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ADRENAL DISORDERS

Abstract #100

AUTONOMOUS MASSIVE MACRONODULAR ADRENALS IN THE SETTING OF CONGENITAL ADRENAL HYPERPLASIA

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Case Presentation: A 74 year old male presented to our Endocrinology clinic for workup of incidentally found adrenal enlargement and nodules on CT. Both adrenals showed diffuse nodular thickening and measured 7.7 cm on greatest dimension on the left and 6.5 cm on the right. The left adrenal had a 4.3 x 2.4 cm nodule (38 HU; 75% washout) and right adrenal had a 2.5 x 1.9 cm nodule (38 HU; 67% washout). On history patient stated that he was born with a birth defect (hypospadiasis and undescended testis bilaterally). Also, at age 12 during an appendectomy, a benign tumor was removed from his pelvis (no records available). Patient claims normal puberty, but he did stop growing early after being the tallest kid in his class briefly. Patient had a male phenotype with male pattern hair growth, height 4’11” and a normal physical except for micropenis, hypospadiasis and absent testis bilaterally. Hormonal workup showed a 17-hydroxyprogesterone (17-OHP) level >50,000 (40-180 ng/dl), DHEAS 150 (10-204 mcg/dl), testosterone 121 (220-1000 ng/dl), FSH 102 (1-10 mU/ml), LH 55 (1-7 mU/ml), Androstenedione 5.3 (0.7-2.2 ng/ml), 11-deoxycortisol 16 (<49 ng/dl), 11-deoxycorticosterone <5, ACTH 38 (8-42 pg/ml). Patient had normal plasma metanephrines, aldosterone, renin, salivary cortisol and normal suppression of cortisol with dexamethasone. After administration of 1 mg dexamethasone, 17-OHP dropped to 2,471 and androstenedione to 2.2. On ACTH stimulation test for adrenal insufficiency, the patient had a sub-optimal response of 9.8, 9.9, 12.1 (baseline, 30, 60 min). US revealed no testis in the scrotum or inguinal area. Review of CT images showed no gonads in the pelvis. Estradiol was 27 (10-60 pg/ml), inhibin <10 pg/ml, AMH <0.003 (2-30 ng/mL). Chromosome analysis revealed XX.

Discussion: Untreated CAH patients tend to have adrenal masses but enlargement to the extent depicted here is unusual. The presence of gonads. Primary or ACTH-independent bilateral macronodular adrenal hyperplasia (BMAH) is usually associated with Cushing’s syndrome and suppressed ACTH. In CAH on the other hand, steroidogenesis is ACTH mediated and levels are usually elevated >70. Our patient had an ACTH in the normal range indicating that the adrenals seemed to have become partially autonomous. The presence of long-term untreated CAH caused the adrenals over time to become autonomous and escape the control of ACTH. Conclusion: A very interesting case depicting the co-occurrence of BMAH and CAH. BMAH is one situation where one should check a 17-OHP level.

Abstract #101

A CURIOUS CASE OF SPINAL EPIDURAL LIPOMATOSIS (SEL): A SIGN INDICATING CUSHING’S SYNDROME

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Objective: Recognizing spinal epidural lipomatosis (SEL) as one of the signs of glucocorticoid excess. SEL is accumulation of excessive fat within the spinal epidural space, most commonly in the lumbar region, compressing the thecal sac, resulting in compressive symptoms. The most common cause being excess glucocorticoids either exogenous or endogenous (Cushing’s syndrome). Also seen in morbid-obesity, while some are idiopathic. Clinical presentation is usually non-specific, varying from completely asymptomatic to pain with radicular symptoms and weakness in lower extremities.

Case Presentation: We report a 74-year old Nepalese women who had MRI-Lumbar Spine for evaluation of chronic back pain which showed epidural lipomatosis. Since spinal epidural lipomatosis is seen in glucocorticoid excess, a 1 mg overnight dexamethasone suppression test (ODST) was performed. Early morning cortisol level was 16.8 ug/dl and Dexamethasone level was 792 ng/dl (Reference range <50 ng/dl). Cut off value of 1.8 ug/dl for AM cortisol was used which indicated cortisol excess. Three consecutive midnight salivary cortisol, and Abdomen/pelvis CT with adrenal protocol were ordered to confirm the diagnosis and assess the adrenal glands. Discussion: The mechanism of epidural lipomatosis caused by glucocorticoid-excess is not exactly known. Epidural
lipomatosis should raise the suspicion for hypercortisolism and patients with hypercortisolism who have back pain should be evaluated for epidural lipomatosis. Careful neurologic examination of patients with Cushing’s syndrome should be performed and should be evaluated with spinal MRI if neurological signs and symptoms are present. In most cases, no specific treatment is required, although causes of endogenous steroid excess and exogenous steroid use should be assessed. In patients with severe symptoms including neurologic deficits, operative decompression is recommended.

**Conclusion:** Spinal Epidural Lipomatosis (SEL) seen on MRI-Spine should raise the suspicion for glucocorticoid excess and prompt further evaluation.

**Abstract #102**

**EXTERNAL BEAM RADIATION THERAPY AS AN ADJUNCTIVE FOR BENIGN PARAGANGLIOMA**

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**Objective:** Paragangliomas (PGL) are catecholamine-secreting extra-adrenal tumors. Management of even nonfunctional PGL needs meticulous preparation and a multidisciplinary approach. Radiotherapy (RT) is reserved for unresectable, malignant or metastatic lesions. We present a case of benign aortocaval PGL that was clinically silent, yet the definitive treatment proved quite challenging.

**Case Presentation:** 71-year-old male with uncontrolled hypertension presented with lumbar and leg pain. CT abdomen revealed a 6.6 cm aortocaval mass. Biopsy was consistent with extra-adrenal pheochromocytoma. The procedure was uneventful. Biochemical testing done only after the biopsy showed elevated plasma metanephrines 715 (0-62 pg/ml), normetanephrines 1615 (0-145 pg/ml), and norepinephrine 1335 (0-874 pg/ml). MIBG scan showed avid uptake in the right suprarenal fossa and no distant metastasis. In addition to PGL, a 1.5 cm lung lesion was identified on PET-CT. Biopsy of this lesion revealed primary adenocarcinoma. Despite preoperative medical optimization over 3 weeks with prazosin, bisoprolol and metyrosine, intraoperatively patient had extremely labile blood pressure necessitating use of nitroprusside drip. Surgery was aborted. PGL was considered unresectable at that time. Patient was treated with external beam RT (25 Gy to the PGL and 50 Gy to the lung lesion). Phenoxybenzamine, metoprolol and metyrosine were continued as outpatient. A follow-up CT six weeks later showed necrosis of the PGL though size remained unchanged. 24-hour urine metabolites were still elevated. Finally, patient underwent uneventful resection of PGL with fast recovery. Follow up biochemical testing was normal. MIBG scan showed no residual uptake and genetic testing was negative.

**Discussion:** Manipulation of PGL, biopsy or resection, presents a unique challenge due to inherent risks associated with excess catecholamine release and variable anatomic presentation. RT is often used for malignant or metastatic lesions. Current guidelines do not support RT for treatment of benign PGL. RT results in decreased catecholamine production and reduced tumor burden without substantial radiological changes. Typical dose used is 45 Gy. Despite these effects, RT alone does not suffice in terms of functional control. Our patient had adrenergic crisis in spite of adequate preoperative preparation. RT dose used in this benign PGL was lower than suggested in literature, yet RT led to tumor necrosis while tumor size was unchanged. Subsequent surgical resection resulted in a favorable outcome.

**Conclusion:** This case highlights the importance of multidisciplinary approach and use of multiple modalities for successful treatment of even benign PGL.

**Abstract #103**

**ADRENAL INSUFFICIENCY AS A HARBINGER OF WORSENING POEMS SYNDROME**

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University of Nebraska Medical Center

**Objective:** POEMS syndrome is a rare paraneoplastic disorder characterized by polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes. Endocrinopathy is a minor criteria for diagnosis of POEMS. POEMS syndrome itself is quite rare, and adrenal insufficiency as an endocrinopathy is also uncommon. We report a case of simultaneous presentation of adrenal insufficiency and primary hypothyroidism in a patient with Castleman’s Disease and POEMS years after development of other endocrinopathies. We propose that adrenal insufficiency and primary hypothyroidism were the markers of worsening of POEMS syndrome.

**Case Presentation:** The patient was 48 years old when he was diagnosed with Castleman’s and POEMS. He was treated with cyclophosphamide, rituximab, and dexamethasone initially before undergoing bone marrow transplant and attaining remission. His initial endocrinopathies around time of diagnosis included Type 2 diabetes and primary hypogonadism. His diabetes required treatment with a sulfonylurea and eventually insulin, and his hypogonadism was treated with testosterone replacement. After his transplant, he was able to stop testosterone.
initially did well post-transplant, but a few years later was evaluated for worsening fatigue and was diagnosed with primary hypothyroidism and started on levothyroxine. He also had weight loss, diarrhea, abdominal pain, and tanned skin, so underwent evaluation for adrenal insufficiency. An ACTH stimulation test showed an elevated baseline ACTH level of 92 pg/ml and stimulated cortisol of 14.3 mcg/dl, consistent with primary adrenal insufficiency. He was started on replacement with hydrocortisone, but despite this, his POEMS worsened. Due to increasing proteinuria and lymphadenopathy, he underwent repeat bone marrow and kidney biopsies and was restarted on rituximab and prednisone for worsening POEMS. He had elevated serum free light chains, denoting B-cell/plasma cell activation from the POEMS as well as elevations of VEGF and IL-6, signifying worsening POEMS. He remains on treatment for primary adrenal insufficiency with hydrocortisone and fludrocortisone was added for worsening orthostasis. He is also back on treatment for hypogonadism.

**Discussion:** POEMS syndrome and Castleman’s Disease are rare disorders, but important to be aware of due to the associated endocrinopathies. Hypogonadism is the most common endocrine abnormality seen in these patients, followed by hypothyroidism and diabetes. Adrenal insufficiency is rare. **Conclusion:** We propose that development of primary hypothyroidism and primary adrenal insufficiency and recurrent primary hypogonadism signified worsening POEMS syndrome. This has not previously been described in the literature.

**Abstract #104**

**PRIMARY ADRENAL LYMPHOMA PRESENTING AS BILATERAL ADRENAL MASSES.**

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**Objective:** Incidentally discovered adrenal masses (“Incidentalomas”) are commonly encountered. Prevalence of Incidentalomas on CT scans increase with age; 7% in patients older than 70 years of age. Although most incidentaloma’s are unilateral about 15% of incidentalomas occur bilaterally. Differential of bilateral masses include metastatic disease, C.A.H., bilateral cortical adenomas and infiltrative processes including infectious. We report a case of Primary adrenal lymphoma (PAL) presenting as rapidly enlarging adrenal masses.

**Case Presentation:** 64-year female admitted to the hospital with worsening back pain, limiting her ADL’s for 3 weeks prior to presentation. CT angiogram done on initial presentation to rule out embolism showed bilateral adrenal masses 6.2cm and 4.4cm on right and left respectively. CT scan done four years ago, had not shown any adrenal masses. Patient reported 30-lbs. weight loss, night sweats, poor appetite in the last 3 months. Age appropriate screening test include normal mammogram and pap smears. She never had a colonoscopy. Exam was negative for lymphadenopathy, fecal occult blood testing. Initial blood testing showed mild normocytic anemia with normal differential. PPD and HIV testing were negative. No travel history or sick contacts were reported. Biochemical adrenal cortical (DHEAS 84.3 ug/dl AM cortisol 21ug/dl, ACTH 85pg/ml, renin 56ng/ml/hr., aldosterone 1.4ng/dl and 24-hour urine for normetanephrines and metanephrines were 362 ug/24hr and <14ug/24 hours) respectively. CT guided biopsy of right adrenal mass showed diffuse large B-cell lymphoma (CD 20, MUM-1 positive, Ki 67 98%, negative for BCL 2, BCL 6 and myc). Pan CT imaging and bone marrow biopsy did not show any lymphadenopathy or marrow involvement. Interval increase was noted in 2 months since last imaging. (7cm right and 6 cm left). FDG- PET scan showed hyper metabolism in both adrenal (SUV 51) but also showed four areas of intense uptake in the heart (Maximum SUV 20.4) and L3 vertebra. R-CHOP therapy was started, repeat PET scan after 3 rounds of chemotherapy showed complete resolution of the adrenal and intracardiac involvement.

**Discussion:** Primary adrenal lymphoma represents 3% of the extra nodal lymphomas. Most common type of adrenal NHL is Diffuse Large B cell lymphoma (DLBCL) phenotype, comprising 70% of cases. This type follows aggressive clinical course which can manifest itself as rapid adrenal enlargement and primary adrenal insufficiency without typical skin pigmentation (because of rapid adrenal destruction). **Conclusion:** PAL should be considered in the differential diagnosis of bilateral incidentalomas and rapidly enlarging adrenal masses.
Abstract #105

ACTH-SECRETING OLFACTORY NEUROBLASTOMA: A CASE REPORT

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Objective: This case report aims to present on diagnosis and management of an ACTH-secreting olfactory neuroblastoma.

