NSGCTs treatment. The case described above is unique in having NSGCTs and PTC occurring simultaneously at initial presentation.
Conclusion: While it is possible that the simultaneous presentation of two separate neoplasms is coincidental, the
possibility of genetically association cannot be excluded given the nature of these tumors.

Abstract #1100

HIGH DOSE OF NUTRITIONAL SUPPLEMENT COULD INTERFERE WITH LABORATORY ASSAY

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Objective: Clinical consultations regarding abnormal Thyroid function tests are a routine problem in the endocrinology world and can be challenging to finding the offending cause. We present a case report to increase awareness of biotin supplement interferences with the Thyroid function test assay.

Case Presentation: A 68 yo female presented to her PCP complaining of weight loss. Labs showed elevated FT4 of (3.01; 0.61-1.37 ng/dL), FT3 (9.5; 2.8-4.4 pg/mL), TT3 (547; 87-178 ng/dL) with normal TSH (1.02; 0.35-4.01 u[IU]/mL), and TT4 (10.37; 4.30-12.50 ug/dL). She was clinically euthyroid. She was taking Biotin 10000 mcg daily for hair loss as prescribed by her Dermatologist for about 6 months. Biotin was withheld prior to repeat testing which resulted in normalization of laboratory values as follows: TSH 0.54 u[IU]/mL, FT4 1.23 ng/dL, FT3 3.1 pg/mL, TT4 9.83 ug/dL, and TT3 110 ng/dL.

Discussion: Biotin is an essential cofactor for multiple biochemical reactions. The recommended daily intake of biotin is 30 mcg per day. Doses above the recommended daily dose are frequently found in nutritional supplements reported to be beneficial for hair and skin care. Many immunoassays use a biotin-streptavidin interaction. Streptavidin has a high affinity for biotin. The binding of biotin to streptavidin is one of the strongest non-covalent interactions known in nature. This phenomena is used in competitive and immunometric immunoassay designs. In both types, excess biotin resulted in low signaling production. In a competitive immunoassay, when tested for triiodothyronine and thyroxine, results were falsely high levels. In immunometric immunoassays, when tested for thyrotropin, excess biotin resulted in falsely low levels. Therefore, biotin interference may result in a biochemical picture of severe hyperthyroidism or an atypical pattern with elevated free thyroid hormone and an inappropriately normal TSH, as it was in our case.

However, clinical assessment of a patient should be based on clinical symptoms and signs as cornerstones of a suspected diagnosis. Laboratory tests are there to confirm or reject the clinical hypothesis. Lab error or inaccurate results are a possibility. In case of a supraphysiological dose of biotin, a falsely abnormal thyroid function result could occur and lead to a wrong diagnosis while possibly exposing the patient to unnecessary treatment and complications.

Conclusion: In our case, we found that the intake of a high dose of Biotin lead to interferences with the thyroid function test results and could lead to unnecessary evaluation. Increased awareness of this laboratory interference among physicians could help to insure correct testing and avoid unnecessary testing.

Abstract #1101

THE VALUE OF CALCITONIN CALCIUM STIMULATION TEST LEVELS AS PREDICTORS OF MEDULLARY THYROID CANCER.

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Objective: Calcitonin, a hypocalcemiant hormone is released by C parafollicular cells as a marker for medullary thyroid cancer (MTC). Since C cell hyperplasia (CCH) is a premalignant state, acute calcium stimulation test (CST) could induce more calcitonin release in CCH or MTC than in normal thyroid. Our objective was to evaluate CST to preclude “gray zone” values of basal calcitonin, diagnose minimal residual disease and help the early diagnosis of CCH, and therefore prevention of MTC through early diagnosis.

Methods: We applied the CST on a series of patients with either nodular goiter, single nodule, RET positive or history of MTC associated with elevation of basal calcitonin values. Calcium gluconate 25 mg/kg adapted on the ideal BMI was administered over 3 minutes under ECG monitoring. Blood was collected before, at 2; 5 and 10 minutes after calcium infusion. Calcitonin was measured using LIAISON XL assay.

Results: The test has been performed on 44 patients, aged (6-70), 19 M, 25 F. Mean calcitonin values (normal range: 1-11.8 pg/ml) were: basal=24.03 pg/ml; at 2 min=309.159 pg/ml; at 5 min=241,33 pg/ml, at 10 min=176.7 pg/ml; 37 subjects had a significant 2 min stimulated calcitonin (>100 pg/ml) and 17 were operated, 3 subjects had an intermediate response (53.31-81.7 pg/ml) and 4 patients had low stimulated values(< 54 pg/ml) therefore they are to be followed-up. CCH and MTC was confirmed histologically in 9 out of 17 patients (3 CCH and 6 MTC); 2 subjects had benign nodular goiter and 2 papillary thyroid microcarcinomas.

Discussion: In the algorrhytm for diagnosis of thyroid
nodule, Calcitonin, a well known marker of CCH and MTC, became increasingly used. In some patients inadequately high basal calcitonin (below 100 pg/ml) could raise concerns about presence of MTC. However, cutoff levels are not established and sex/ tumor size/ age differences in the stimulation test are not well understood. If the CCH is a premalignant state for MTC, the pathway from CCH to MTC could be revealed by CST (figure).

Conclusion: Stimulated calcitonin may be useful in the early diagnosis and follow-up of CCH and MTC and could reduce false negative rate of basal calcitonin measurement.

Abstract #1102

LITHIUM INDUCED THYROTOXICOSIS

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Medstar Health

Case Presentation: A 57-year-old female with seizure and bipolar disorder on lithium therapy presented with complaints of lethargy and altered mentation. Laboratory findings revealed supratherapeutic lithium levels of 1.8 mmol/L (0.6-1.2 mmol/L) with suppressed thyroid-stimulating hormone (TSH) at 0.015 uIU/ml. On examination, she did not have exophthalmos and the thyroid was not palpable. Burch-Wartofsky score was 25, suggesting impending thyroid storm, and therapy with propylthiouracil and metoprolol was initiated. Further workup confirmed thyrotoxicosis with elevated free thyroxine (FT4), 3.25 ng/dL, and free triiodothyronine (T3), 337 pg/mL. Evaluation for the underlying etiology was notable for negative thyroid-stimulating immunoglobulin (TSI), thyroid peroxidase antibodies, 29 IU/mL, and thyroglobulin antibodies, <30 IU/mL. Ultrasound revealed a heterogeneous, hypoechoic, hypervascular nodule in the right mid thyroid lobe with intranodular coarse calcification and an avascular, isoechoic nodule in the lower portion of the left lobe. Over the course of the hospitalization, the TSH level improved to 0.03 uU/ml, free T4 decreased to 1.68 ng/dL, and free T3 normalized with gradual improvement in mentation to baseline.

Conclusion: Hypothyroidism secondary to use of lithium is well known, but thyrotoxicosis secondary to its use is less common. Different mechanisms have been postulated for lithium-induced thyrotoxicosis, one of which is an escape phenomenon from the inhibitory effect of lithium leading to intrathyroidal iodine retention. Another mechanism is development of autoantibodies in susceptible individuals. Lithium increases B cell activity and decreases the ratio of suppressor cells to cytotoxic T cells. Patients on lithium therapy have an increased propensity to develop anti-thyroid antibodies. Another mechanism is a direct toxic effect of lithium resulting in painless, non-tender goiter secondary to ultra-structural lysosomal and mitochondrial damage, like that in amiodarone-induced thyroiditis. In our patient, thyrotoxicosis was postulated as a precipitant of her encephalopathy. Given the absence of anti-thyroid antibodies, the possible mechanism of lithium-induced thyrotoxicosis was from direct toxic effect or from an escape phenomenon. In patients taking lithium, as in other drugs that can cause thyroid dysfunction, the American Thyroid Association guidelines recommend clinical and biochemical monitoring at 6-month intervals. It is important to consider the potential thyrotoxic effect of lithium in maniac-depressive patients because it may precipitate “breakthrough mania” in these patients.

Abstract #1103

METABOLIC STATUS CONFIGURATION IN PATIENTS WITH AND WITHOUT CHRONIC AUTOIMMUNE THYROIDITIS

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Objective: Chronic autoimmune thyroiditis is caused by an abnormal immune response to autoantigens, often being associated with other autoimmune diseases. Hashimoto’s thyroiditis is considered the most common cause of primary hypothyroidism which can lead to important metabolic comorbidities.

Methods: We conducted a retrospective study on a group of patients with chronic autoimmune thyroiditis and another one with patients without chronic autoimmune thyroiditis (control group). This is a single center experience in a tertiary center of endocrinology. Biochemical, endocrine and anthropometric assessment are provided in order to establish the metabolic status. We evaluated anthropometric data (BMI: Body Mass Index), blood pressure, seric glucose level and lipidic profile and also history of high blood pressure, type 2 diabetes mellitus, and dyslipidemia (anomalies of serum cholesterol). For statistical analysis we used Student’s t-test (statistical significance at p<0.05).

Results: The entire cohort included 295 patients with a female predominance (93.55% vs 6.44% males). We enrolled a group of 109 patients (with a mean age of 54.26 years+/− 12.7) with chronic autoimmune thyroiditis, diagnosed based on positive TPO (anti-thyroxperoxidase)
PTH levels did not decrease, and postoperative PTH and enlarged at 15 mg and 75 mg, respectively. Intraoperative right lower and left upper parathyroid glands, which were underwent partial parathyroidectomy with resection of the neck showed bilaterally enlarged parathyroid glands. He was negative. A computed tomography (CT) scan of the tomography/computerized tomography (SPECT/CT) scan 99m sestamibi with single-photon emission computerized parathyroid hormone (PTH) at 578 pg/mL. Dual-phase Tc-phosphate was 1.9 mg/dL with inappropriately elevated fatigue. Initial serum calcium was 14.0 mg/dL, and serum polyuria, polydipsia, worsening arthralgias, osteodynia, and kidney stones and chronic joint pain. His symptoms included parathyroid cyst in a 62-year-old Caucasian male with severe hypercalcemia secondary to a functional intrathymic Of these, only 10% are functional. We report a rare case of only 0.6% of all reported thyroid and parathyroid lesions. 300 documented cases of parathyroid cysts, which make up in the neck or anterior mediastinum. There are fewer than Case Presentation:

Medstar Union Memorial Hospital

Ariane Davis, MD, Pamela Schroeder, MD, PhD, Rani Kulkarni, MD

Abstract #1104

INTRATHYMIC PARATHYROID CYST: A RARE CAUSE OF HYPERPARATHYROIDISM

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Case Presentation: Parathyroid cysts are rare lesions found in the neck or anterior mediastinum. There are fewer than 300 documented cases of parathyroid cysts, which make up only 0.6% of all reported thyroid and parathyroid lesions. Of these, only 10% are functional. We report a rare case of severe hypercalcemia secondary to a functional intrathymic parathyroid cyst in a 62-year-old Caucasian male with kidney stones and chronic joint pain. His symptoms included polyuria, polydipsia, worsening arthralgias, osteodynia, and fatigue. Initial serum calcium was 14.0 mg/dL, and serum phosphate was 1.9 mg/dL with inappropriately elevated parathyroid hormone (PTH) at 578 pg/mL. Dual-phase Tc-99m sestamibi with single-photon emission computerized tomography/computerized tomography (SPECT/CT) scan was negative. A computed tomography (CT) scan of the neck showed bilaterally enlarged parathyroid glands. He underwent partial parathyroidectomy with resection of the right lower and left upper parathyroid glands, which were enlarged at 15 mg and 75 mg, respectively. Intraoperative PTH levels did not decrease, and postoperative PTH and serum calcium continued to increase to 878 pg/mL and 14.7mg dL, respectively. A postoperative CT of the chest with contrast revealed an intrathymic cystic mass measuring 76 x 34 mm. CT guided aspiration of the mediastinal mass yielded 10 mL of turbid brown fluid and intact PTH of 273,200 pg/ml. The patient underwent right -sided robot-assisted excision of the mediastinal mass. A thin-walled cyst measuring 11 x 6 x 0.4 cm was excised. Intraoperative serial PTH levels decreased from 1224 pg/mL to 86 pg/mL ten minutes after cyst excision. His postoperative course was uneventful and his total serum calcium rapidly normalized. Discussion: Primary hyperparathyroidism is commonly caused by a parathyroid adenoma, multiple adenomas, or gland hyperplasia. Approximately 95% of patients with primary hyperparathyroidism are cured after initial endoscopic neck surgery. Although a missed abnormal parathyroid gland is the most common cause of a failed parathyroidectomy, one rare cause is an ectopic location of the parathyroid adenoma or cyst. Routine preoperative diagnostic tools, such as ultrasonography or parathyroid scintigraphy, may be negative. The diagnosis is suggested when chest imaging shows a cystic mass in the mediastinum and is confirmed by fine needle aspiration with a high PTH level or through a surgical biopsy, which may reveal tissue that stains positively for PTH.

Conclusion: Our case emphasizes the importance of preoperative localization and also suggests the need to consider rare entities when standard investigations are negative in patients with primary hyperparathyroidism.

Abstract #1105

USE OF ELASTOGRAPHY TO DETERMINE THE EXTENT OF SURGERY PREOPERATIVELY IN A THYROID NODULE WITH INDETERMINATE CYTOLOGY RESULTS

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Objective: To demonstrate the use of a noninvasive tool such as strain elastography in distinguishing benign from malignant thyroid nodule and its value in surgical approach and extent. We present a case of a patient with indeterminate cytology with suspicious gene expression classifier test with low elastography score found to have benign pathology post hemi-thyroidectomy.

Case Presentation: 67 year old male after a fall was noted to have an incidental finding of a 2.5 cm left thyroid lesion on CT of cervical spine. He had no dysphagia, dysphonia, neck pain or sore throat. He did not have any radiation exposure nor family history of thyroid cancer. Physical exam was significant for left thyroid...
mass palpable on deglutition with neither tenderness nor cervical lymphadenopathy. Labs were normal: TSH at 2.1 uIU/mL (0.4-4.5), FT4 at 1.2 ng/dL (0.8-1.7), FT3 at 2.8 pg/mL (2.0-4.4) and Thyroid Peroxidase Antibody at 13 IU/mL (0-34). Ultrasound thyroid revealed asymmetric thyroid gland with enlarged left lobe, dominant left nodule measuring 2.82 cm in greatest dimension with no significant cervical adenopathy. The nodule was solid, isoechoic, with hypoechoic possibly cystic area medially within the nodule, heterogeneous with smooth borders and Grade 3 Doppler flow with presence of microcalcifications. The elastography showed a score of 2, based on strain elastographic scores by Rago criteria indicating elasticity in a large part of the nodule. FNA biopsy revealed indeterminate cytologic results with suspicious gene expression classifier testing. He was referred to ENT. Indirect laryngoscopy yielded insufficient view. Fiberoptic nasopharyngolaryngoscopy revealed mobile true vocal folds and no suspicious lesions. He underwent left hemithyroidectomy and is doing well. Final pathology showed benign Hurthle cell type follicular adenoma.

**Discussion:** Elastography is a dynamic technique that provides an estimation of nodule stiffness by measuring the degree of distortion using an ultrasound probe. Stiffness of thyroid nodules has been stated as an independent predictor of thyroid malignancy. Since its popularity a decade ago, many studies and a few meta-analysis have demonstrated promising sensitivity, specificity and negative predictive value associated with elastography. One study reported it to be more accurate than US and doppler US, and another highlighted improved diagnostic performance of elastography when combined with high resolution US.

**Conclusion:** Continuous use of this technique is needed to identify the depth of its use to prevent unnecessary total thyroidectomies.

**Abstract #1106**

**DRAMATIC RISE OF SERUM THYROGLOBULIN AFTER LYMPH NODE FINE NEEDLE ASPIRATION**

_Yewande Adepoju, DO, Rodhan Khthir, MD_

Marshall University

**Objective:** Thyroglobulin (TG) has been used to monitor the recurrence of differentiated thyroid cancer. TG in fine needle aspiration (FNA) washout has been shown to be more sensitive when evaluating for lymph node metastasis. We present a case of dramatic rise of serum TG few days after FNA of a suspicious cervical lymph node in a patient who underwent total thyroidectomy and radioactive iodine ablation for papillary thyroid cancer. Case Presentation: A 68-year-old man with history of papillary thyroid cancer (T3N0Mx) status post total thyroidectomy and radioactive iodine ablation presented for an outpatient follow-up visit. He was diagnosed 5 years ago and has been maintained on Levothyroxine for TSH suppression post-surgically. TG levels have been low with undetectable antibody. Multiple whole body scans have been unremarkable. In addition, he has had serial thyroid ultrasounds, which showed small, benign appearing bilaterally lymph nodes until 4 months ago. Ultrasound showed bilateral lymph nodes with a suspicious 1.3 cm right anterior lymph node. 2 months later, a repeat ultrasound showed mild enlargement of the suspicious lymph node. FNA of the lymph node was done. Cytology study was negative for malignancy but lymph node washout TG was 204,410 ng/ml (confirmed by dilution). 2 weeks after FNA, a routinely scheduled serum TG was done and was 22.6 ng/ml (previously 0.40 ng/ml 6 months prior) with negative antibody. 6 weeks post-FNA, serum TG level was repeated and resulted as 0.53 ng/ml. Neck CT with contrast revealed non-specific cervical and upper mediastinal lymphadenopathy. Since he is a high-risk patient, he was referred for lymph node dissection.