Methods: Case review and follow-up of the patient was done.

Case Presentation: R.H., 47 year-old female, presented with hypercortisolism, such as weight gain, easy bruisability, bilateral lower extremity edema, hypertension, hyperglycemia and hypokalemia. She had elevated cortisol levels, unsuppressed with dexamethasone suppression test. This points to Cushing’s syndrome. Elevated ACTH pointed to an ACTH-dependent Cushing’s syndrome. Incidentally, patient also had anosmia with rhinorrhea. On MRI, she had left nasal mass eroding the cribiform plate. Endoscopic endonasal excision of left intranasal mass done. Histopathology revealed olfactory neuroblastoma. Immunologic stains were done with positive results on ACTH, synaptophysin, chromogranin, S-100. Upon removal of the mass, hypercortisolism, hypertension, hyperglycemia and hypokalemia were resolved. This confirmed an ACTH-secreting olfactory neuroblastoma. PET scan was done revealing metastasis to the bones. Patient underwent cisplatin-based combination chemotherapy for six cycles. Repeat cortisol and ACTH were normal. No recurrence of the tumor. PET scan done after chemotherapy revealed negative for metastases.

Discussion: There are only 18 cases of ectopic ACTH-secreting olfactory neuroblastoma in the international registry. The youngest of which presented in a 3 year-old male and the oldest case was that of a 70 year old male. Olfactory neuroblastoma is a rare malignant tumor that arise from the olfactory epithelium with neuroendocrine origin. The mean age is 53 years old and predominantly in males. The most common presentation is nasal obstruction. Other symptoms include epistaxis, anosmia, or nasal pain. Local extension affects the eyes, ears, eustachian tube and frontal sinus. Staging is based on Kadish clinical staging system. Bone metastasis in the patient is staged D. The mainstay of treatment of olfactory neuroblastoma is surgical resection. Metastatic olfactory neuroblastoma is managed with chemotherapy of cisplatin-based combination regimens due to its positive outcome in head and neck cancers and neuroendocrine-type cancers. There are no formal guidelines on posttreatment surveillance. Local recurrence of olfactory neuroblastoma is 10-15 years. Prognosis of metastatic disease shows five-year overall survival rates of 80-90%. Normal cortisol and ACTH show no recurrence of the ACTH-secreting tumor.

Conclusion: ACTH-secreting olfactory neuroblastoma with metastasis on the bones is a rare case in a 47-year old female who presented with Cushing’s syndrome. It is effectively managed with surgical resection and cisplatin-based chemotherapy.

Abstract #106

CONGENITAL ADRENAL HYPERPLASIA PRESENTING WITH GIANT ADRENAL MYELOLIPOMAS

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Objective: To present a case of giant adrenal myelolipomas in a patient with congenital adrenal hyperplasia (CAH) 21-a hydroxylase deficiency and review the presentation of this rare disorder and treatment considerations.

Case Presentation: A 40-year-old male presented with a year of progressive abdominal and back pain. He carried the diagnosis of CAH made at 2 months of age, with a history of non-adherence to steroid replacement. He had been off prednisone for 1.5 years at presentation. CT abdomen and pelvis showed symmetric large predominantly fat containing masses involving both adrenals. The right adrenal mass measured 20cm and the left measured 18.5cm most consistent with adrenal myelolipomas. His hormonal evaluation on no steroid replacement showed a random cortisol of 6.5 mcg/mL, renin of 425 pg/ml (3-45 pg/ml), 17-OH progesterone elevated at 26,800 ng/dL, and ACTH level of 29 pg/mL. Bilateral adrenalectomy was performed and pathology was consistent with myelolipomas. The right adrenal gland measured 27.5 x 19.9 x 7.8 cm, weighing 1913 gm, the left measured 26.2 x 16.8 x 13.2 cm, weighing 1823 gm.

Discussion: Adrenal myelolipomas constitute a rare entity but appear more frequent in inadequately treated CAH. The combination of an environment of androgen excess together with the persistent high ACTH may promote the development. In CAH adipocyte differentiation promoters and androgen receptor over expression potentially promote growth. Significant over expression of lymphocyte markers and inflammatory cytokines are the first evidence for adipose specific gene overexpression in a giant myelolipoma. Left-sided myelolipoma are usually larger than the right, attributed to the space limiting constraints by the liver on the right side. A reviewed of 37 cases of giant adrenal myelolipomas found a median age of 46 and no gender difference. 11 cases were associated with CAH prior to the diagnosis of myelolipoma. Massive growth of
this neoplasm can produce symptoms such as flank pain and abdominal discomfort, rupture, hemorrhage, or necrosis. Surgical intervention is required in symptomatic tumors and is usually recommended in tumors bigger than 7 cm, to avoid potential risk of rupture, torsion and hemorrhage. **Conclusion:** Adrenal myelolipomas are most commonly associated with inadequately treated CAH and clinicians should have high suspicion in long standing untreated patients presenting with abdominal and back pain.

**Abstract #107**

**A CASE OF MEN2A TREATED FOR LARGE, BILATERAL ADRENAL PHEOCHROMOCYTOMAS WITH ADRENAL SPARING SURGERY**

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The Cleveland Clinic Foundation

**Objective:** Multiple endocrine neoplasia 2A syndrome (MEN2A) is a familial disorder characterized by medullary thyroid carcinoma, pheochromocytoma and primary parathyroid hyperplasia. Hereditary adrenal pheochromocytomas present bilaterally in nearly 50% of MEN2 patients by the age of 50. Once the disease is present bilaterally, total adrenalectomies are recommended to minimize the risk of future recurrences. However, such approaches result in significant morbidities related to adrenal insufficiency and long-term steroid dependence. Cortical sparing adrenal surgeries have therefore been increasingly advocated, particularly when small, bilateral pheochromocytomas are present.

**Case Presentation:** A 29-year-old woman, with a previously established severe delayed hypersensitivity reaction to class A steroids precluding the use of fludrocortisone, hydrocortisone and prednisone, presented with large, bilateral adrenal masses. Her right adrenal mass measured 4.7 x 3.8 cm and her left mass measured 1.8 x 1.3 cm on MRI. The patient’s 24-hour urine metanephrines and normetanephrines measured greater than 5 times the upper limit of normal confirming a diagnosis of pheochromocytoma. A Fine needle aspirate of a concomitantly diagnosed thyroid nodule was positive for medullary thyroid carcinoma, and subsequent genetic analysis confirmed the diagnosis of MEN2A. Upon collaboration with Allergy and Endocrine Surgery, decision was made to pursue adrenal sparing surgery to avoid or minimize the use of corticosteroids post-adrenalectomy. The patient underwent a successful total right and sub-total left adrenalectomy; no steroids were used perioperatively. Her free plasma metanephrines and normetanephrines normalized post-surgery. She was started on dexamethasone only (class C corticosteroids) for a suboptimal ACTH-stimulation test on post-op day 2. At her most recent 9-month follow-up, she had been successfully tapered down to 0.25 mg of dexamethasone every other day. Her free plasma metanephrines and normetanephrines remained within normal limits and a CT of the abdomen and pelvis obtained at her last follow-up showed no evidence of disease recurrence.

**Conclusion:** Adrenal sparing surgery should be considered in the management of hereditary, bilateral pheochromocytomas to avoid definitive adrenal insufficiency. MEN2 patients presenting with bilateral pheochromocytomas should be evaluated at a referral center for such approaches.

**Abstract #108**

**NORMOTENSIVE HYPERALDOSTERONISM CASE REPORT**

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MCG

**Objective:** Primary hyperaldosteronism is characterized by difficult to control hypertension, an increase in aldosterone excretion, and suppression of the renin-angiotensin system. Hypertension is the hallmark feature of this disorder. We report a case of primary hyperaldosteronism in a 41-year-old woman without hypertension which was first suspected because of persistent symptomatic hypokalemia.

**Case Presentation:** A 41 year-old Caucasian female was referred to Endocrinology clinic for a history of hypokalemia and a left adrenal mass. She had never been on any anti-hypertensives, specifically no diuretics. She was started on potassium chloride 20mEq daily for hypokalemia by her referring physician. Systolic blood pressures taken in the clinic over a period of 9 weeks ranged from 132 to 145 mmHg. Laboratory studies showed potassium of 3.7mEq/L with BUN and creatinine 11mg/dL and 0.6mg/dL respectively and no other electrolyte abnormalities. An aldosterone-renin ratio was suggestive for primary hyperaldosteronism with plasma aldosterone concentration (PAC) 32 ng/dL and 0.6ng/dL respectively and no other electrolyte abnormalities. An aldosterone-renin ratio was suggestive for primary hyperaldosteronism with plasma aldosterone concentration (PAC) 32 ng/dL (normal value <=21) and the plasma renin activity (PRA) 1.1 ng/mL/hr; aldosterone/renin ratio of 29.

Computed tomography of the abdomen showed a 1 cm left adrenal nodule which measured 10 Hounsfield units (HU). Workup for pheochromocytoma and Cushing’s were negative. A salt suppression test was also consistent with primary hyperaldosteronism. Adrenal vein sampling (AVS) was performed and results showed an elevated aldosterone to cortisol ratio on the right side and suppression on the left. Inferior vena cava: aldosterone 55
ng/dL, cortisol 30.08 mcg/dL, aldosterone to cortisol ratio 1.83; right adrenal vein: aldosterone 5170 ng/dL, cortisol 1096.87 mcg/dL, aldosterone to cortisol ratio 4.71; left adrenal vein: aldosterone 55 ng/dL, cortisol 1394.20 mcg/dL, aldosterone to cortisol ratio 0.04.

Given the findings on AVS, the patient underwent a laparoscopic right adrenalectomy. Microscopic histopathology revealed a 2 mm collection of cells which likely represented a very small adenoma, with scattered micro nodules throughout the cortex. After adrenalectomy her serum potassium level returned to normal (4.2-4.4mEq/L) and peripheral plasma aldosterone was 9.2 ng/dL.

Conclusion: We described a patient with primary hyperaldosteronism who presented with muscle cramping and a low potassium in the setting of a normal blood pressure. Our case highlights the need to consider the diagnosis of primary hyperaldosteronism as a cause of hypokalemia, in the absence of hypertension and the need for AVS to accurately locate these adrenal tumors.

Abstract #109

GIANT BILATERAL ADRENAL MYELOLIPOMAS AND BILATERAL TESTICULAR ADRENAL REST TUMORS IN A PATIENT WITH CONGENITAL ADRENAL HYPERPLASIA

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UMASS

Objective: Myelolipomas are rare and benign neoplasms, predominant occurring in the adrenal glands. Tumors exceeding 8 cm are called giant myelolipomas. Few cases of bilateral giant adrenal myelolipoma (GAM) have been reported, especially in the setting of congenital adrenal hyperplasia (CAH). Testicular adrenal rest tumors (TART) are lesions in the rete testis, which could be associated with CAH. We present a case of CAH associated with GAM and TART.

Case Presentation: A 31-year-old man presented with bilateral flank pain. He was diagnosed with congenital adrenal hyperplasia at the age of 3 (21-hydroxylase deficiency), but had not taken any therapy in 25 years. Physical exam revealed normal vital signs, distended abdomen and enlarged testicles (11 cm x 8 cm); lab results showed: 17-hydroxyprogesterone 13,500 ng/dL, total testosterone > 1600 ng/dL, Cortisol 4.1 mg/dL, ACTH 37.5 pg/ml. CT abdomen revealed enlarged adrenal glands bilaterally.

He was treated with Dexamethasone, but ACTH continued to increase, and 17-hydroxyprogesterone remained elevated. MRI abdomen showed myelolipomas in the adrenal glands. Subsequently he underwent a bilateral adrenalectomy: the right gland measured 26 cm, weighing 2500 grams; the left measured 29 cm, weighing 4500 grams. The glands were predominately myelolipomatous tissues with nodular cortical hyperplasia. Treatment with Hydrocortisone and Fludrocortisone was initiated.

The patient continued to have enlarged testicles, and three years later, his 17-hydroxyprogesterone was 13574 ng/dL, total testosterone 5099 ng/dL and hematocrit of 61%, suggesting adrenal rests within the testes. He underwent a bilateral orchiectomy, with pathology revealing that both testes were completely replaced by proliferation of adrenal cortical cells. He was subsequently started on testosterone replacement.

Discussion: CAH is rare disease with incidence of 1:15,000 live births. With inadequate therapy, patients may face complications like TART and GAM. The incidence of TART in CAH is as high as 94%, and is believed to be due to aberrant migration of adrenocortical cells to the testes during embryogenesis. Elevated ACTH can stimulate TART formation, which in this patient caused significant elevation in testosterone level. Treatment is usually with glucocorticoids, but refractory cases require orchiectomy, as seen here. Our patient also had a giant myelolipoma, a neoplasm composed of mature adipose tissue and hematopoietic elements. This metaplasia can be similarly triggered by ACTH.