**Discussion:** TG is the marker for monitoring the recurrence of thyroid cancer. Detectable TG in FNA washout has been shown to be more sensitive compared to cytology result for recurrence of disease. Our patient exhibited high TG level in FNA washout which represents disease recurrence and developed dramatic increase in serum TG level after the biopsy (44 times baseline TG). The level went back to its baseline within 6 weeks. TSH level was low normal during both tests. This shows that with FNA, there may be spillage of TG into the circulation which may transiently elevate serum TG level if there is a local recurrence in the setting of elevated wash-out TG.

**Conclusion:** This case shows the transient elevation in serum TG after FNA. We recommend to avoid measuring serum TG shortly after fine needle aspiration of suspicious lymph node.

**Abstract #1107**

**NIVOLUMAB INDUCED HYPOTHYROIDISM: UNUSUAL REPLACEMENT REQUIREMENTS**

_Bhairavi Sheshadri_

WMC Medical Center

**Objective:** Nivolumab is a fully human immune checkpoint inhibitor antibody (anti PD-1 Ab) that is indicated for the treatment of multiple malignancies. Immune checkpoint inhibition can lead to multiple immune-related endocrinopathies and, based on randomized trial data, nivolumab has been shown to induce hypothyroidism in...
abstracts – thyroïd disease

Objective: Thyroid nodules are a common incidental finding during routine exam or radiographic procedure. Once found, further evaluation is necessary depending on nodule size and ultrasonographic appearance. Further evaluation involves fine needle aspiration biopsy (FNA); a procedure that carries a very low risk profile with one of the rarest being vocal cord paralysis with incidence of 4 in 10,000-15,000 FNAs. We describe a case where a patient developed vocal cord paralysis two weeks after undergoing FNA leading to uncovering of an underlying lung malignancy.

Case Presentation: A 61 year-old male presented to our hospital with diarrhea, fatigue, hair loss and mild bilateral leg swelling for one month. He was being treated for metastatic renal cell carcinoma and had been on nivolumab biweekly treatment for the past 7 months. Prior to this he was on pazopanib. Thyroid function tests revealed hypothyroidism which was attributed to an immune-mediated adverse reaction to nivolumab. Levothyroxine was initiated. Despite 200mcg QAM (weight 107kg: 1.87 mcg/kg), TSH rose from 29.37 to 57.33 over the next 7 days. Levothyroxine was increased to 300mcg and he was discharged on this dose. As an outpatient, his levothyroxine dose was gradually reduced to 150mcg over the next year. At that point nivolumab was restarted biweekly. Over the next two months, thyroid requirements continued to decrease and he is currently on levothyroxine 100mcg daily. In addition, the patient was on a PPI and on prednisone for Crohn’s disease. Prednisone was dosed at 50mg daily at the time of admission and was gradually tapered off.

Conclusion: Our patient initially required much higher than expected doses of levothyroxine, which then gradually decreased to more usual doses over the next 18 months. It is unclear if this was due to a unique mechanism in immune-mediated hypothyroidism secondary to nivolumab. There may have been additional effects on thyroid hormone levels from the concurrent administration of prednisone and proton pump inhibitors, or even his previous treatment with pazopanib. Our report suggests that these patients require close monitoring of thyroid function and an increased awareness to the complex interactions associated with the management of these toxicities.

Abstract #1108

VOCAL CORD PARALYSIS POST-FINE NEEDLE BIOPSY OF THYROID NODULES

Harris Baloch, MD, Katherine Vu, DO, Thanh Hoang, DO

Walter Reed National Military Medical Center

Objective: Thyroid nodules are a common incidental finding during routine exam or radiographic procedure. Once found, further evaluation is necessary depending on nodule size and ultrasonographic appearance. Further evaluation involves fine needle aspiration biopsy (FNA); a procedure that carries a very low risk profile with one of the rarest being vocal cord paralysis with incidence of 4 in 10,000-15,000 FNAs. We describe a case where a patient developed vocal cord paralysis two weeks after undergoing FNA leading to uncovering of an underlying lung malignancy.

Methods: Case report.

Case Presentation: A 38-year-old male, father of two daughters with PTEN mutation, was tested positive for longstanding multinodular goiter and hypothyroidism. At presentation for routine follow up, patient noted to have interval growth in her thyroid nodules, largest measuring at 3.2x2.4x2.5cm and 4.3x2.4x2.6cm with intense hyperemia noted on images. Given the significant interval increase in size, patient underwent thyroid FNA. Pathology results showed follicular lesion of undetermined significance (FLUS) with subsequent molecular analysis negative for any mutations or gene fusions. Two weeks following FNA patient complained of voice hoarseness that she described developing immediately following the FNA and persistently worsening. These symptoms continued to persist several weeks later, leading to further evaluation for presence of any masses or thyroid nodules causing compressive symptoms. CT neck showed medialization of the right vocal cord with necrotic appearing lymph nodes in the aortopulmonary window measuring 2.2x2.1cm. A CT chest confirmed presence of multiple ground glass opacities with multiple enlarged lymph nodes. Tissue sampling of lymph nodes demonstrated poorly differentiated adenocarcinoma of the lung (Stage III B). Treatment with etoposide/cisplatin/radiation was initiated but patient continued to progress to Stage IV with metastases to brain and liver. Patient expired 10 months after her initial presentation for thyroid FNA.

Discussion: This case highlights an unusual presentation of an aggressive lung cancer masquerading as vocal cord paralysis following a thyroid FNA. Clinicians have to be mindful of complications arising from every day procedures like thyroid FNA but at the same time need to keep a wide differential for other possibilities.

Conclusion: Unfortunately, early diagnosis did not help this particular patient but remaining mindful of odds of having vocal cord paralysis from FNA and investigating other etiologies in a timely manner can make the difference in patient care.

Abstract #1109

PAPILLARY THYROID CARCINOMA WITH PTEN MUTATION

Sablaa Ali, DO, Yusef Hazimeh, MD, Christopher Barnes, DO

Arnot Ogden Medical Center

Objective: Phosphatase and tensin homolog (PTEN) mutation has been associated with increased risk for multiple malignancies. We present a case of recurrent papillary thyroid carcinoma in the setting of this hereditary disorder.

Case Presentation: 38-year-old male, father of two daughters with PTEN mutation, was tested positive for
that mutation in 2007. In early 2013, thyromegaly was noticed on routine exam. Ultrasound revealed a 3.5 cm right thyroid nodule, and fine-needle aspiration showed malignant cells. He underwent thyroidectomy. Pathology demonstrated papillary thyroid cancer (PTC), measuring 6.5 cm in the right lobe and 3.2 cm in the isthmus. There was intra-lymphatic, vascular and capsular invasion. He had 17/19 lymph nodes (LN) positive for malignancy. (Stage was T3N1bMx). He received radioiodine (RAI) ablation. Post-treatment whole-body scan was consistent with residual thyroid tissue versus carcinoma in the surgical bed. Six-month follow-up ultrasound did not reveal any residual thyroid tissue. His thyroglobulin levels were undetectable, however he had positive thyroglobulin antibody. He lost follow-up for about 2 years. He came back to Endocrinology and he was found to have a right thyroid area mass. His TSH was 0.29 uIU/ML (normal 0.34 - 5.6). Ultrasound of the thyroid bed revealed 2 masses. He underwent a second surgery in November 2016. That revealed multiple lymph nodes on the right side measuring up to 4.3 centimeter, and consistent with papillary thyroid carcinoma with extra nodal extension.

**Discussion:** PTEN gene is located on chromosome 10q23.3. It encodes a phosphatase enzyme which acts as tumor suppressor. PTEN point mutation has been reported in thyroid carcinoma. Germ line mutations in this gene have been described in a variety of rare autosomal dominant syndromes, and has been associated with increased risk of multiple cancers. Our patient had PTC, treated surgically and with RAI. No residual thyroid tissue on ultrasound six-month after the first surgery. Although he lost follow-up with us, he was still taking his Levothyroxine, and TSH was suppressed. He was found to have recurrence of the tumor in multiple large lymph nodes with extranodal extension.

**Conclusion:** The presence of PTEN mutation has been shown to have an association of increased thyroid malignancy. We think that the presence of this germline mutation might be associated with more aggressive PTC and higher risk of recurrence. Consideration should be given to perform early thyroid cancer screening for carriers of this mutation. Close postoperative follow-up is needed.

**Abstract #1110**

**THERAPEUTIC PLASMA EXCHANGE IN A CASE OF THYROID STORM**

Megan Minch, MD, William Moore, MD, Samuel Fineberg, MD, Monica Agarwal, MD

University of Alabama at Birmingham

**Objective:** We present a case of thyroid storm treated with therapeutic plasma exchange (TPE). TPE is a type of apheresis procedure in which plasma is removed and replaced with a solution such as colloid (albumin and/or plasma) or combination of crystalloid and colloid solution.

**Case Presentation:** A 28-year-old man had presented with weight loss and palpitations and was diagnosed with Graves disease but did not seek further care. Several months later, he presented with abdominal pain and vomiting. He was found to have severely depressed LV ejection fraction and atrial fibrillation with RVR, and he subsequently suffered cardiac arrest. Following resuscitation, he developed multiorgan failure requiring mechanical ventilation, pressor support, hemodialysis and had severe hepatic dysfunction; AST 986 U/L (12-39), ALT 752 U/L (7-52) and PT 34 (12-14). Thyroid tests revealed TSH 0.13 (0.45-5.3), Free T4 4 ng/dL (0.61-1.12) and Free T3 10.4 pg/ml (2.5-3.9). TPO antibodies >1000 units (<100), TSI antibodies >700 (<140), and TSH receptor antibodies 25 IU/L (<1.75). He was started on lithium, cholestyramine, and hydrocortisone. Beta-blockers were held due to cardiac decompensation, and thionamides were avoided due to hepatic dysfunction. TPE was initiated with significant improvement in T4 and T3. Methimazole was started as hepatic function improved, and Lugol’s iodide was added before thyroidectomy. He successfully underwent total thyroidectomy.

**Discussion:** Numerous case reports have suggested TPE as a potential therapy for thyroid storm. However, there are no clear guidelines for its use. TPE is typically reserved for cases of severe symptoms, failure of conventional treatments, or contraindications to traditional therapies. It is the fastest method for lowering thyroid hormone. TPE removes cytokines, putative antibodies, and thyroid hormones with their bound protein. TPE has a recommendation of category III (optimum role of apheresis therapy not established, and decision making should be individualized) and grade 2C (weak recommendation based on observational studies or case studies) for thyrotoxicosis by the American Society for Apheresis. TPE has a transitory effect and thus should be associated with additional therapies. In our patient, TPE resulted in a rapid lowering of thyroid hormones.

**Conclusion:** Though indication for use is not well...
established, TPE is reported as a therapeutic option in patients with thyroid storm in specific circumstances. Responses in the literature vary, though its use often leads to biochemical and clinical improvement. Additionally, it could be used to render the thyrotoxic patient euthyroid prior to thyroidectomy.

Abstract #1111

METASTATIC CLASSICAL PAPILLARY THYROID CANCER WITH UNDETECTABLE BASAL THYROGLOBULIN LEVEL AND LACK OF METASTATIC UPTAKE ON RADIO-IODINE SCAN

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Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Cincinnati, Cincinnati College of Medicine

Objective: Metastatic Classical Differenced Papillary Thyroid Cancer (DPTC) has rarely been reported with negative thyroglobulin (Tg) and Radioiodine Whole Body Scans (WBS). We present such a case of metastatic DPTC with negative Tg, Tg antibodies (ab) and WBS.

Case Presentation: A 46 year old male with prior history of hypertension, Type 2 Diabetes Mellitus and no family history of endocrine malignancies, was found to have palpable neck mass. Patient was evaluated with a thyroid ultrasound showing 0.7x1.8x1.2 cm left sided thyroid nodule. Chest CT scan showed incidental findings of multiple non-calcified lung nodules (largest in the left lower lobe 1.05 cm).

Patient underwent core needle biopsy of the largest lung nodule, which stained positive for cytokeratin 7, TTF-1, Tg, PAX-8, HMBE-1 stains, hence suggesting well DPTC. Ultrasound guided FNA of the thyroid nodules concurred the PTC diagnosis.

Patient underwent total thyroidectomy with lateral and central neck dissection. Pathology confirmed a unifocal classic well DPTC (2.8x1.8x1.4 cm) with gross extra thyroidal and extra nodal extension. 8 out of 78 lymph nodes were positive. No angio or preneural invasion was identified. According to AJCC 8th Edition, patient was classified as Stage II PTC pT4aN1bM1. He was categorized as high risk of mortality and recurrence, therefore to suppress his TSH to 0.05-0.1, levothyroxine PO 225 mcg/day was started.

Labs showed TSH 0.03 (0.34-5.60 uIU/mL), Free T4 1.64 (0.61-1.76 ng/dL), Tg <0.2 (1.6-59.9 ng/mL), Tg by LC-MS/MS <0.2 ng/mL and Tg ab <20.0 (1.4-29.2 ng/mL).

Pre-therapy RA1-123 WBS with Recombinant Thyrogen, showed a focal radioiodine uptake (24 hr) of 1% in the neck, consistent with residual thyroid tissue.

The patient was treated with radioiodine 1-131 at the dose of 224 mCi with dosimetry. Post therapy WBS on day 5 was similar to the pre-therapy WBS with no evidence of metastatic disease. Stimulated Tg was 2.3 ng/ml (Immunoassay) and 2.6 ng/ml by LC-MS/MS with TSH 58.13 uIU/mL.

Conclusion: Metastatic DPTC is associated with marked elevation of basal and stimulated serum Tg. However 3-5% DPTC cases could have undetectable or very low Tg levels even after immunoassays interferences have been ruled out. In our patient there were no signs of dedifferentiation of primary or metastatic tumor. The pathophysiology may involve selective defects of thyroglobulin synthesis and sodium iodide symporter by the cancer cells while maintaining other aspects of thyroid cellular differentiation. Serum Tg many not be a reliable tumor marker for surveillance and follow-up in all patients with DPTC.

Abstract #1112

PRIMARY THYROID LYMPHOMA, A UNIQUE CASE REPORT

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1. University of Connecticut, 2. Hartford Hospital

Objective: Primary Thyroid Lymphoma (PTL) is a rare disorder, representing less than 2 percent of all primary malignancies of the thyroid. Prompt recognition and diagnosis is essential as this is a rapidly progressive disorder whose management differs greatly from all other thyroid malignancies.

Case Presentation: 59 year old female with a history of hypothyroidism due to Hashimoto’s disease who presented with rapid onset and progressive dysphagia. She first noted swelling in her neck 4 months prior and had thyroid ultrasound showing 0.7x1.8x1.2 cm left sided thyroid nodule. Chest CT scan showed incidental findings of multiple non-calcified lung nodules (largest in the left lower lobe 1.05 cm).

Patient underwent core needle biopsy of the largest lung nodule, which stained positive for cytokeratin 7, TTF-1, Tg, PAX-8, HMBE-1 stains, hence suggesting well DPTC. Ultrasound guided FNA of the thyroid nodules concurred the PTC diagnosis.

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Conclusion: Metastatic DPTC is associated with marked elevation of basal and stimulated serum Tg. However 3-5% DPTC cases could have undetectable or very low Tg levels even after immunoassays interferences have been ruled out. In our patient there were no signs of dedifferentiation of primary or metastatic tumor. The pathophysiology may involve selective defects of thyroglobulin synthesis and sodium iodide symporter by the cancer cells while maintaining other aspects of thyroid cellular differentiation. Serum Tg many not be a reliable tumor marker for surveillance and follow-up in all patients with DPTC.
doxorubicin, vincristine and prednisone (R-CHOP) chemotherapy. She received 4 doses as an inpatient and had rapid improvement in symptoms with ability to tolerate thin liquids and soft diet. She was discharged to home, and as an outpatient completed 6 cycles of R-CHOP chemotherapy. Repeat CT scan of the neck revealed that the previously demonstrated large mass in the left lobe of the thyroid had largely resolved.

**Conclusion:** Primary Thyroid Lymphoma presents as a rapidly enlarging neck mass or goiter with compressive symptoms, most often in the setting of background Hashimoto’s disease. Treatment of this disorder is unique to other thyroid cancers as there is no role for routine thyroidectomy or surgical intervention. The mainstay of therapy remains R-CHOP chemotherapy, with the majority of patients responding very well to this treatment.