Conclusion: Our patient had GAM and TART as manifestations of untreated CAH. These complications are rare and have been reported in tandem in very few published cases.

Abstract #110

AN UNUSUAL CASE OF CONCOMITANT HYPERALDOSTERONISM AND HYPERCORTISOLISM IN A PATIENT WITH ADRENAL INCIDENTALOMA.

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Objective: Present an unusual case of adrenal nodule co-secretion of aldosterone and cortisol.

The first case of a single adenoma producing both aldosterone and cortisol was reported in 1997. Since then concomitant hyperaldosteronism and hypercortisolism has been reported in several cases. The exact prevalence of aldosterone and cortisol co-producing tumors is not known. Co-secretion of aldosterone and cortisol should be suspected if a patient has primary aldosteronism, an adenoma larger than 2.5 cm and a positive 1-mg overnight dexamethasone suppression test (ODST).
Case Presentation: We present a case of 66 year-old male with a left adrenal incidentaloma that was an exophytic lesion, 3.6 x 4.3 x 4.2cm, with Hounsfield Units <10. He had hypokalemia and uncontrolled hypertension (HTN) despite being on potassium supplements and 6 different blood pressure medicines including lisinopril. After stopping interfering drugs and optimizing blood pressure control on verapamil and hydralazine, the supine plasma aldosterone was high at 29ng/dl (ref. range 3-16), as was the plasma aldosterone/plasma renin activity (PRA) ratio of 112.9 (ref. range: 0.9-28.9). ODST was positive with AM cortisol of 9.4ug/dL and an adequate dexamethasone level. The initial evaluation indicated concomitant hyperaldosteronism and subclinical Cushing’s syndrome. Hypercortisolism was further confirmed by 3 consecutive high midnight salivary cortisol levels. Plasma metanephrines and normetanephrines were within the reference ranges. Early morning plasma ACTH level was 11pg/mL (ref. Range 6-50). Due to a recent stroke with left-sided weakness and uncontrolled HTN, the salt-loading test was not feasible. Captopril challenge test (25 mg PO) confirmed primary hyperaldosteronism. Aldosterone was high at 33ng/dL at baseline and remained elevated at 23ng/dL and 28ng/ dL, respectively, at 60 and 120minutes. PRA was low at 0.22ng/ml/h (ref. range: 0.25-5.82) at 120min. Due to his multiple co-morbidities and cortisol co-secretion, we opted to proceed with laparoscopic adrenalectomy without prior bilateral adrenal venous sampling.

Discussion: Several clinical complications are important for aldosterone and cortisol co-producing tumors. These include the increased risk of cardiovascular events, hypertension, metabolic abnormalities and decreased bone mineral density. Cortisol co-secretion may cause false negative results in adrenal venous sampling.

Conclusion: Aldosterone and cortisol co-secreting adrenal adenomas are often not readily apparent. Correct diagnosis is imperative to avoid post-operative adrenal crisis and to guide management of secondary adrenal insufficiency.

Abstract #111

AURICULAR OSSIFICATION IN A PATIENT WITH CONGENITAL ANTERIOR PITUITARY HYPOPLASIA.

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Texas Tech University Health Science Center

Objective: The auricle of the ears is vulnerable to local trauma (Cauliflower ear in boxers) and frostbite, which is the common etiological factor in hardening of the auricular cartilage. Metabolic disorders implicated in other reported cases include ochronosis, Acromegaly, hypercalcemia and adrenal insufficiency. We report a case of progressive stiffening of ears in a patient with long standing pan hypopituitarism.

Case Presentation: 37-year-old male with history of hypopituitarism which was diagnosed a few weeks after birth. He was a product of full term normal pregnancy; however early neonatal period was complicated by frequent hospitalizations and bout of meningitis. Anterior pituitary hormone replacement was initiated from early neonatal period. Growth hormone replacement was used briefly for 2 years. He could achieve puberty and mid parental height by age 15. Never required desmopressin. No developmental delays were noticed however he did not finish high school, and never hold any steady job. Medications include LT4 112 mcg, Androgel 1.62% 2 depressions daily, Hydrocortisone 15 mg in AM and 5 mg in the evening. Patient reports 50% adherence with medications. Recent labs showed normal Free T4, and low testosterone level 145ng/ml. Previous MRI showed hypoplasia of anterior lobe of the pituitary gland along with infundibulum and ectopic posterior pituitary gland along the undersurface of optic chiasm. Over the last few years he complained of hardening of his external ears with progressive difficulty and pain on bending them. Pain can wake him up from sleep while turning in bed. On exam, bilaterally hard, stiff ears with no redness and warmth on palpation were noted. No tenderness to palpation of nasal and tracheal cartilage was noted. CT scan of the face and external ears showed extensive calcifications of the external ears.

Discussion: Although pathogenesis remains ambiguous, but presence of calcified external ears in adrenal insufficiency and particularly secondary adrenal insufficiency is of interest as it previously occurred mainly in patients treated with desoxycorticosterone (D.O.C) before the glucocorticoids became available. D.O.C use in the past is like that occurring in the patient with long standing hypopituitarism, who presumably had normal amounts of mineralocorticoids but decreased glucocorticoids because of deficient ACTH production. Hypercalcemia and hyperphosphatemia have been reported in adrenal insufficiency but the association is not always present in the reported cases of petrified ears with adrenal insufficiency.

Conclusion: Auricular ossification can be a complication of long standing secondary adrenal insufficiency.
Abstract #112

PLANTING SEEDS: A CASE OF METASTATIC HEPATOCELLULAR CARCINOMA TO BILATERAL ADRENAL GLANDS

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Objective: To show the importance of early recognition of HCC with extra-hepatic metastasis, to review diagnosis and management of bilateral adrenal tumors including extrahepatic metastasis of HCC to the adrenal glands.

Case Presentation: A 54 year-old man with history of hypertension was found to have a 2 cm right hepatic lobe lesion and a 6 cm left adrenal mass on CT imaging during routine surveillance. After being lost to follow up for one year, repeat CT scan showed growth of the left adrenal mass to 15 cm with a new 6 cm right adrenal mass and progression of the liver lesion to 3 cm. Laboratory analysis was negative for plasma catecholamines, 24-hour urine cortisol, and renin and aldosterone levels. The patient underwent bilateral adrenalectomy with resection of liver mass with unremarkable post-operative hospitalization. He was successfully weaned down to physiologic dosing of corticosteroids. All three lesions were positive for hepatocellular carcinoma.

Discussion: Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world with an estimated annual incidence of 0.5 to 1 million cases.(1) It is commonly associated with viral hepatitis, alcohol use, and non-alcoholic steatohepatitis(2). Extra-hepatic metastasis is the most common cause of death among patients with HCC(3). Metastasis of HCC to the adrenal glands accounts for approximately 10% of metastatic cases which is the fourth most frequent site of distant metastasis.(1,3,4)

Bilateral adrenal masses are uncommon and have many possible etiologies: bilateral adrenal hyperplasia, infection, lymphoma, metastasis from extra-adrenal sites, and bilateral tumors such as pheochromocytoma(5). According to some sources, metastatic disease is the most frequent cause of bilateral adrenal masses. In any case of unilateral or bilateral adrenal masses, biochemical evaluation of the mass should be investigated for pheochromocytoma, cushing’s syndrome, and hyperaldosteronism. After biochemical analysis, radiological imaging can help differentiate the etiology of the adrenal mass based on certain radiologic characteristics (7). Quickly determining the etiology of the mass is essential because time is of the essence as overall survival of patients with HCC and extra-hepatic metastasis is poor regardless of treatment modality(8).

Conclusion: We present this case of bilateral adrenal metastasis from HCC to show the importance of early recognition of HCC with extra-hepatic metastasis, to review incidence and evaluation of bilateral adrenal tumors, and discuss the management of HCC with extrahepatic metastasis to the adrenal glands. Recognizing this presentation early is important as prognosis is usually poor.

Abstract #113

IATROGENIC CUSHING & SECONDARY ADRENAL SUPPRESSION BECAUSE OF DRUG INTERACTION IN A PATIENT ON H.A.A.R.T. FOR H.I.V

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Objective: Highly active antiretroviral therapy (HAART) has revolutionized H.I.V. treatment. Longevity has substantially increased in treatment adherent patients. Chronic disease e.g. Osteoarthritis, Osteoporosis are expected to rise. Resulting polypharmacy can result in significant drug-drug interactions with HAART therapy. We report a case of Iatrogenic Cushing/Secondary Adrenal suppression after Intramuscular injection of Triamcinolone.

Case Presentation: 54-year-old HIV positive female (20-year HAART therapy use) reported fatigue, easy bruising and difficulty climbing stairs. Initial workup showed normal electrolytes and an AM cortisol level of 0.8 mcg/dL. Problems started five months prior to initial visit and progressively worsened. She denied orthostatic dizziness, palpitations or increased skin pigmentation. She also reported loss of axillary/pubic hair, easy bruising, 10 lbs. weight gain and reddish skin complexion. Initially patient denied steroid use (Intraarticular, oral, topical or suppositories). Later she recalled receiving two Intramuscular injections for respiratory infection. Records showed she had received Intramuscular steroid injections (40 mg IM triamcinolone on 1st visit and Solumedrol 40 mg IM on 2nd visit, 6 & 7 months respectively) prior to this presentation. OTC fluticasone as needed was prescribed which she stopped after 2-week use. Her HIV regimen was stable and included (Atazanavir 300 mg daily, Ritonavir 100 mg daily, Etravirine 200mg BID & Reltigavir 400 mg BID). Central obesity, thin extremities, skin bruises and difficulty standing from squatting was noted on exam. Cosyntropin stimulation (using 250 mcg of ACTH) was done. Baseline ACTH < 5, DHEAS 6 and cortisol was 0.9; cortisol increased to 4 and then 5 at 30 and 60 mins respectively. Urine synthetic glucocorticoid screen showed Triamcinolone level of 1.9 mcg/dl (Normal value <0.1); all other steroid including methylprednisolone and...
Discussion: Protease Inhibitors (PI) are an integral part of HAART. Ritonavir is a potent inhibitor of cytochrome P450 3A4, enzyme and helps increase the level of 2nd PI in a HIV regimen resulting in reduced pill burden and dosing frequency. Most steroids (inhaled, oral, IM, intranasal) are also metabolized by CYP-P450 3A4; and can lead to significantly elevated levels in blood. Lipodystrophy commonly seen in patients treated with HAART can increase absorption of highly lipophilic steroid (fluticasone and triamcinolone) which can lead to slow and sustained release months after last dose.

Conclusion: Significant drug interactions can occur with PI based HAART. One should avoid use of steroids in such patients.

Abstract #114

THE COLOR OF YOUR SKIN DOES MATTER—AN INTERESTING CASE OF SCHMIDT SYNDROME

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Objective: Review physical findings in Schmidt-Syndrome. Schmidt-Syndrome refers to autoimmune adrenal-insufficiency (Addison’s disease) with autoimmune-hypothyroidism and/or type-1 diabetes mellitus (T1DM). It is part of a larger syndrome known as Autoimmune Polyendocrine Syndrome type II (APS II). APS II is a polygenic disorder in which two or more of following disorders may be present: autoimmune thyroid disease, Addison’s disease, T1DM, primary hypogonadism, myasthenia gravis and celiac disease. Prevalence of Schmidt Syndrome is 1:20,000 in general population with females to males ratio of 3:1.

Case Presentation: We present a case of 31 year old Caucasian female who was referred to us for newly diagnosed hypothyroidism secondary to Hashimoto’s thyroiditis. She was started on levothyroxine 25 mcg by her primary care which she had not yet started taking. Her chief complaints were extreme fatigue and exertional shortness of breath. Vitals were within normal range. Physical examination was unremarkable except for peculiar bronzed/tanned skin for a Caucasian. We asked her if she had tanned her skin. She said that she had never been to a tanning salon or used tanning products. She worked as physical therapy assistant and denied excess sun exposure. This raised our suspicion for ACTH excess. We asked her not to start levothyroxine until we did ACTH stimulation test to rule out adrenal insufficiency, as it may precipitate an adrenal crisis. ACTH stimulation test confirmed primary adrenal insufficiency with 30min and 60min cortisol levels to be 8.6 ug/dl and 7.1 ug/dl respectively. ACTH level was 1883(0-46 pg/ml). 21-hydroxylase antibodies and anti-TPO antibodies were strongly positive. Celiac screen was negative.

Discussion: These investigations were triggered by the color of her skin. ACTH is derived from a bigger precursor molecule called pro-opiomelanocortin(POMC). POMC is also the precursor for melanocyte stimulating hormone (MSH). MSH stimulates melanocytes, giving the skin a bronze color. Treatment of Schmidt Syndrome is same as that of individual disorders. Antibody screening for other associated disorders may help identify patients at risk for developing autoimmune gland failure. These patients should be screened for antibodies against insulin, GAD to test for type I diabetes predisposition, and tissue transglutaminase autoantibodies to screen for celiac disease. Patients with APS-II and their families should be counselled about other associated autoimmune conditions and asked to monitor for disease specific symptoms for early detection.