**Abstract #1114**

**A UNUSUAL CAUSE OF EUTHYROID HYPERTHYROXINEMIA**

Hammad Hussain, MD

Mayo Clinic Health System

**Objective:** We describe a patient with euthyroid hyperthyroxinemia (EH) that was found to have point mutation in transthyretin gene

**Case Presentation:** 73 years old female was referred for abnormal thyroid level. She had removal of “thyroid nodule” 30 years ago and pathology was benign. Later her surgeon started levothyroxine in order to “suppress growth of new nodules”. She used levothyroxine since then with monitoring of TSH. Two years ago she had free T4 checked for the first time, which was elevated with normal TSH. Further testing reported both elevated total and free T4. Free T4 by equilibrium dialysis was also elevated. T3 checked on several occasions was normal. Alpha-subunit of pituitary was 0.4 ng/mL. HAMA antibodies was undetectable. Previously based on elevated T4 there has been attempt to reduce levothyroxine dose but she experienced fatigue, cold intolerance and constipation with decreased dose and in fact thyroid function tests throughout dose reduction remained essentially unchanged. Thyroxine binding protein electrophoresis reported elevated total T4 at 14.7 (4.5-11.7 mcg/dl), increased binding to pre-albumin at 74.7% (48.8-70.4 mcg T4/dL), decreased binding to albumin at 7.1% (11.5-34.1 mcg T4/dL), and normal binding to TBG at 18.2% (10.3 - 24.9 mcg T4/dL). There is no known family history of thyroid disease. Thyroid ultrasound reported sub-centimeter nodules. Considering genetic anomaly that resulted in increasing binding of thyroid hormone to thyroxine binding pre-albumin, genetic analysis was performed that revealed mutation of transthyretin (TTR) gene.

**Discussion:** TTR is protein of hepatic origin that transports 20-30% of serum thyroxine. There have been reports of clinically euthyroid individuals with hyperthyroxinemia secondary to increased binding of T4 with TTR. This patient was noted to have c.385G>A mutation. This specific mutation has not been associated with familial amyloidosis, but has been described in a Portuguese family that has EU. It raises protein bound fraction of total T4, but does not affect free T4. Unfortunately free T4 assays done in standard chemistry laboratory may be affected by extremes of binding abnormality. Therefore elevated free T4 may be inaccurate in this case. This condition does not require treatment. Offspring have 50% likelihood of inheriting this gene and have EH. Therefore if their thyroid level is checked and is abnormal, they may not need further evaluation or treatment.

**Conclusion:** It is important to identify increased thyroxine binding to tranthyretin causing EH. These patients do not require further treatment.
documented mixed systolic and diastolic HF. The primary end point of this study is maintenance levothyroxine dose (mcg/kg) used in patients with and without HF. Secondary endpoints include average EF in HF patients with elevated thyroid stimulating hormone (TSH) compared to normal TSH, percentage of patients with elevated TSH in the HF population compared to patients without HF, and average dose of levothyroxine in patients with normal TSH (range 0.27-4.5 mcIU/mL). The primary end point was analyzed using ANOVA. Secondary end points were analyzed using ANOVA and Chi-square tests.

**Results:** A total of 300 patients, 109 (36%) male with a mean age 69.9 + 13.6 years were included in the study with 100 patients in each arm. Average levothyroxine doses (mcg/kg) were 1.49, 1.59, and 1.51 for no HF, HF-HF, and other types of HF, respectively (p=0.62). Average EF was 43%, 45%, and 36% for HF patients with decreased TSH, normal TSH, and elevated TSH, respectively (p=0.035). The percentage of patients in the HF group with elevated TSH was 18% (n=53), compared to 6% (n=19) in the no HF group (p=0.347). The average dose of levothyroxine in patients with normal TSH was 87.5 mcg (1.5 mcg/kg) and not significantly different between the HF and no HF groups.

**Conclusion:** No differences were detected in levothyroxine dose in HF patients compared to patients without HF. An elevated TSH was associated with a lower EF in patients with HF. Given the risks associated with hypothyroidism in HF patients, future studies may be needed to address appropriate initiation and titration of doses for HF patients.

Abstract #1115

**SQUAMOUS CELL CARCINOMA OF THE THYROID**

Susan Shey, MD, Susana Harbutt, MD, Melissa Weinberg, MD

CPMC

**Objective:** Highlight squamous cell carcinoma (SCC) of the thyroid

**Case Presentation:** A 74 year old male with T2DM and HTN presented with 3 weeks of dysnea, dysphagia, and odynophagia. He had stridor, thyromegaly, and left cervical lymphadenopathy on exam. All thyroid labs were within normal range. CT head and neck showed multiple thyroid nodules compressing the trachea with a calcified 2 cm left lobe nodule and left vocal cord paralysis. Whole body PET CT revealed cervical and left supraclavicular lymph nodes and many pulmonary nodules consistent with metastatic disease. Pathology from FNA of the left calcified thyroid nodule revealed SCC of the thyroid. He underwent total thyroidectomy but failed intraoperative extubation and tracheostomy was placed. Surgical pathology showed bilateral SCC of the thyroid with extrathyroidal extension and positive margins. He had a poor prognosis from an oncology standpoint and was recommended palliative chemotherapy after adequate recovery post-op. He was discharged from the hospital, but was admitted 4 months later with respiratory distress and hemoptysis from the tracheostomy site. With his poor prognosis and concerns for tracheal metastasis causing airway obstruction, he was transitioned to comfort care with home hospice.

**Discussion:** Squamous cell carcinoma of the thyroid is a rare condition that is responsible for <1% of primary thyroid malignancies. The mean age of diagnosis is early 60s, seen more commonly in females (F:M = 2:1). Typically, it presents with a rapidly growing neck mass that can cause dysphagia, dyspnea, and/or hoarseness, but by this point the malignancy is already advanced. Metastases are common to the cervical lymph nodes, but can also spread to lungs, bone, liver, kidneys, and heart. In general, there are no guidelines to treatment. Primarily, surgical resection is the treatment of choice with the goal of negative margins, but because of high risk of relapse, usually adjunct radiation is necessary despite SCC of the thyroid being radio-resistant. There is poor response to chemotherapy, but cisplatin can be used with radiotherapy in cases of margin positive SCC. The primary cause of death is laryngeal or tracheal involvement leading to respiratory failure, which seemed to be the case in our patient. Overall, the prognosis is poor, with median survival of 9 months and most patients dying within 1 year after diagnosis.

**Conclusion:** Squamous cell carcinoma of the thyroid is a rare primary thyroid malignancy that remains difficult to treat as it generally presents at an advanced stage, has poor prognosis, and has limited treatment guidelines.

Abstract #1116

**RADIOACTIVE IODINE THERAPY FOR GRAVES DISEASE: WHAT PREDICTS FAILURE?**

Kalyani Regeti, MD, Rajinkanath Yatavelli, MD, Harsha Karanchi, MD, Binod Pokhrel, MD

LSU health Shreveport

**Objective:** RAI ablation with I-131 is used as permanent treatment option for patients with Graves’ disease. About 10-15% of these patients fail treatment for reasons not clearly defined. We evaluated the failure rate, mean RAI I-131 dose used and factors leading to failure of RAI ablation in patients with Graves’ disease at our institution.

**Methods:** Single center, retrospective chart review of 170 adult patients (age> 18 years) with Graves’ disease who underwent Radioactive Iodine I-131 ablation therapy.
between years 2011-2016.
Primary end point was failure rate of RAI therapy defined as persistent hyperthyroidism 6 months post RAI treatment. Secondary end points were mean RAI dose used and factors leading to RAI failure.

Results: Mean age was 40 (range: 18-67), n:170.
1.I-131 failure rate was 19.7%
2.Mean dose of I-131 used was 22.8 +/- 5.3 (mean +/- SD)
3.Factors predicting failure were age < 40 (26.5 vs 12.8%, p: 0.03), free T3/free T4 ratio >3.7 at diagnosis (26 vs 8.3%, p:0.01), free T3/Free T4 ratio >3.7 at pre-RAI therapy (31 vs 7.5%, p:0.0002), RAI 4/24 hr uptake > 0.8 (34.2 vs 8%, p:0.0009).
4.In multivariate analysis, men had higher failure rate (OR:6.3 (95% C.I of 1.5-26.2).
Pre-therapy Free T3/T4 ratio <3.7 were 82% less likely to have failure.

Discussion: Literature review showed female sex, younger age, larger goiters, and higher free T3 have been associated with rapid I-131 turnover. Large goiters and higher 5/24 hour uptake ratios have been independently associated with high failure rates.
I-131 RAI doses used at our institution for RAI ablation of Graves’ disease were typically higher than fixed doses described in literature.

In our analysis, male sex, age <40, higher free T3/Free T4 ratio and higher diagnostic RAI scan 4/24 hour ratio>0.8 were predictors of higher failure rate. We were unable to look at goiter size due to limitations of availability of goiter dimensions from ultrasound

Conclusion: In the setting of male sex, younger patients and higher free T3/Free T4 and higher RAI scan turnover, it may be important to be wary of higher failure rates.
Discussion of failure rates with RAI is important in informed decision making.
At this time, there is limited data on predictors of failure of RAI therapy in Graves’ disease and appropriate management of patients with higher likelihood of failure.