Conclusion: This case report highlights the importance of thorough physical examination and physical finding of hyperpigmentation in patients with Addison’s disease.

Abstract #115

DISSEMINATED NOCARDIA VETERANA IN METASTATIC ADRENOCORTICAL CARCINOMA

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Case Presentation: We present a 76 year-old male with history of hypertension who was admitted by his primary care physician for workup of a 6.2x3.7cm heterogeneous adrenal mass and multiple pulmonary nodules. He had a 40-pound weight loss over 3 months with fatigue and multiple cellulitic areas on his extremities. He was found to be hypertensive and hypokalemic. His hospital course was complicated by pulmonary embolism, atrial fibrillation, and aspiration pneumonia. Biochemical workup revealed elevations in 24-hour urine free cortisol (3036mcg/d), AM cortisol after 1mg dexamethasone suppression (50mcg/dL), 11-deoxycortisol (511ng/dL), androstenedione (3.09ng/mL) and estradiol (95pg/mL). Random evening cortisol was elevated (46mcg/dL) with concurrent normal ACTH (7pg/mL). Total testosterone, plasma aldosterone, renin activity and 24-hour urine fractionated metanephrines were normal. Ketoconazole therapy was initiated for hypercortisolism. Spironolactone and amiloride were used to control his hypertension and hypokalemia. The patient developed a left elbow abscess while on antibiotics and one of the large pul-
Pulmonary nodules became cavitary. Deep wound cultures grew Nocardi a veterana, raising suspicion for disseminated nocardiosis. Subsequently, the patient underwent video-assisted thoracoscopic surgery, which provided histological diagnosis of metastatic adrenocortical carcinoma (ACC). Shortly after, the patient clinically deteriorated and passed away in hospice. While on ketoconazole 500mg twice daily, the 24-hour urine free cortisol level decreased by half (1420mcg/dL).

Discussion: ACC is a rare (1-2 cases per million) and highly aggressive malignancy. 50-80% of patients with ACC have been shown to have hypercortisolism, predisposing them to numerous complications including venous thromboembolism and opportunistic infection, both of which our patient had. Previous case reports have shown nocardiosis associated with other causes of hypercortisolism, such as Cushing’s syndrome and ectopic Cushing’s, however it has not been directly linked to ACC. Nocardiosis is an aerobic gram-positive infection commonly presenting in the lungs, central nervous system and skin. Our patient had skin abscesses that were positive for Nocardi a veterana along with a cavitary lung lesion highly suspicious for infection. Other case reports have also described pulmonary nodules initially thought to be malignancy in patients with hypercortisolism and nocardiosis.

Conclusion: It is important for clinicians to be aware of opportunistic infections such as nocardiosis in the differential diagnosis of pulmonary lesions in patients with ACC. Timely treatment with antibiotics is warranted when suspicion of infection is high.

Abstract #116

A RARE CASE OF LIFE-SAVING ENDOCRINE CONSULTS IN THE EMERGENCY ROOM (RECURRENT GRAVES’ THYROTOXICOSIS RESULTING IN ADRENAL CRISIS)

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Objective: Endocrinologists understand the need to rule out adrenal insufficiency in patients with hypothyroidism prior to initiating levothyroxine; however, adrenal insufficiency in the setting of endogenous thyrotoxicosis is not as commonly encountered. We present a case where a routine request for endocrine consultation in the emergency room for care of a patient with recurrent hyperthyroidism resulted in a new diagnosis of central adrenal insufficiency.

Case Presentation: A 35-year-old Hispanic female presented to the emergency room with concerns of weight loss, diffuse musculoskeletal pain, nausea and vomiting. The endocrine consult service was contacted for discharge recommendations due to a diagnosis of recurrent thyrotoxicosis. The patient’s medical history was significant for Graves’ disease (previously in remission) and pregnancy with uncomplicated cesarean section 5 months prior. The patient noted a significant deterioration in her health post-delivery including fatigue, diffuse pain, and a 50 pound weight loss. She was unable to breastfeed, though reported having menses. Initial evaluation was significant for hypotension with tachycardia (blood pressure 90/51 mmHg, pulse 106). On exam, she was cachectic with severe muscle tenderness to palpation, diffuse thyroid enlargement, tremor, and hypereflexia. Laboratory workup showed overt hyperthyroidism: TSH <0.01, Free T4 of 4.01 (0.71-1.40 ng/dL), and Total T3 of 3.6 (1.0-1.7 ng/mL). Her basic metabolic panel demonstrated normal electrolytes (NA 139, K 4.0) and kidney function (Creatinine 0.5). The endocrine consult team requested an ACTH stimulation test to be performed prior to planned discharge, which revealed severe adrenal insufficiency (Cortisol 0.1 > 0.2 ug/dl). Further workup confirmed secondary adrenal insufficiency (ACTH before stimulation test < 5.0 pg/mL), normal gonadotropin axis (FSH 8.1, LH 8.1 Estradiol 58.6 pg/mL), and low prolactin (< 1.4). No pituitary abnormalities were identified on MRI of the brain.

Discussion: This case demonstrates how endogenous thyrotoxicosis can result in adrenal crisis. Our patient had recurrent Graves’s hyperthyroidism, and new onset secondary adrenal insufficiency with partial hypopituitarism. ACTH deficiency with preserved gonadotropin axis is commonly seen in lymphocytic hypophysitis, which is often associated with pregnancy.

Conclusion: It is important to recognize the possibility of adrenal insufficiency in patients with autoimmune hyperthyroidism who have an atypical presentation. Had we not taken the time to listen carefully to the patient’s story, she would have been treated for recurrent hyperthyroidism alone, and not for her new diagnosis of adrenal insufficiency – a potentially lethal mistake.
Abstract #117

CAN I TRUST MY LAB RESULTS?

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Objective: The incidence of adrenal incidentalomas is increasing due to frequent and advanced imaging techniques and is around 8.7%. 24 hour urine free cortisol is one of the recommended screening tests. Currently, most labs in United States use liquid chromatography tandem-mass spectrometry (LCMS) as it achieves the best accuracy in diagnosing Cushing Syndrome among patients presenting with suspected hypercortisolism. It offers better specificity and accuracy than the previously used immunoassay-based methods though every test can have artifactual errors. We present a case of lab error due to malfunctioning of a refrigerator.

Methods: Case report

Case Presentation: A 60 year old female was incidentally found to have a 2.54 x 2.72 cm right adrenal mass on CT abdomen done for work up of liver hemangiomas. The adrenal mass measured 18.3 Hounsfield units on non-contrast images. The patient then underwent a standard work up for adrenal incidentaloma which included measurement of 24 hour urine free cortisol levels. All the work up came back within normal range but her 24 hour urine cortisol levels were reported as undetectable with no other synthetic steroid present in urine as well. The sample collection was also adequate with 2350 ml urine collected in 24 hours. She was not on any external steroids other than an occasional use of fluticasone nasal spray. Her random cortisol at 2:35 PM had previously been recorded at 7.1 ug/dL. Suspecting this to be a lab artifact or improper collection, the results were discussed with the patient. She mentioned following the procedure properly, her refrigerator working appropriately as well and no explanation could be found. Later on, the patient called back saying that she had kept the urine container at the back of the refrigerator and it had frozen over. The same test was then performed using the same method (LCMS) while making sure the sample was not frozen. The results on this occasion showed cortisol 8.3 mcg/24 hours with urine collection of 1933 ml.

Discussion: Gas chromatography-mass spectrometry and high pressure liquid chromatography are considered reference tests or gold standard for urine free cortisol levels. With the costs of rapid liquid chromatography coming down and its results closely correlating with the reference tests, these have been used commercially on larger scales. It is important to remember that no test is infallible and small oversights can lead to a large variation in test results.

Conclusion: This case underscores the continued importance of clinical judgment and experience in the changing world of Evidence Based Medicine where lab tests and imaging techniques are sometimes considered more valuable than a physician’s instinct.

Abstract #118

HYPERTENSIVE CRISIS DURING ADRENALECTOMY FOR UNDIAGNOSED PHEOCHROMOCYTOMA

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Objective: To present a case of a male normotensive patient with an incidentally found three centimeter adrenal mass, with normal preoperative hormonal work up, who then developed hypertensive crisis intraoperatively and was found to have a pheochromocytoma.

Case Presentation: A 55-year-old man with history of hyperlipidemia presented to his primary care physician for an adrenal mass discovered on imaging during an emergency room visit for viral gastroenteritis. He denied any history of hypertension, orthostasis, palpitations, diaphoresis, or diarrhea. On MRI, it was a three centimeter, well-defined, round, heterogenous mass in the left gland showing predominantly T2 hyperintense signal centrally with heterogeneous contrast enhancement. His serum metanephrines were mildly elevated to 0.68 nmol/L (upper limit of normal 0.49 nmol/L), and his serum normetanephrines were elevated to 1.5 nmol/L (upper limit of normal 0.89 nmol/L). Other laboratory workup included a normal dexamethasone suppression test and normal serum aldosterone and renin. The patient was referred for robotic adrenalectomy. During the procedure, his systolic blood pressure rose to over 300 mmHg. The procedure was aborted. He was treated with antihypertensive drips and was able to come off all medications within twenty-four hours. Two weeks later, repeat serum metanephrines and normetanephrines were 1.69 nmol/L and 3 nmol/L, respectively. He was started on doxazosin and atenolol and had an uneventful adrenalectomy. The final surgical pathology confirmed the diagnosis of pheochromocytoma.

Discussion: Twenty percent of pheochromocytomas are biochemically silent with normal concentrations of catecholamines. Measurement of their metabolites is a more sensitive way to make a diagnosis. These levels are
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typically elevated four-fold over the upper limit of normal in 80% of patients with pheochromocytoma. When a pheochromocytoma is still small, borderline elevations in serum metanephrines should be further investigated before the patient is referred for surgery.

**Conclusion:** The diagnosis of pheochromocytoma can be difficult if the tumor is symptomatically silent. Metanephrine testing should be completed before any surgery, and the size of the tumor and appearance on imaging should be considered during interpretation.

Abstract #119

TOO TIRED TO WALK: A RARE CASE OF ADDISON’S DISEASE MASKED BY HYPOTHYROIDISM

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**Objective:** Addison’s Disease occurs in the US in 1 out of every 100,000 people yet it can be a diagnosis that can be elusive and life-threatening if not suspected. Often the fatigue that many Addison’s Disease patients present with can be misdiagnosed as resulting from hypothyroidism. The diagnosis of adrenal insufficiency is made with an ACTH stimulation test. The purpose of this study is to report a case of Addison’s Disease that was diagnosed initially as hypothyroidism and upon lack of symptom improvement, further investigation lead to the diagnosis of Addison’s Disease.

**Case Presentation:** 22 year old female of Mediterranean descent presented to the hospital complaining of dizziness and fatigue. She was given antivert in the ER and discharged. Her symptoms did not improve so she presented to the ER again. A TSH level was checked and was elevated at 15 and free T4 was low at 0.76. The patient was diagnosed as having hypothyroidism and given synthroid and referred to endocrinology. She revealed that for the past five months she was feeling progressively more tired to the point that now it was difficult for her to walk. She could not wake up early to get to her classes and sometimes found herself falling asleep in the middle of the day. Moreover, she reported an unintentional ten pound weight loss within the past 5 months. Sodium was 135 and potassium 4.4. An ACTH stimulation test was done with 0.25mg of cosyntropin. Baseline cortisol was <0.2 and ACTH 1103. Then, 30 minutes later cortisol was <0.2 and 45 minutes later cortisol was still <0.2. The patient was given IV steroids after the diagnosis was made and discharged home on cortef 20mg in the morning and 10mg in the evening. Adrenal antibodies were positive >1300 confirming a diagnosis of autoimmune thyroid disease. The patient returned 2 weeks later on appropriate replacement and her symptoms had improved tremendously.

**Discussion:** The patient had Addison’s Disease that was misdiagnosed. Glucocorticoid replacement should be done prior to replacing thyroxine in patients in whom adrenal insufficiency is suspected to avoid an Addison’s crisis. The diagnosis of hypothyroidism had initially masked the diagnosis of Addison’s Disease.

**Conclusion:** It is integral to keep a high suspicion for Addison’s Disease in patients who lack improvement in response to therapy and especially those with autoimmune disease as they are at increased risk for other autoimmune endocrinopathies.

Abstract #120

ADRENAL INSUFFICIENCY IN PREGNANCY- A DIAGNOSTIC CHALLENGE

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**Objective:** Adrenal insufficiency (AI) is extremely rare in pregnancy and diagnosis is complex as demonstrated in this case.