Abstract #1117

CENTRAL HYPOTHYROIDISM DUE TO SEVERE CUSHING’S SYNDROME FROM AN ACTH-PRODUCING PHEOCHROMOCYTOMA

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Marshall University

Objective: TSH suppression due to an elevated cortisol is well documented, but is rarely severe enough to suppress thyroid function. We report a case of hypercortisolism causing central hypothyroidism.

Case Presentation: A 46-Year-old woman presented with palpitations, tremors, headaches, and worsening diabetes and hypertension control for 3 months. She also noted irregular menstruation, weakness, cold intolerance, easy bruising, and 100 Lb weight loss during that time.
The endocrine service was consulted to rule out hyperthyroidism after a finding of a suppressed thyroid stimulating hormone of 0.057 mIU/mL (Ref 0.4-4 mIU/mL). She had no prior history of thyroid disease.

On exam, she had a moon face, significantly changed from her driver’s license, supraclavicual and dorsocervical fat pads, wide purple abdominal striae, thin skin, bruises, edema and muscle wasting. This raised suspicion for other endocrine disorders.

Further investigation showed a suppressed free thyroxine level of 0.67 ng/dL (0.8-1.4 ng/dL) and a low-normal Free Triiodothyronine. Metanephrines were elevated. Cortisol levels were significantly elevated with no suppression after dexamethasone. ACTH, testosterone and DHEA-S were elevated, gonadotropins suppressed and prolactin normal.

There was no pituitary lesion on MRI, but abdominal CT showed a 3.8 cm left adrenal mass.
A diagnosis of severe Cushing’s syndrome due to an ACTH-producing pheochromocytoma was made. Hypothyroidism was likely due to the severe hypercortisolism. She was started on levothyroxine replacement. After controlling her blood pressure, she had a left adrenalectomy. Levothyroxine was held post-operatively. All her symptoms resolved. A week later her thyroid function was normal. A year later she was free of Cushing’s, pheochromocytoma and thyroid disease.

Discussion: The suppressive effect of both endogenous and exogenous glucocorticoids on TSH secretion is well documented, but is usually mild and asymptomatic. However, our case had significant central hypothyroidism due to severe hypercortisolism. ACTH-producing pheochromocytoma is a rare cause of ectopic Cushing’s syndrome, and our case is only the third reported in the literature with this condition producing central hypothyroidism. Cortisol levels in ectopic Cushing’s are much higher than other causes of hypercortisolism, which could explain the severity of hypothyroidism. Complete resolution of thyroid dysfunction after treatment of hypercortisolism confirms the diagnosis.

Conclusion: Central hypothyroidism due to elevated cortisol levels could be clinically significant. ACTH-producing pheochromocytoma is a rare cause of this condition. Treatment of hypercortisolism results in resolution of the hypothyroid state.
Abstract #1118

PROPOSING A NEW DIAGNOSTIC ENTITY WITH THE NOMECLATURE “SILENT STORM” AS A SYNDROME THAT REQUIRES IMMEDIATE ATTENTION

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Objective: To propose a new diagnostic entity and nomenclature “Silent Storm” as distinct syndrome as distinct syndrome that requires immediate attention for early diagnosis and timely treatment

Methods: A 35 year old male with non-ischemic dilated cardiomyopathy with EF < 10% and history of Non-Sustained Ventricular Tachycardia on Amiodarone 200 mg daily developed nausea and later mild shortness of breath, admitted to the hospital Cardiac Unit for CHF exacerbation. He was found to have abnormal thyroid function tests done routinely with suppressed TSH and elevated Free T4 and T3. Endocrinology was consulted for evaluation of his thyroid status. Denies recent contrast use, no fever, no tenderness and no dysphagia. Patient appeared euthyroid. Patient was sitting comfortable in bed, talkative speaking full sentences and tolerating diet well. His temperature was normal and blood pressure was holding up with infusion of Milrinon with mild tachycardia. His mental status was normal, and found to have mild edema on exam. Patient was diagnosed with Amiodarone-Induced thyroiditis and was treated with high doses of Methimazole 40 mg TID; SSKI 4 drops Q6H; Lithium 300 mg with targeting serum level of 0.5-1.3; and Prednisone 60 mg QD. Charcoal Hemoperfusion was later considered but the patient clinical status deteriorated rapidly in the CCU with cardiogenic shock, multi-organ failure and sadly he passed despite maximal intensive care.

Case Presentation: On admission: Free T4: 6.47 ng/dL, Total T3: 249 ng/dL with TSH of 0.006 mIU/L. TPO-antibody is negative, TRAB-antibody is negative, TSI-antibody is negative, and Anti-TG antibody is negative. US of Thyroid showed heterogeneous enlargement of thyroid with normal vascularity and no discrete nodules. His TFT was responding to therapy Free T4: 3.98 ng/dL, Total T3: 100.4 ng/dL

Discussion: Patient was recognized as having a true thyroid storm despite his lack of classic features. The probability of him having a storm was low per Wartofsky score. We believe his significant decrease of physiological reserve, made him unable to mount normal response we usually see in profound hyperthyroidism and thyroid storm. However, his significant biochemical evidence of severe hyperthyroidism despite lack of symptoms and the rapid deterioration in the setting of CHF made us recognize the patient has thyroid storm.

Conclusion: Silent Storm or Silent Thyroid Storm is a thyroid storm that occurs in patients with severely decompensated heart failure and present with no overt storm signs and symptoms. Silent Storm requires immediate recognition by medical community to increase awareness for timely diagnosis and management of this high mortality syndrome.

Abstract #1119

TREATMENT PROCRASTINATION HURTS IN HURTHLE CELL THYROID CANCER

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Objective: Hurthle cell thyroid cancer (HCC) is relatively rare and accounts for 3% of differentiated thyroid cancer (DTC). It has more aggressive clinical behavior and higher rate of metastases, when compared with other DTC. We present a case of HCC, where untimely adjuvant therapy led to an unfavorable outcome.

Case Presentation: A 40-year old morbidly obese man, was incidentally found to have a 5.3 cm right thyroid nodule on CT thorax, done for neck pain after a fall. Thyroid ultrasound showed enlarged heterogenous thyroid lobe; 6.6 x4.3 x4.4 cm that was likely replaced by neoplasm. Thyroid function test was normal. He had FNA and pathology was suspicious for hurthle cell neoplasm. He had total thyroidectomy, pathology revealed right lobe multifocal HCC, largest was 6 cm, with capsular invasion and multifocal angioinvasion. Patient missed scheduled radioactive iodine (RAI) therapy due to his reluctance and procrastination. He was lost to follow up despite several attempts to reach out to him. 15 months later, he presented with neck pain after a fall. CT neck and chest showed expansive mass in C3 vertebral body with pathological fracture, lung nodules and enlarged right cervical lymph node. Biopsy of spine revealed metastatic HCC. Thyroglobulin level (TG) was 2662 ng/ml (<35 ng/ml), with negative antibody and TSH of 1.67 uIU/ml (0.27-4.2 uIU/ml). He had C3 corpectomy, surgical decompression and fusion of C2 to C4. He received external beam radiation to the spine and RAI therapy with 194 mCi. Post RAI scan showed no evidence of iodine avid lesions. One-week post RAI, he presented with painful mass in left upper extremity, biopsy of which revealed metastatic HCC. He was started on Tyrosine Kinase Inhibitor (lenvatinib) and denosumab. Despite these treatments, his clinical condition did not improve, and TG level remained elevated. He succumbed to his disease, about 2 years from initial diagnosis.

Discussion: Increasing age, tumor size, male sex and wide
vascular invasion are predictors of poor outcome in HCC. Treatment of HCC, is based on same ATA guidelines as that for other DTC, with surgery as first line, and adjuvant therapy including TSH suppression, RAI therapy, external beam radiation and systemic chemotherapy. Timely management with these treatment modalities have shown favorable outcome and decreased recurrence in HCC. The 10-year disease specific survival of HCC without metastasis is about 90%, but decreases to 60% with metastasis. Distant metastases and recurrence is common in invasive HCC; thus, adjuvant therapy should not be delayed as happened in our patient. 

**Conclusion:** Patients should be informed of the aggressive behavior of HCC and thus need for earlier adjuvant therapy and close follow up.

**Abstract #1120**

**EPIDEMIOLOGY AND RISK OF MALIGNANCY IN INDETERMINATE THYROID NODULES**

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Northern Ontario School of Medicine

**Objective:** Millions of people are now diagnosed with incidental thyroid nodules. Around 30% of nodules belong to the indeterminate category. We conducted a retrospective chart review to characterise the epidemiology, pattern of care and the risk of malignancy of indeterminate thyroid nodules under the category of atypia of undetermined significance (AUS).