**Case Presentation:** A 28 year old female at 32 weeks gestation with twin pregnancy presented with generalized weakness and headaches of 2 weeks duration associated with transient blurring of vision. Medical history was significant only for unexplained infertility. Clomiphene citrate resulted in a twin pregnancy. Social history was unremarkable. Her vitals, including orthostatics, were normal. Physical exam revealed edema in both legs but was otherwise unremarkable. Laboratory studies were as follows: sodium 116mmol/L (135-145), serum osmolality 242 mosm/kg (280-295), urine osmolality 486 mosm/kg (40-140) and urine sodium 34 mmol/L. Sodium levels did not respond to 3% normal saline. 8:00 am cortisol was 1.7 mg/dl (5-23), adrenocorticotropic hormone (ACTH) 10 pg/ml(6-50), thyroid stimulating hormone 2.51 U/ml (0.27-4.20), and free thyroxine level 0.8 ng/dl (0.8-1.8). She denied exogenous steroid use. Other labs were normal. MRI brain without contrast showed a normal pituitary, 10mm in size. Cosyntropin stimulation testing was deferred due to undefined values in twin gestation and worsening renal and liver function, labor was induced at 34 weeks resulting in normal vaginal delivery.
Stress dose hydrocortisone was given in the peripartum period, followed by maintainece doses. There were no complications with breast-feeding. Cosyntropin testing done 3 months post delivery revealed baseline serum cortisol of 13.1 mg/dl and ACTH 26pg/ml. Cortisol 30 and 60 minutes post cosyntropin showed adequate response, of 19.4 and 22.8mg/dl respectively.

**Discussion:** Refractory hyponatremia should raise concern for AI, which if untreated, could be life threatening for mother and baby. The presentation of central AI in the last trimester, and normal testing after delivery, makes lymphocytic hypophysitis a likely cause. Signs and symptoms of AI overlap with those of pregnancy, thus delaying the diagnosis. This along with changes to hypothalamic-pituitary-adrenal axis, cortisol metabolism and end organ response to cortisol in pregnancy makes the diagnosis complex.

**Conclusion:** Hyponatremia in pregnancy warrants evaluation for AI as prompt management is necessary to reduce maternal-fetal mortality.

**Abstract #121**

**DXA PROFILE IN MENOPAUSAL PATIENTS FOLLOWED FOR ADRENAL INCIDENTALOMA: A LONGITUDINAL STUDY**

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**Objective:** Adrenal incidentalomas (AI) still display controversies related to definition and best management, knowing the increasing frequency due a large number of investigations as abdominal ultrasound or computer tomography (CT) or magnetic resonance imagery.

**Methods:** This is a retrospective study performed in a single tertiary center of Endocrinology. The inclusion criteria are: menopausal status of at least 12 months, the confirmation of an AI based on specific endocrine assays and at least two central DXA (Dual-Energy X-Ray Absorptiometry) scans (GE Lunar Prodigy machine) while the females were followed-up. The exclusion criteria are: concurrent or prior malignancy of any type, previous or concurrent specific anti-osteoporotic therapy for osteoporosis regarding any time of drugs (not vitamin D and calcium). Adrenal scanning is based on CT scan.

**Results:** 18 women (N=18) had an average age at diagnosis of 61.5+/-.9.5 years, the mean tumour diameters were of 2.19+/-.085 cm, respectively of 1.48+/-.0.85 cm. Mean baseline plasma cortisol was of 14.97+/-.0.72µg/dL (Normal:6-21), and ACTH (Adrenocorticotropic Hormone) of 8.15+/-.6.93pg/mL (Normal:3-66pg/mL), 25-hydroxvitamin D of 15.84+/-.6.16ng/mL (Normal:30), years since menopause (YSM) of 14.65+/-.9.36, L1-4 lumbar BMD (Bone Mineral Density) of 0.972+/-.0.167g/sqcm, L1-4 T-score of -1.5+/-.1.13SD (ranges: -1 to -3.3SD), femoral neck BMD of 0.885+/-.0.131g/sqcm (T-score of -1.5+/-.1.1SD), total hip BMD of 0.949+/-.0.181g/sqcm (T-score of -0.7+/-.1.4SD). After 12 months: L1-4 BMD was of 1.009+/-.0.139g/sqcm, femoral neck BMD of 0.917+/-.0.145g/sqcm, total hip BMD of 0.93+/-.0.156g/sqcm. After 24 months, BMD was for the three regions of 0.89+/-.0.75g/sqcm (T-score of -2.4+/-.0.63SD), 0.791+/-.0.09g/sqcm (T-score of -1.8+/-.0.72SD), 0.867+/-.0.5g/sqcm T-score of -1.12+/-.0.43SD. Baseline ACTH, cortisol (at baseline and after low dose of dexametasone test) was not corelated with BMD. After 24 (not 12) months, BMD was statistically significant diferent than baseline.

**Discussion:** The age-dependent BMD loss might be overlapped with tumor-associated BMD changes.

**Conclusion:** Despite the general concept of AI and harmless general profile, in special subgroups as menopausal population, DXA may reveal time-dependent changes.

**Abstract #122**

**SECONDARY ADRENAL INSUFFICIENCY: A COMPLICATION OF EPIDURAL STEROID INJECTION**

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**Objective:** To describe a case of secondary adrenal insufficiency due to multiple epidural steroid injections.

**Methods:** Epidural steroid injections (ESI) are commonly used to treat radicular back pain. Epidural steroid administration is considered to have limited systemic absorption. We report a case with secondary adrenal insufficiency due to hypothalamic-pituitary-adrenal axis (HPA) suppression as a result of multiple epidural steroid injections.

**Case Presentation:** A 47-year-old woman presented for evaluation and treatment of hypothyroidism and thyroid nodules. She reported intermittent palpitations for one year and severe fatigue. She had chronic neck pain and lower back pain. She received ESI (triamcinolone and bethamethasone) in the neck and lumbar spine every 2-3 months for one year. She also received two occipital nerve blocks with triamcinolone for cranioocular headaches in one year. On physical examination, her pulse was 85 beats per minute, blood pressure 139/74 mm Hg, weight 177.4
lbs, and BMI 28.7 kg/m². She endorsed 19 lbs of weight gain in that year. Thyroid gland was normal in size and symmetric with no palpable nodules. Her serum cortisol and ACTH were checked for evaluation of fatigue revealing very low levels at <0.02 mcg/dL and <1.1 mcg/dL. Thyroid hormone levels were normal. Serum cortisol after 0.250 mg intravenous cosyntropin at 30 and 60 minutes was 2.9 and 4.8 mcg/dL. She was started on a 10 mg hydrocortisone tab in the morning and 5 mg in the late afternoon with improvement in fatigue. She was recommended to minimize epidural steroid injections. Her HPA axis recovered after two and a half years while on hydrocortisone. She is currently doing well off hydrocortisone.

Discussion: The risk of HPA axis suppression with epidural steroid injections is under-recognized. The optimal dose, frequency, and number of injections per year are not clearly established. HPA axis suppression for 21 days after a single epidural injection of 40 mg triamcinolone has been reported in prior studies with return to recovery after 19.9 ± 6.8 days. To avoid suppression of the HPA axis, experts recommend avoiding more than one injection in 30 days and more than three injections per year. Long term studies on patients receiving epidural steroids and their complications are lacking.

Conclusion: We report an interesting case of adrenal insufficiency secondary to epidural steroid injections. Providers treating patients with frequent/multiple epidural steroid injections need to be aware of this potential complication.

Abstract #123

TOPICAL STEROID USE LEADING TO SEVERE ADRENAL INSUFFICIENCY IN A PATIENT WITH PSORIASIS

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Objective: To describe a case with severe adrenal insufficiency due to prolonged use of topical steroids.

Methods: Adrenal insufficiency secondary to topical steroid use is uncommon. We report a case with psoriasis that developed severe adrenal insufficiency due to prolonged use of topical steroids, which took three years for his hypothalamic-pituitary-adrenal axis (HPA) to recover.

Case Presentation: A 63-year-old white male was referred to the endocrine clinic for evaluation of low serum cortisol. He had a history of psoriasis diagnosed 23 years ago and had been using topical steroids (Clobetasol Propionate 0.05%) on several parts of his body daily for 18 years. The patient complained of a 24 pound weight gain over two years and facial puffiness. He also complained of increasing fatigue for the past 5 years. Random serum cortisol was checked with concern for Cushing’s and was noted to be very low at 0.2 ug/dL. ACTH was also noted to be low at <1.1 pg/mL. The labs were indicative of secondary adrenal insufficiency. The patient was started on hydrocortisone 10 mg in the morning and 5 mg in the evening with significant improvement in fatigue. A pituitary MRI was also obtained that showed a 2 mm hypoenhancing lesion within the midline of the pituitary gland consistent with Rathke’s cleft cyst versus pituitary microadenoma. The patient was started on apremilast (Phosphodiesterase-4 enzyme inhibitor) and phototherapy for psoriasis. The patient decreased his use of topical steroids to once a month. Cosyntropin stimulation test (0.250 mg intravenously) showed subnormal response after 2.5 years and a normal response with rise in serum cortisol to 18.7 ug/dL at 60 minutes after 3 years. Hydrocortisone was then stopped. A repeat pituitary MRI showed a stable pituitary tumor.

Discussion: The most common cause of secondary adrenal insufficiency is iatrogenic. Adrenal insufficiency secondary to long-term topical steroid use has been uncommonly reported. One study showed 40% of patients with abnormal cortisol response to exogenous ACTH after two weeks of topical glucocorticoids usage. In addition, a meta-analysis evaluating fifteen studies and 320 patients showed 4.7% patients with adrenal insufficiency after topical steroid use.

Conclusion: The present case described a patient with a long-term history of psoriasis who developed secondary adrenal insufficiency secondary to long-term topical steroid use and who with decreased topical steroid use recovered. Clinicians need to be aware of potential side effects of prolong topical steroid use.

Abstract #124

SCREENING OF DIABETIC PATIENTS USING U500 INSULIN UNCOVERS A HIGH PERCENTAGE OF UNDIAGNOSED HYpercortisolism CONSISTENT WITH CUSHING’S SYNDROME.

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Objective: Studies screening patients with diabetes for hypercortisolism indicate 2-10% of patients have undiagnosed Cushing’s syndrome (CS) and those authors concluded that such a low percentage makes screening of all diabetics for CS prohibitive. However, patients with
Abstract #125

CHALLENGES IN DIAGNOSIS AND MANAGEMENT OF CUSHING’S SYNDROME: A CASE SERIES

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Objective: While the diagnosis of Cushing’s syndrome (CS) is often unequivocal, determining the etiology and effectively managing the condition remain a challenge. We present three cases of CS with varied presentations, etiologies, and management.

Case Presentation: Case 1: A 71 year-old male with coronary artery disease (CAD) presented with fatigue and weakness, Cushingoid features, insulin resistance, and hypokalemic metabolic alkalosis (HMA). Laboratory evaluation showed an elevated 24-hour urinary free cortisol and ACTH level. He failed the 1mg and 8mg dexamethasone suppression tests. He underwent inferior petrosal sinus sampling (IPSS), which was consistent with a pituitary source of ACTH. Total hypophysectomy was performed for a presumed pituitary microadenoma, but pathology instead showed corticotrophi hyperplasia. The patient continues to have persistent CS, which is managed medically with mifepristone. However, due to recent intolerances, bilateral adrenalectomy is being considered.

Case 2: A 35 year-old male developed diabetes mellitus (DM), CAD, pulmonary embolism, and osteoporosis over a period of 1 year, and was noted to have Cushingoid features and HMA. Random cortisol and ACTH levels were very elevated. Pituitary MRI revealed a 3mm microadenoma, however he failed the 8mg dexamethasone suppression test. The patient then underwent IPSS, which was consistent with a pituitary etiology. Pituitary microadenoma was resected and pathology confirmed ACTH-secreting adenoma. He is being monitored closely postoperatively and has exhibited signs of adrenal insufficiency.

Case 3: A 40 year-old female with history of metastatic pancreatic neuroendocrine tumor (PNET) presented with altered mental status, skin hyperpigmentation, and HMA. Laboratory evaluation showed an elevated 24-hour urinary cortisol and ACTH level. High dose dexamethasone suppression and CRH stimulation tests were suggestive of ectopic ACTH secretion. Pituitary MRI did not reveal any significant mass. ACTH staining of previously resected PNET ovarian metastases showed positive immunoreactivity, confirming the source of ACTH. Given lack of surgical options due to metastatic disease, she is being managed on combination therapy with octreotide, ketoconazole and mifepristone.

Conclusion: Our three cases demonstrate the difficulty in practically applying the theoretical diagnostic algorithm to determine the etiology of CS. In addition, these cases also demonstrate that treatment in CS should be individualized.

Abstract #126

THE IMPORTANCE OF A TAN IN SEPTIC SHOCK; A PICTURE SPEAKS LOUDER THAN WORDS

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Case Presentation: Autoimmune adrenalitis is the main cause of Addison’s disease or primary adrenal insufficiency (PAI). Because PAI’s identification depends on careful history-taking, proper diagnosis can be challenging. In a national registry 60% of the patients with PAI reported being evaluated by two or more doctors before reaching the correct diagnosis.