**Methods:** The study cohort consisted of all patients who underwent cytological testing at Health Sciences North, Sudbury, Ontario, between January 1, 2011, and December 31, 2015. Demographic, clinical and histopathological data were obtained from electronic medical records.

**Results:** We identified 139 subjects (84% women, median age: 58.5 years) with indeterminate thyroid nodules during the study period. Almost 60% of patients underwent surgical procedures such as total thyroidectomy, hemithyroidectomy and completion thyroidectomy (Table 1). The incidence of histopathology confirmed malignancy was only 32% however 22% of patients with confirmed malignancy had microcarcinoma. Male gender, age<50 years and sonological features were discriminative of malignant potential. Around 52% of cases with confirmed malignancy showed at least 1 suspicious sonological feature. One-in four patients underwent repeat biopsy (n=36/139). In this subgroup most patients had either ALUS or benign features. Two of the 36 patients had a malignancy on repeat cytological study. Only 40% (forty) of the non-surgical subjects underwent repeat FNAB during the observation period.

**Discussion:** Our results suggest that only one forth of patients with indeterminate thyroid nodules are at risk of malignancy. In the absence of molecular testing, the management of indeterminate thyroid nodules involves unwanted diagnostic surgeries, repeated cytological studies, morbidity, risk of surgical complications and huge health care expenditure.

**Conclusion:** We report the clinical trajectory and incidence of malignancy in patients presenting with indeterminate thyroid nodules. This is the first report describing the epidemiology and clinical features of indeterminate thyroid nodules in patients living in Northern Ontario, Canada. Our results support the argument that molecular diagnostics should be proposed in the management of indeterminate nodules in order to avoid unwanted diagnostic surgeries and morbidity.

**Abstract #1121**

**A CASE OF REVERSIBLE PARALYSIS**

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**Objective:** Thyrotoxic periodic paralysis (TPP) is a life threatening complication characterized by acute onset of reversible painless paralysis and hypokalemia in setting of hyperthyroidism. Severity ranges from mild weakness to life threatening paralysis. Incidence is rare, with male predominence, occurring in second and fourth decade of life. Prevalence is 2% of Asian patients with hyperthyroidism and 0.1-0.2% in American Caucasians with thyrotoxicosis. Inciting factors include stress, alcohol ingestion, and high carbohydrate ingestion. We present a case of TPP in a biracial male where early recognition of disease led to rapid improvement without complications.

**Case Presentation:** 21-year-old Hispanic-American Indian male presented with inability to move both lower extremities. 12 hours prior he had a large amount of pizza and awoke with significant weakness that progressed to complete paralysis. One month ago he was diagnosed with Grave’s disease but did not start treatment as recommended and had repeated episodes. No other past surgical or social history existed. Family history was negative for periodic paralysis or thyroid disorders. Review of systems was positive for nausea, vomiting, and diarrhea. Initial vitals remarkable for tachycardia. Exam revealed a well-nourished male, with rapid speech and bilateral exophthalmos. No thyroid bruit on neck exam. Fine motor tremor of hands was noted. Strength of bilateral proximal lower extremities was 2+/5, distal lower extremities 5/5,
with proximal upper extremity 4+/5, distal 5/5. Initial serum potassium was 2.7 mEq/L, magnesium 1.7 mEq/L, TSH <0.005 mIU/L, free thyroxine (T4) 4.28 ng/dL, free triiodothyronine (T3) 16.6 pg/mL, TSH receptor antibody 14.09 IU/L. Parenteral potassium replacement was started. After 24 hours of treatment, patient reported complete resolution of symptoms. He was diagnosed with TPP due to untreated Grave’s Disease, started on methimazole and propranolol and discharged home safely with follow up with Endocrinology.

Discussion: Pathogenesis of TPP is thought to be due to thyroid hormone sensitization of Na+/K+-ATPase causing increased intracellular shift of potassium resulting in proximal muscle weakness. Another theory relates mutations in Kir2.6, an inwardly rectifying potassium channel causing hypokalemia induced inexcitability of skeletal muscles during periods of hyperthyroidism.

Conclusion: Treatment of hyperthyroidism is best to prevent TPP. Correction of life threatening hypokalemia should occur but overcorrection should be avoided. Early recognition as a potential etiology for muscle weakness can minimize diagnostic tests, decrease length of stay, and help educate patients on how to prevent future episodes.

Abstract #1122

FATAL THYROTOXICOSIS IN UNDIAGNOSED GRAVES’ DISEASE PRECIPITATED BY WEIGHT LOSS SUPPLEMENTATION

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Saint Peters University Hospital, New Brunswick, New Jersey

Objective: To report a case of fatal thyrotoxicosis in a susceptible patient taking a weight loss supplement.

Case Presentation: A 26-year-old female presented to the emergency department for evaluation of multiple complaints including loose stools, palpitations, and sweating. She also reported hyperactivity and amenorrhea. She was previously diagnosed with a condition of the thyroid, but had no follow-up. There was no known exposure to iodine and no irregular use of prescribed medication. There was a family history of thyroid disease. Her blood pressure was 119/89 mmHg, pulse rate was 160 bpm and irregular, and respiration rate was 27 breaths per minute. Her temperature was 96.9F, oxygen saturation was 99% on room air, and body mass index was 30 kg/m2. Findings included diaphoresis, proptosis with periorbital edema, and enlarged thyroid. The extremities were cool, with bilateral tremor and edema present. Electrocardiogram showed atrial fibrillation, and after attempts at rate control she became hypotensive requiring cardioversion and intubation.

Work up revealed free T4 at > 6.00 ng/dL, TSH at 0.108 mIU/L, and elevated anti-thyroid stimulating hormone receptor antibodies. She was diagnosed with Graves’ disease and managed for thyroid storm. Upon further investigation, it was disclosed that she was using weight loss supplements for the last month, and was consuming double the recommended dose. Her hospital course thereafter was complicated by multi-organ failure, and she expired after one month of intensive care.

Discussion: Nearly one third of nonprescription weight loss products marketed in the United States contain clinically relevant amounts of thyroid hormone. Although the chemical composition of the product in this case could not be analyzed, given the patient’s presentation and those characterized in previous reports, it was likely contaminated with thyroid hormone exceeding therapeutic doses. While undiagnosed Graves’ disease is uncommon in the general population, the estimated prevalence of weight loss supplementation use approaches twenty percent. Products with disclosed or surreptitious addition of thyroid hormone may induce a rapid rise in serum thyroid levels, intensify sensitivity to catecholamines, or augment the response to hormone and precipitate fatal thyrotoxicosis in susceptible individuals.

Conclusion: Weight loss supplements may contain clinically significant amounts of thyroid hormone, and use of these products should be evaluated when determining inciting factors for thyrotoxicosis. The unique epidemiology of this case highlights the potential for contaminated weight loss products to result in devastating consequences in patients at risk of hyperthyroidism.

Abstract #1123

PAPILLARY THYROID CARCINOMA WITH ANAPLASTIC TRANSFORMATION

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Objective: To present a natural history of Papillary thyroid carcinoma (PTC) transformation to anaplastic thyroid carcinoma (ATC) with poor prognosis

Case Presentation: A 55-year-old male presented with shortness of breath since 1 week before admission. Five years prior to this episode, he had lumps on the neck and behind his right ear. He underwent surgery and pathological report revealed PTC with lymph node metastases. He refused to receive any medical treatment afterwards. Four
months prior to admission he noticed that lump developed above his right clavicle. The mass extended to his skin that then burst out forming ulcer that eventually became larger. Moreover, the ulcer has foul odor and discharge. On physical examination, he was hemodynamically stable, tachypnea, normal body mass index, pale conjunctiva, and left lobe of thyroid was palpable. An extensive irregular mass with ulcers on his neck extending to the chest with pus and necrotic tissues. Lymph nodes were found on both sides of his neck and right axilla. Bilateral rhonchi was found without any wheezing and edema on his all extremities. Laboratory result showed anemia (hemoglobin of 5.7 g/dL), leukositosis (23,900 cel/mm3), hyponatremia hypoosmolar hypovolemia (Natrium 127mmol/L), hypoaalbuminemia of 2.2 g/dL, hypercalcemia (calcium 10mg/dL, corrected 11mg/dL). Thyroid function was in hypothyroid range (TSHs 18.2 mU/L, fT4 0.27 ng/dL). Thoracic CT scan demonstrated mass in right thyroid extending to the left infiltrating surrounding muscles and destructing right clavicle and scapula bones. Mass extended to right superior mediastinum and multiple nodes were found in both lungs. He received blood transfusion, fluid resuscitation, antibiotic, albumin correction, and treatment for his hypercalcemia. Also, Levothyroxin was initiated. He underwent biopsy for the mass and pathological result came back with anaplastic thyroid carcinoma. Following his symptoms alleviated, patient refused to receive any further medical treatment.