A 45-year-old female fitness buff (TM) with no medical history presented with 3-weeks of fatigue and mental slowness. Three days prior to presentation she had onset of non-bilious emesis, abdominal pain and chills. She denied diarrhea or sick contacts and had just returned from a lengthy beach vacation. On admission she was confused, hypotensive (77/45 mmHg) and tachycardic; further
testing revealed lactic acidosis, severe hyponatremia (107 mmol/L) and a urinary tract infection (UTI). She was treated for septic shock due to UTI in the intensive care unit (ICU). Despite appropriate treatment, she remained hypotensive and weak with slow mentation. She underwent extensive evaluation over the next 2 weeks, all of which was negative; her electrolyte abnormalities were attributed to laxative abuse, although TM denied their use. TM’s initial cortisol level was low-normal, eliminating the differential diagnosis of PAI for her ICU physicians. However, she had received a dose of intravenous hydrocortisone for septic shock just prior. She continued to have recurrent hyponatremia with repeated transient normalization of serum sodium with saline infusions. On day 17, the patient was transferred to a different unit and the persistent symptoms lead to a workup for adrenal insufficiency. Her ACTH levels were elevated, her morning cortisol level was 2.3 µg/dl with no response to cosyntropin stimulation, and 21-hydroxylase antibodies were found, confirming PAI. Her symptoms and sodium returned to normal with initiation of hydrocortisone and fludrocortisone.

**Conclusion:** The presentation of PAI is easily confused with septic shock, psychiatric disorders or gastrointestinal infections; TM’s presenting symptoms were consistent with these. The absence of hyperkalemia and the initial cortisol level misled the admitting physicians in their diagnosis. Moreover, the hyperpigmentation was initially attributed to a tan instead of up-regulation of pituitary hormones in response to adrenal failure. With proper diagnosis and treatment, patients with PAI have normal life expectancy compared to age-matched controls. A delay in PAI diagnosis can be fatal within 2 years if not diagnosed and treated appropriately, demonstrating the importance of maintaining a high index of suspicion when patients do not improve with appropriate treatment of alternate diagnoses.

**Abstract #127**

**PHEOCHROMOCYTOMA WITHOUT BIOCHEMICAL EVIDENCE: UNINTENTIONAL TREATMENT WITH BIOPSY OR SILENT PHEOCHROMOCYTOMA?**

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**Objective:** To demonstrate through case presentation the possible initial treatment of pheochromocytoma with embolization, as well as reinforce the importance of biochemical evaluation prior to adrenal mass biopsy.

**Case Presentation:** A 58 year old male presented to the hospital with a several month history of right sided abdominal pain. CT abdomen showed an indeterminate 1.9 cm right adrenal mass. MRI of the adrenal mass showed decreased signal intensity on T2 weighted images, and therefore described as a benign adenoma consistent with adipose tissue. CT guided biopsy was done on the adrenal mass with a small amount of hemorrhage adjacent to the mass. Two hours later evaluation of the hemorrhage was done with CT abdomen demonstrating a large perinephric and suprarenal hematoma with active bleeding. Coiling of all three adrenal arteries was completed with successful hemostasis. Biopsy results later returned consistent with pheochromocytoma, however, further evaluation with serum metanephrines and normetanephrines was negative. The adrenal gland was surgically excised three months later with confirmed pheochromocytoma.

**Discussion:** Pheochromocytomas present symptomatically about half of the time or, as with our patient, are asymptomatic and discovered incidentally on imaging. Approximately 5% of adrenal incidentalomas are pheochromocytomas, with detection prior to biopsy crucial to avoid hypertensive crisis or hemorrhage. They have unique characteristics on imaging, including increased signal uptake on T2 weighted MRI, which make the diagnosis more likely. However, because imaging is not 100% specific, biochemical testing is imperative for all patients with adrenal incidentalomas, especially if biopsy is planned. Plasma free metanephrines or 24-hour urine fractionated metanephrines have relatively good sensitivity and specificity. However, in some very rare instances, pheochromocytomas can be biochemically silent. In our case, we speculate that the normal biochemistry may represent a biochemically silent tumor; it is also possible that during the emergent embolization procedure to halt the bleeding there may have been enough ischemia to the adrenal to inadvertently cure the patient of an active pheochromocytoma.

**Conclusion:** Our case reinforces the recommendation that biochemical testing of adrenal incidentalomas should be completed prior to biopsy to avoid post-procedure complications. This case demonstrates possible treatment of a pheochromocytoma initially with embolization, which has been reported previously in a limited number of cases including inoperable masses and those which have ruptured.
Abstract #128

PHEOCHROMOCYTOMA WITH INVASION OF LIVER, KIDNEY, AND INFERIOR VENA CAVA

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Case Presentation: Background: Pheochromocytomas are rare catecholamine-secreting tumors of chromaffin cells in the adrenal medulla, with estimated annual incidence of 0.8/100,000 person-years. Most are sporadic, but approximately 30 percent occur as a part of a familial disorder. Symptoms occur in roughly half of patients; the classic symptom triad is episodic headache, sweating, and tachycardia. Roughly 10% of catecholamine-secreting tumors are malignant. Indicators of malignant potential are local invasion or distant metastases, which may occur up to 20 years after resection. Efforts to identify other prognostic markers have met with mixed results.

Case report: A 73 year-old man with gallstone pancreatitis and pneumonia presented from an outside hospital for escalation of care. History revealed he had suffered recent flank pain, weight loss, hematuria, and uncontrolled hypertension (previously well controlled for 20 years on lisinopril). Other medical history was significant for hyperlipidemia, pre-diabetes, and osteoarthritis.

A CT & MRI scan both demonstrated a 12 cm right adrenal mass showing central necrosis and local invasion of the liver and inferior vena cava (IVC). Serum catecholamine and metanephrine labs were consistent with pheochromocytoma. He underwent initial exploratory laparotomy at an outside hospital without preoperative alpha blockade with intraoperative blood loss of 1 liter and the mass was deemed unresectable. This was his only prior abdominal surgery.

After his gallstone pancreatitis & pneumonia resolved, he received approximately two months of alpha blockade. He then underwent an en bloc resection of the right kidney, right adrenal gland, segment 6 of the liver, & the right lateral aspect of the IVC with reconstruction of the vena cava with a Gore-Tex patch, & cholecystectomy (given his history of gallstone pancreatitis). Pathology revealed vascular invasion, involvement of the renal cortex, perinephric adipose tissue, and the wall of the IVC; a metastasis was seen in one of two lymph nodes.

Conclusion: This is a case of a malignant pheochromocytoma with local invasion of the liver, right kidney, and IVC, successfully resected en bloc with evidence of a lymph node metastasis.

Abstract #129

ADRENA L INCIDENTALOMA DIAGNOSED AS ASYMPTOMATIC PHEOCHROMOCYTOMA

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Case Presentation: A 39 year old Haitian-American woman, previously without significant past medical history presented with vague lower abdominal pain and gas. A CT of the abdomen revealed an incidental right adrenal mass 6.3cms in largest dimension. The washout characteristics were indeterminate. A subsequent MRI of the abdomen with contrast showed a right adrenal mass, 6.4cm in largest dimension that was hyperintense on T2 imaging (Image 1). It was felt to be consistent with a pheochromocytoma. The results of biochemical testing are included in table 1. She did not have classic symptoms for a pheochromocytoma, such as palpitations, sweats or pounding headaches. She reported no significant change in weight and denied panic attacks. Her highest recorded blood pressure (BP) was 138/89. She was started on doxazosin (Cardura) as an outpatient. Based on the imaging and unequivocal biochemical findings, a clinical diagnosis of pheochromocytoma was made. She underwent right adrenalectomy after one month of doxazosin and two days of preoperative aggressive inpatient intravenous hydration with normal saline without complications. The pathology revealed pheochromocytoma with negative resection margins (Images 2-4). Post operative plasma metanephrine levels were normal.

Discussion: Pheochromocytomas are catecholamine-secreting tumors originating in the medulla of the adrenal glands in 90% of cases. They are rare tumors, with an annual incidence of 2 to 8 cases per million people. Based on screening studies for secondary causes of hypertension in outpatients, the prevalence of pheochromocytoma has been estimated at 0.1% to 0.6. Our patient sought medical attention due to seemingly unrelated symptoms and was found to have an adrenal incidentaloma on radiographic imaging. The clinical presentation of pheochromocytomas are variable and many patients will not have the complete classic triad of headache, sweating, and palpitations. About half the patients will have paroxysmal hypertension. Once a pheochromocytoma is suspected, the diagnosis is based on demonstration of catecholamine overproduction by measurement of urine or plasma catecholamines and their metabolites.

Conclusion: Pheochromocytomas are very rare tumors. Even more rare, is for a pheochromocytoma to be entirely asymptomatic and to be associated with a persistent normal blood pressure. When this does occur, it is more likely to be seen in association with an adrenal incidentaloma,
as occurred in our patient. Her tumor was discovered in a relatively early phase. Aggressive treatment of a pheochromocytoma is mandatory; otherwise, severe hypertension with potentially lethal outcomes such as stroke or myocardial infarction may eventually ensue.

Abstract #130

A PATIENT WITH UNDIAGNOSED PARA-GANGLIOMA PRESENTING WITH ACUTE APPENDICITIS

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Objective: Paragangliomas are rare neuroendocrine tumors that originate from sympathetic nervous system outside of adrenal glands. This is a pediatric case of parareureteral paraganglioma manifested as acute appendicitis.

Case Presentation: An otherwise healthy 10-year-old female admitted to the PICU for management of hypertensive urgency and abdominal pain found to be secondary to acute appendicitis confirmed by abdominal ultrasound and underwent laparoscopic appendectomy. Intraoperatively a vascular mass was noted posterior to the uterus. After completion of appendectomy, imaging revealed an avidly enhancing mass in the pelvis along with significantly elevated normetanephrines. Patient was started on alpha blockade and then beta blockade in preparation for surgical resection of paraganglioma. Genetic testing for possible germline mutations as etiology of paraganglioma was sent.

Discussion: Genitourinary tract paragangliomas are rare neoplasms and ureteral paragangliomas are rarest form of the disease that can be missed on regular imaging for common disease process work up. Given the fact the patient underwent first surgery with undiagnosed paraganglioma deems risk for hypertensive crisis. This warrants obtaining detailed history and physical examination along with requesting appropriate lab values and imaging modalities before confirming diagnosis.

Conclusion: Paragangliomas usually manifest with hypertensive episodes and specially in pediatric population medical team needs to be sensitive to such symptoms and obtain thorough work up including metanephrines and proper imaging to avoid risk of morbidities and mortalities involved in procedures with no prior stabilization of blood pressure.

Abstract #131

MEDICAL MANAGEMENT OF MILD HYPER-CORTISOLISM AND PRIMARY ALDOSTERONISM IN A PATIENT WITH ACTH-INDEPENDENT MACRONODULAR HYPERPLASIA PRESENTING WITH RESISTANT HYPERTENSION

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Objective: Co-secretion of cortisol and aldosterone from adrenal nodules has been reported (Spath, 2001; Hayashi 1998) and is typically managed surgically. We present a case of hypercortisolism and primary aldosteronism (PA) managed medically with glucocorticoid and mineralocorticoid receptor antagonists.

Case Presentation: Case: A 71 y/o man with resistant hypertension was referred for suspected PA. Prior to presentation his BP ranged from 170/90 to 230/100 mmHg on 5 anti-hypertensive agents. His screening aldosterone to renin ratio was elevated at 53 ng/dL:ng/mL/hr with serum potassium 3.8 mmol/L (3.5-5.3). Plasma metanephrines performed prior to referral were normal, as was 24-hr UFC 34.5 µg/d( 4-50).

Results: Physical examination was notable only for obesity with BMI 31 kg/m2. Oral salt load test confirmed PA with a 24-hr urine aldosterone of 17.9 µg/d. He declined adrenal vein sampling and surgery. Spironolactone was initiated at 100mg/d. Abdominal CT performed to exclude adrenal cortical carcinoma demonstrated four bilateral adrenal adenomas ranging from 1.9 to 3.5 cm. Random ACTH was undetectable, suggesting ACTH-independent macronodular adrenal hyperplasia (AIMAH). 1mg DST 2.6 µg/dL. Late-night salivary cortisol was normal x 2. BP control improved on spironolactone. However, he developed worsening anxiety, weight gain of 10 lbs and pre-diabetes over the next year. Repeat 1mg DST was 3.4 µg/dL. Surgery was again declined, and mifepristone 300 mg/d was initiated. After 3 months of therapy, he reported weight loss, improved energy and less anxiety. ACTH 2 months following mifepristone initiation rose to 29 pg/dL.