Discussion: ATC is a rare form of thyroid carcinoma comprising approximately 1% of thyroid malignancy. Most of ATC developed on the thyroid gland itself or spreading to surrounding neck lymph nodes as part of metastatic from well-differentiated that underwent anaplastic transformation from existing PTC. Poor prognosis in ATC associated with older age, male gender, leukositosis, tumor size, extrathyroidal invasion, and presence of distant metastases as found in this patient.

Conclusion: PTC is a well-differentiated with good prognosis that may evolve into poorly differentiated thyroid carcinoma (ATC). This case represents an observation of natural history of this transformation since the patient refused most of medical treatment.

Abstract #1124
SECOND PRIMARY THYROID CANCER CHARACTERISTICS IN PATIENTS WITH SKIN MALIGNANCIES
Kathleen Gallagher, BS, Chelsea Isom, MD, Christina Bailey, MD, Rondi Kauffmann, MD, Naira Baregamian, MD
Vanderbilt University Medical Center

Objective: Thyroid cancer (TC) is the most common endocrine malignancy and rarely presents as a second primary malignancy in patients with skin cancers. In this study we aim to assess clinicopathologic characteristics of TC as a second primary malignancy.

Methods: A retrospective review was performed of patients who underwent thyroid surgery and skin cancer resection (melanoma, merkel cell carcinoma, mucinous carcinoma) over the last 10 years. Preoperative TC detection, TSH level, clinicopathologic features of each malignancy, and patient characteristics were evaluated. Outcome measures included time to TC diagnosis, mode of detection, type of surgical treatment, need for radioactive iodine (RAI) ablation and status at last follow up visit.

Results: We identified 239 patients with second primary tumor malignancies who underwent surgical resection of skin malignancies, and 13 patients (5.4%) were diagnosed with TC as second primary malignancy with mean age of 54.2±16.1 years and had undergone resection of both malignancies. Skin malignancy was diagnosed first (n=12, 92.3%), and malignant melanoma (n=11, 84.6%) was the predominant type. Most melanomas presented at a later stage (III, n=6, 54.5%) and were intermediate thickness (median Breslow depth 1.7 mm, IQR 0.87-5.5). Time to TC diagnosis was short (median 148 days). Preoperative TSH levels were all within normal range. PET scan (n=7, 53.8%) was the most commonly used initial imaging modality. All patients underwent preoperative fine needle aspiration (FNA) of thyroid nodules that demonstrated either malignant (n=6, 46.1%), indeterminate (AUS/FLUS, n=5, 38.5%), or suspicious for malignancy (n=2, 15.4%) cytology. Total thyroidectomy (n=8, 61.5%) was commonly performed. Thyroid tumor was small (median size 11 mm, IQR, 2.5-17), seldom demonstrated extrathyroidal extension (n=1, 7.7%), or tumor capsular invasion (n=3, 23.1%), and presented at an early stage (stage I, 76.9%, stage II, 23.1%). The predominant tumor type of TC was classic papillary (n=9, 69.2%), no metastatic malignant tumors were detected in the thyroid. Few patients required postoperative RAI ablation (n=2, 15.4%). Median length of follow-up was 883 days (IQR, 468-1948). At last clinic visit, 84.6% (n=11) of patients were disease free, with 2 deaths attributed to melanoma and colon cancer.
Conclusion: Patients with skin malignancies are quickly diagnosed with TC as a second primary malignancy at the time of postoperative metastatic work up using PET scan imaging. TCs have low-risk tumor pathologic features, and rarely require RAI. Thyroid lobectomy may be an adequate surgical approach for the small, low-risk tumors in this unique patient population.

Abstract #1125

AN UNUSUAL PRESENTATION OF GRAVES OPH-THALMOPATHY

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Texas Tech University Health Sciences Center

Case Presentation: A 65-year-old man was followed in Endocrinology clinic for post-surgical hypothyroidism. He was a nonsmoker. He had Graves’s disease diagnosed ten years ago without eye symptoms. Methimazole was started after initial diagnosis. He had difficulty achieving euthyroid state for three years despite frequent dose adjustments. Suppression therapy failed, necessitating total thyroidectomy for definitive treatment. Post-surgery, thyrotoxicosis completely resolved. He was started on Levothyroxine replacement and remained euthyroid on a stable dose for several years.

Ten years after his initial Graves’ disease diagnosis, he developed bilateral eye irritation. He had rapid symptom progression within weeks leading to proptosis, photophobia, diplopia, and eye pain. Exam revealed periorbital edema, exophthalmos, lid lag, conjunctival congestion and ophthalmoplegia. Laboratory data showed TSH, 5.1 mIU/mL (0.3-5.3), FT4, 1.2 ng/dL, (0.7-1.4), Thyroid Stimulating Immunoglobulin (TSI) antibodies, 459 (normal <139%). He was diagnosed with Graves Ophthalmopathy.

Discussion: Graves ophthalmopathy is a potentially sight-threatening ocular disease due to risk of compressive optic neuropathy. It occurs in 5-7% of patients with Graves’ disease and is more common in females and smokers. The temporal relationship between ocular expression and systemic thyrotoxicosis is occurrence of orbitopathy usually at or within two years of diagnosis. It is unusual to develop eye disease, several years after onset of Graves’ disease. Our patient had thyroid eye disease lagging initial Graves’ disease diagnosis by ten years, which is the longest that we know so far.

Thyroid eye disease is usually seen in association with hyperthyroidism and tends to improve with resolution of systemic thyrotoxicosis. Graves ophthalmopathy has a close association with Graves’ hyperthyroidism, due to their common immunoreactivity against the thyrotropin receptor.

Eye disease occurrence with euthyroidism, as in our case is very rare. Only 5% of patients with Graves’ ophthalmopathy are euthyroid or hypothyroid and tend to have low titers of circulating antibodies. Our patient had elevated TSI antibodies in a clinically euthyroid state, several years after total thyroidectomy, which is very unusual.

Conclusion: Thyroid orbitopathy can have a separate clinical course, unrelated to systemic thyrotoxicosis.

Abstract #1126

SALIVARY GLAND MALIGNANCY AS A COMPLICATION OF THYROID CANCER MANAGEMENT.

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Objective: Radioactive iodine (I-131) ablation is commonly used in the management of differentiated thyroid cancer. Several secondary malignancies are reported in association with RAI use, most common being GI cancers (gastric and colon), breast cancer, bladder cancer and rarely salivary gland cancers. We present a case of young woman with differentiated thyroid cancer, treated with surgery and RAI who developed salivary gland cancer 15 yrs after the treatment.

Case Presentation: 33 year old female who initially presented in 2002 at age of 18 for evaluation of a left thyroid nodule. Fine needle aspiration was positive for papillary carcinoma. Patient underwent a total thyroidectomy - pathology showed a 1 cm papillary carcinoma in the left lobe, 5mm papillary carcinoma in the right lobe along with numerous foci of papillary micro carcinoma and a 1 mm extra thyroidal nodule within the surrounding soft tissue. Three of four level six nodes removed were positive for papillary carcinoma. She subsequently received 125 mci of I-131 due to the nodal and microscopic extrathyroidal disease. Whole body scan post ablation showed uptake deep in the neck, follow up ultrasound showed 1.3 cm suspicious node in rt paratracheal region. Pt had a repeat neck dissection in the right and left paratracheal regions revealing twelve positive paratracheal nodes on right, one on left, plus a deep right jugular node. After neck dissection she received one dose of I-131 - 150 mci. Since then pt has been closely monitored with periodic imaging. TCs have low-risk tumor pathologic features, and rarely require RAI. Thyroid lobectomy may be an adequate surgical approach for the small, low-risk tumors in this unique patient population.
ultrasounds and thyroglobulin panel testing. TSH was maintained between 0.1-0.5, Thyroglobulin level has remained 0.1 – 0.3 ng/mL. Neck ultrasounds performed over the past 15 years showed no evidence of recurrent structural disease. Most recently patient noted a lump in the right side of the neck. Ultrasound showed no lymph nodes in neck but showed a 10 mm complex cystic lesion in the right parotid gland. Lesion was eventually resected and it turned out to be a mucoepidermoid carcinoma, thought to be related to I-131 exposure.

**Discussion:** Salivary gland problems such as sialadenitis and xerostomia are commonly seen after RAI but salivary gland cancers are rare. Evidence shows that people who receive RAI ablation have 27% increased risk of developing other malignancies compared to general population. Increased incidence of cancer is noted with a single or cumulative dose of RAI of 150 mci or greater.

**Conclusion:** Several studies have shown that low dose RAI of 30 mci is equally effective for remnant ablation. Hence currently higher doses of 150 mci and above are reserved for bulky nodal disease or distant metastasis.
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