Discussion: Hypercorticolism secondary to AIMAH is a rare cause of Cushings syndrome. Concurrent PA has been described in adrenal nodular disease (Spath, 2001) as well as AIMAH (Hayashi 19982). Surgery is typically the preferred approach in managing PA due to an adenoma as well as hypercortisolism due to AIMAH. We present a case in which medical management of (i) hypercortisolism with mifepristone, a glucocorticoid receptor antagonist, and (ii) PA with spironolactone, a mineralocorticoid receptor antagonist, was successful.
Conclusion: In this patient with bilateral adrenal nodular disease not desiring surgical management, medical management of aldosterone excess with spironolactone and glucocorticoid excess with mifepristone resulted in improvement in symptoms and hemodynamic parameters.

Abstract #132

AN UNUSUAL CASE OF DOPAMINE AND CATECHOLAMINE COPRODUCTION PHEOCHROMOCYTOMA: DOPAMINE COPRODUCTION RAISES THE POSSIBILITY OF MALIGNANT PHEOCHROMOCYTOMA

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Objective: Most pheochromocytomas produce norepinephrine and/or epinephrine. Tumors that co-produce dopamine are rare and the accurate prevalence of such tumors is unknown. Studies suggest that co-production of dopamine could be an indication that it is a malignant pheochromocytoma.

Case Presentation: We present a case of 52 year old male with history of hypertension who presented to the hospital with headache and nausea and followed by cardiac arrest while in emergency-room. He had CPR, was found to be in shockable rhythm and was admitted with anoxic encephalopathy. During his complicated ICU stay, a CT-scan of chest/abdomen/pelvis ordered for identifying possible cause of sepsis revealed a left adrenal incidentaloma measuring 6.4 x 5.3 x 6.8 cm, with heterogenous-hypervascularity. Initial laboratory workup for adrenal mass showed plasma epinephrine >13970 (0-61pg/ml), nor-epinephrine >10370 (0-874pg/ml), dopamine 2361(0-48pg/ml), serum aldosterone <1 (0-30ng/dl), renin 24.18 (supine 1.31-2.33ng/ml/hr) and plasma ACTH 55.60 (7.2-63.3pg/ml). 24hour urinary free cortisol 59 (0-50 ug/24hr), 24HR urine-metanephrines 17988 (45-290ug/24hr), nor-metanephrines 4113 (82-500ug/24hr). Diagnosis of possible-malignant-pheochromocytoma was made based on markedly increased catecholamines, dopamine-coproduction and tumor size. Surgical removal was recommended but deferred due to patients' grave prognosis.

Discussion: About 10% of pheochromocytomas are malignant. Unlike other tumors, no molecular or cellular markers or pathological characteristics can identify a pheochromocytoma as malignant. The only way to diagnose malignant pheochromocytoma is the presence of metastases in the non-chromaffin tissues that could be very difficult. Previous report suggested that increased urinary dopamine levels might raise the likelihood of malignant-pheochromocytoma. Surgery is the main treatment for both benign and malignant pheochromocytoma. Treatment with iodine-131-meta-iodobenzylguanidine (1131-MIBG) and systemic chemotherapy in adjunct with surgery are useful as well. No effective treatment currently exists for patients with malignant pheochromocytomas and prognosis remains poor.

Conclusion: The correct and timely diagnosis of malignant pheochromocytomas is important to enhance treatment and prevent adverse outcomes like cardiac arrest. We suggest that dopamine-coproduction could be a sign of malignancy. Therefore, more studies are needed to evaluate the importance of dopamine levels in the diagnosis and possibly the treatment of malignant pheochromocytomas.

Abstract #133

RAPID ADRENAL RECOVERY AFTER SURGERY FOR NON ACTH DEPENDENT CUSHING SYNDROME FOLLOWING MIFEPRISTONE TREATMENT

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Objective: Cushing syndrome treated with unilateral adrenalectomy is often followed by prolonged recovery of normal hypothalamic pituitary adrenal axis requiring post-operative steroid replacement for many months. A case of non ACTH dependent Cushing syndrome was treated with Mifepristine for several months prior to surgery. Restoration of normal pituitary adrenal function and withdrawal from steroid replacement was accomplished within two weeks of adrenalectomy.

Methods: Mifepriste treatment was used preoperatively in a case of Cushing Syndrome

Case Presentation: The patient is a 52 year old lady referred for evaluation of a left adrenal mass. She had been evaluated elsewhere for functionality and the mass was deemed non-functional. She had a history of IGT, hypertension and hypokalemia. She gained 40 lbs. over the prior two years and had increased appetite. Exam was negative for classical findings of Cushing syndrome other than obesity. CT showed a 1.5 cm left adrenal mass with HU 37. Serum aldosterone, PRA , and catecholamines were normal. AM cortisol was 12-18mcg/dL with ACTH levels 3-6pg/ml. She continued to require KCL. After 8...
months she agreed to surgery and underwent laparoscopic adrenalectomy after withholding mifepristone treatment for 2 weeks. She was discharged on dexamethasone replacement. Post surgery dexamethasone was tapered in 2 weeks with no symptoms. After steroid withdrawal AM cortisol was 11-13mcg/dL, and ACTH was 70-98pg/ml. She has continued to lose weight intentionally with no recurrence of hyperglycemia, hypertension or hypokalemia. **Discussion:** Prolonged steroid therapy with slow tapering after removal of a cortisol secreting adenoma frequently takes months before recovery of normal function in the remaining adrenal gland. This case demonstrated very rapid recovery of normal adrenal function after pretreatment with Mifepristone. Treatment was both effective and well tolerated.  

**Conclusion:** Mifepristone therapy for non ACTH dependent Cushing syndrome is effective therapy for hypercortisolism and appears to offer the advantage of rapid recovery of the pituitary adrenal axis after surgical treatment of the disease. Larger scale investigation this approach may be warranted.

**Abstract #134**

**PEDIATRIC CUSHING DISEASE: DESMOPRESSIN VERSUS OVINE CRH STIMULATED INFERIOR PETROSAL SINUS SAMPLING**

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**Case Presentation:** An 8 year, 7 month old male was referred for evaluation of precocious puberty. He developed pubic hair, body odor and acne at 7 years of age. During the previous year he had gained 10 kg and his height deviated from the 90th to 75th percentile. Physical examination revealed hypertension, height +0.64 SD, weight +2.95 SD, BMI +2.68 SD, plethoric moon face, Tanner 3 pubic hair, 5 mL testicles bilaterally, and mild facial acne. Cortisol level drawn at 1430 was 16.4 mcg/dL and testosterone was 14 ng/dL.

Presentation was concerning for Cushing syndrome and 1 mg overnight dexamethasone suppression test was performed with AM cortisol 2.0 mcg/dL and ACTH 15 pg/mL. Despite the indeterminate results, over a 3 month period he gained an additional 4.1 kg without height gain and appeared more Cushingoid. A 48-hour low dose dexamethasone suppression test was performed; baseline 8 am cortisol was 22.1 mcg/dL, 48-hour cortisol was 5.8 mcg/dL, and ACTH was 29 pg/mL. With biochemical evidence of Cushing disease, MRI of the brain was performed revealing a heterogeneous filling defect within the left and right lateral aspects of the pituitary. A microadenoma was not visualized, but could not be excluded. Inferior petrosal sinus sampling (IPSS) was performed to further evaluate the patient. Notably, our institution is now using desmopressin in place of ovine corticotropin-releasing hormone (oCRH) as the stimulant for IPSS. The results were negative for microadenoma. Clinical and biochemical picture were not consistent with these findings. Repeat IPSS at the NIH using oCRH revealed increase of ACTH in the right IPS from 162 pg/mL to 1250 pg/mL at 3 minutes with right petrosal sinus to peripheral ratio of 30.6 confirming diagnosis of Cushing disease (stimulated ACTH IPSS/peripheral ratio greater than 3 suggestive of pituitary source of ACTH). He then underwent transphenoidal surgery with successful removal of adenoma and subsequent cure of his Cushing disease.

**Conclusion:** Following nationwide shortage of oCRH, desmopressin was used as an alternate stimulant to perform IPSS. While desmopressin stimulated IPSS has shown sensitivity and specificity of over 90% in multiple adult studies and case reports in pediatrics have suggested efficacy, formal pediatric studies have yet to be conducted. Desmopressin stimulated IPSS failed to detect Cushing disease in our patient while a subsequent oCRH stimulated IPSS confirmed the diagnosis. Additional studies of desmopressin as a stimulant for pediatric IPSS are warranted and clinicians should be aware of the potential lack of sensitivity of desmopressin stimulated IPSS.

**Abstract #135**

**AN UNUSUAL CASE OF ALDOSTERONE-PRODUCING ADENOMA PRESENTED WITH SEVERE HYPOKALEMIA, MYOPATHY, RHABDOMYOLYSIS, AND DEVELOPED RENAL FAILURE RESULTING FROM MYOGLOBINURIA.**

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**Objective:** We present a case of Aldosterone-producing Adenoma (APA) with profound hypokalemia, severe myopathy, who developed acute renal failure due to myoglobinuria resulting from rhabdomyolysis. She was treated initially medically with resolution of renal failure, followed by resection of adenoma, resulting in resolution of HTN, hypokalemia and myopathy.

**Results:** A 35 yrs. old lady presented with BP of 180/120, and myopathy. Labs: serum K+ 1.7 mmol/l, Na+ 146 mmol/l, metabolic acidosis pH 7.53, HCO3 40, CK 5061 IU/l, plasma renin activity < 1 ng/ml/hr, plasma aldosterone 693 pmol/l (Ref. value up to 582), abnormal
Abstract #136

IATROGENIC CUSHING’S SYNDROME PRESENTING SEVERE ATIPICAL SKIN LESIONS EXTENDED IN THE BODY

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Results: Cushing’s syndrome comprises a wide variety of signs and symptoms, that are result of a high exposure of body tissue to glucocorticoids. The most common cause is iatrogenic from prescribed corticosteroids. Skin tends to become thin, fragile, and more susceptible to bruises and infections, wounds heal poorly, and striae appear in areas of weight gain. Although some skin lesions are not rare, it is not common to see widespread skin lesions in these patients. We describe the case of a 61-year-old female patient with history of high blood pressure and rheumatoid arthritis, and generalized tremor associated with a cerebellar vascular event; she had been receiving intramuscular betamethasone every fifteen days for the last 3 years. The patient had extremely thin and fragile skin, presented with widespread lesions with ecchymosis, ulcers and necrosis located in arms, forearms, chest and legs. Her family referred that the patient had progressive muscular weakness that prevented her from walking, and had been bedridden for 2 months; associated with an altered mental status for the last two weeks. She arrived into our emergency service with a 2-day history of a very intense headache, nausea, vomiting and fever. Blood pressure (BP) was not audible, cardiac frequency was 120 bpm, neurological examination was normal except for a 3/5 muscle strength according to the oxford scale, plantar response was indifferent. The abdomen presented striae, telangiectasia and central adiposity. White blood cells: 22,300, 83% neutrophils, 11% lymphocytes, with increased CSF proteins 474 mg/dl, glucose 84 mg/dl, 57 cells (70% monocytes), creatinine: 2.18mg/dl, albumin: 1.5 g/dl, rheumatoid factor was positive, serum cortisol was suppressed. She was diagnosed with Iatrogenic Cushing’s syndrome, in septic shock, with possible source of infection attributed to the skin lesions and meningitis. Wide spectrum antibiotics were initiated (meropenem and vancomycin), as well as norepinephrine, hydrocortisone, and IV albumin. The skin lesions were attributed as a severe manifestation of the Cushing’s syndrome by the Dermatology and Endocrinology services. The symptoms resolved within 72 hours of treatment; as she improved a steroid tapering program was prescribed with oral deflazacort and she was sent home.
Conclusion: Forty-five days later, she returned to our service with joint and skeletal pain, anxiety, altered consciousness (Glasgow 6/15), and no audible blood pressure. She had suspended the steroid treatment abruptly; BP was elevated with a dose of 500mg IV hydrocortisone, noting the presence of adrenal insufficiency. Unluckily, the patient died a few days later due to pulmonary complications.

Abstract #137

ISOLATED PRIMARY ALDOSTERONE DEFICIENCY

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Objective: We present a case of critical hyponatremia with low serum osmolality that turned out as isolated primary aldosterone deficiency.

Results: A 60-yr. old female had completed 6 cycles of R-CHOP & XRT for diffuse large B cell lymphoma. She presented with confusion, disorientation, hypotension, dehydration & seizure. She had serum Na+ 116mmol/l, urine Na+ 119mmol/l, serum osmolality 260 mos/kg, urine osmolality 464, abnormal FENa 56%, normal renal functions (Cr 46, GFR >60), FT416.7 pmol/l, TSH 0.985 mu/l (WNL). MRI brain: edema, probable lymphoma recurrence. She received dexamethasone. Thereafter, serum ACTH was suppressed to <1, & cortisol was 32 mmol/l (RR:137-689). However, synacthen test revealed peak cortisol 549 indicating normal adrenal fasiculata reserve. Dexam does not interfere with cortisol assay. Also, dexam does not have mineralocorticoid activity. The possibilities of SIADH versus cerebral salt wasting (CSW) were considered since in addition to hyponatremia, two disorders share inappropriately high urine osmolality & urine sodium is usually >40 mmol/L due to volume expansion in SIADH & salt wasting in CSW. ADH determination does not help to differentiate the two. Patient received initially water restriction under observation with no improvement. Thereafter she received hypertonic saline (2%-3% NaCl), oral sodium chloride 2g TID again without improvement. Further evaluation consisted of determination of serumincreased direct renin of 154.7 mu/l and serum aldosterone 193 pmol/l (Ref. value 332-582), findings compatible with isolated primary aldosterone deficiency. Upon resumption of florinef serum Na+ returned and remained normal at 135.

Discussion: Patient had isolated hypoaldosteronism defined as normal synacthen response, hyponatremia, despite elevated renin, implying deficient aldosterone production. Most probable cause of hypoaldosteronism appears to be severe illness resulting in decreased aldosterone production that can occur in critically ill patients with volume expansion playing a contributory role. Other causes of acquired hypoaldosteronism that include non-steroidal anti-inflammatory drugs, calcineurin inhibitors, angiotensin inhibitors, heparin therapy are not applicable to her. A primary cause such as inborn enzymic errors or genetic causes are unlikely since she had no previous episodes of hyponatremia.

Conclusion: Analysis of the basic pathophysiology is crucial for appropriate management. Serum aldosterone & plasma renin are useful in distinguishing primary from secondary aldosterone insufficiency, but aldosterone values are only interpretable when renin is high. Our patient had primary aldosterone insufficiency.
with hypertension, hypokalemia and primary amenorrhea, however, she has a female 46 XX karyotype. Both patients were started on Dexamethasone with very good control of the BP and correction of long standing hypokalemia.

Discussion: We present two Saudi siblings diagnosed with the rare diagnosis of 17-A-OHD after presenting with hypertension, persistent hypokalemia and failure of puberty for many years that responded well to dexamethasone. Some of the difficulty in the late diagnosis of both cases may be related to the fact that both cases didn’t present with ambiguous genitalia at birth which normally hints to the diagnosis earlier.

Conclusion: The diagnosis of 17-A-OHD is a challenging one. While the response of hyperyension and hypokalemia to dexamethasone is very good, the psychosocial and reproductive implications of the diagnosis are huge and require a multidisciplinary approach.

Abstract #139

A CASE OF HYPERTENSIVE ENCEPHALOPATHY DUE TO PHEOCHROMOCYTOMA CRISIS

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Objective: Pheochromocytomas are rare neuroendocrine tumours arising from the chromaffin cells developed inside the adrenal gland. Hypertension is caused by endocrine causes in just 5% of cases and in a small procent of 0.1–0.2% of patients it is related to pheochromocytomas or other catecholamine producing tumors. The classical clinical presentation specific for pheochromocytoma consist in the triad: headache, palpitations and perspiration. In addition, medical conditions such as severe acute hypertension, recent onset cardiomyopathy, aortic dissection, new-onset diabetes and pulmonary edema, could be one of the atypical clinical expressions of a pheochromocytoma

Methods: We report the case of a 24-year-old young woman who was referred to Parhon Institute with the diagnosis of hypertensive encephalopathy in the context of an adrenal tumour.

Case Presentation: On admission in Craiova County Hospital, the patient complained of severe headache, blurred vision, nausea and vomiting having a blood pressure of 270/150 mmHg. At the county hospital, the patient had undergone cranial computed tomography (CT) which excluded acute cerebral hemorrhage and confirmed the presence of cerebral edema. Thereafter, therapy with beta-blockers (bisoprolol), alpha blockers (doxazosin), diuretics (furosemide) and magnesium sulfate was initiated, obtaining the decrease and the control of the blood pressure values and also the reduction of cerebral edema. Furthermore, thoraco-abdominal CT revealed a left adrenal mass of 48/37 mm. The patient was subsequently transferred to Parhon Institute for further investigations. Thus, hormone assessment indicated elevated values of plasmatic metanephrines (1227pg/ml, normal range 10-90 pg/ml), urinary metanephrines (960 ug/day, normal range 50-350 ug/day) and seric chromogranin A (156ng/ml, normal range 20-125 ng/ml) with normal results for pituitary, thyroid, parathyroid, mineralocorticoid and glucocorticoid hormones.

Discussion: Based on clinical findings and investigations the patient was diagnosed with pheochromocytoma, which was subsequently laparoscopical resected. Histopathological and immunohistochemical examination confirmed the diagnosis of pheochromocytoma. Blood samples were collected for genetic testing.

Conclusion: We present the clinical case of a 24-year-old young woman with symptoms of hypertensive encephalopathy in which further investigations revealed the presence of a pheochromocytoma. With proper medical and surgical treatment, the patient’s clinical outcome was favorable.

Abstract #140

A CASE OF PRIMARY ADRENAL INSUFFICIENCY FROM TUBERCULOUS ADRENALITIS

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Objective: Primary adrenal insufficiency (PAI) is uncommon, but requires prompt recognition, as it can be life threatening and cause significant morbidity. We present an interesting case of PAI from tuberculous adrenalitis with concomitant genitourinary tuberculosis (TB).

Case Presentation: A 63 year old Malay lady with no past medical history presented to our hospital with 2 weeks of non-vertiginous orthostatic dizziness associated with fatigue, nausea and generalised hyperpigmentation of her skin. She had no respiratory or genitourinary symptoms. On examination, she was dehydrated with orthostatic hypotension (blood pressure 137/63 sitting and 114/60 standing). Areas of hyperpigmentation were noted over pressure areas and her oral mucosa. Investigations on admission showed hyponatremia (Sodium 129 mmol/L) and hyperkalemia (Potassium
ABSTRACTS – Adrenal Disorders

5.8 mmol/L) with acute kidney injury (Creatinine 1.5 mg/dL). Given the clinical presentation and electrolyte abnormalities, primary adrenal insufficiency was suspected. 8 am cortisol was low (2.9 mg/dL), with high paired adrenocorticotropic hormone levels (1027 pg/mL). A cosyntropin stimulation test was non-responsive (cortisol level 2.7 mg/dL 60 minutes post-stimulation). Adrenal androgen levels were low. Renin and aldosterone levels were performed only after high dose hydrocortisone replacement thus not interpretable. A Computed Tomography scan revealed scattered lung granulomas and bilateral enlarged adrenal glands.

The patient persistently declined adrenal biopsy as she was asymptomatic after glucocorticoid and mineralocorticoid replacement. Post-discharge, the patient was noted to have persistent sterile pyuria. Subsequent urinary investigations detected Mycobacterium TB on both polymerase chain reaction and culture. Repeated laryngeal swabs were negative for TB. The patient’s TB was successfully treated over 6 months, during which the dose of oral hydrocortisone was increased. Follow-up imaging showed near resolution of the adrenal enlargement.

Discussion: Tuberculous adrenalitis is rare in Singapore, which has seen significant reductions in rates of TB over the past 50 years. In this patient, a high index of suspicion led to the diagnosis of tuberculous adrenalitis which was treated successfully. During TB treatment, it is important to increase the dose of hydrocortisone as its half-life is shortened by rifampicin.

Conclusion: Tuberculous adrenalitis may be asymptomatic after treatment of PAI. Therefore, it is important to maintain a high index of suspicion for infective and infiltrative causes of adrenal failure, particularly if imaging studies show adrenal enlargement.

Abstract #141

GIANT PHEOCHROMOCYTOMA IN A PATIENT WITH NEUROFIBROMATOSIS TYPE 1 - A CASE REPORT AND A REVIEW OF LITERATURE

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Objective: The prevalence of pheochromocytoma in neurofibromatosis type 1 (NF1) is increased, with incidence reaching 50% in hypertensive patients. Pheochromocytoma can be asymptomatic and screening only hypertensive NF1 may miss a significant proportion and lead to delayed diagnosis. We present a case of giant pheochromocytoma in NF1, whose initial presentation was an ischemic stroke.

Case Presentation: A 49-year-old lady with NF1 was admitted for 3 days of right sided weakness. A large abdominal mass was noted incidentally on examination. Retrospectively, she had paroxysms of palpitations and diaphoresis in the preceding months, but had dismissed them as anxiety. On examination, blood pressure was 165/70 mmHg and pulse rate was 100 beats per minute. There was no discrepant blood pressure between both arms. Peripheral pulses were equal. Neurological examination confirmed right hemiparesis. Cardiorespiratory examination was normal. A large firm mass measuring 15cm was felt on the right side of the abdomen. An acute ischemic stroke was confirmed on the MRI of the brain, where an infarct in the left internal capsule contributed by a stenosis in the M1 segment of the left middle cerebral artery was seen. A 24-hour urinary metanephrines showed marked elevations of metanephrines and normetanephrines at 54619 nmol/day (reference interval (RI) 264-1729 nmol/day) and 111500 nmol/day (RI 480-2424 nmol/day) respectively. A CT scan of the abdomen revealed a large heterogeneous 18 cm left adrenal mass with cystic areas of necrosis. The right adrenal was normal. Despite adequate pre-op preparation with oral phenoxybenzamine and atenolol, she had intra-op fluctuations in blood pressure between systolic 70-170 mmHg. Histology confirmed a 20 cm x 14 cm x 10 cm composite pheochromocytoma. One month later, hypertension recurred despite normal urinary metanephrines. An I131-MIBG scan did not detect any tracer avid lesion. Screen for other causes of secondary hypertension was negative. After 3 years, her blood pressure remained well controlled with prazosin and nifedipine.

Discussion: Pheochromocytomas are rare but life-threatening tumours. While size does not correlate with symptoms, increased size has been shown to correlate with increased risk of malignancy. Recent evidence suggests that pheochromocytomas in NF1 are often asymptomatic and have increased risk of malignancy. The current recommended strategy for screening for pheochromocytoma only in hypertensive NF1 may lead to a delay in diagnosis, risking larger tumours with increased surgical risks and malignancy.

Conclusion: More prospective studies in NF1 are necessary to understand the behavior of this rare disease and recommend a cost-effective screening method.
Abstract #142

CORTISOL LEVEL AND ACADEMIC STRESS IN MEDICAL VS NON-MEDICAL STUDENTS

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Objective: The purpose of this study was to explore whether medical students who are under higher academic stress have higher cortisol concentration compared to non-medical students.

Methods: In this study, we measured am serum cortisol in fifty medical students (22 dental and 28 medical) and fifty non-medical (26 Art and 24 Business students). Assuming a higher academic stress among medical vs non-medical students, we analyzed am cortisol to see if there is significant difference between the two groups.

Results: Four colleges were included in this study Medicine (28.0%), Dental (22.0%), Business (24.0%) and Art (26.0%). The mean age of participants was 22.2 years with SD of 1.5. The mean Am cortisol level was 332.61 with SD of 141.46. Mean weight in kg was 78.97 with SD of 16.04, and the mean waist circumference was 89.29 cm with SD of 14.30. The Independent Samples t Test was used to test the null hypothesis that several means are equal, against the alternative hypothesis, (medical students have more stress and therefore higher cortisol level than non-medical students), there was no significant difference between the two groups (P value =0.348), However, there was significant difference between each single college using analysis of variance (F= 3.906, DF 3, P 0.011). In a regression model to look for confounders including weight, waist circumference, college, and age against the dependent factor cortisol, only age was significant, (P-value = 0.027)

Discussion: Stress due to performance in highly competitive academic environment has been a topic of great interest in many studies. The present study examined the relationship between stress level among colleges of high stress and competition (Medical and Dental) vs less stressful ones (Art, Business). Cortisol levels were measured as hormonal indicator for stress.

Conclusion: There was no significant difference between medical and non medical students cortisol level.

Abstract #143

ACTS LIKE PHEOCHROMOCYTOMA, LOOKS LIKE CUSHING’S SYNDROME- A MYSTERIOUS PRESENTATION OF A RARE ADRENAL CORTICAL CARCINOMA

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Objective: Adrenocortical carcinoma (ACC) occurs in only 0.5-2 adults per million per year and is associated with a 5-year survival rate of less than 30%. The objective of this case is to create awareness regarding the challenging diagnosis of ACC which can present with unclear symptoms like catatonia.

Case Presentation: A 50-year-old woman presented with worsening malaise over 2 days and a history of multiple hospitalizations for hypertensive urgency, dyspnea and facial flushing. Soon after admission, the patient had an episode of tachycardia at 170 beats per minute, blood pressure of 180/100 mmHg, and psychosis which resolved without any treatment within 20 minutes. She appeared anxious and kept repeating a phrase while staring at no particular object. On exam, the patient was obese with abdominal striae and pale mucous membranes. Initial laboratory results were unremarkable. CT scan of her abdomen showed a 10x6x10cm lobulated, partially calcified, septated left adrenal mass. An octreoscan showed abnormal uptake in the left adrenal area, concerning for pheochromocytoma. Treatment for presumed pheochromocytoma was started immediately with α blockade. However, testing for plasma metanephrines and catecholamines were negative and the 24-hour urine metanephrine test only showed a mild elevation of normetanephrines. The following day, the patient had another psychotic episode, but this time with catatonia and was unable respond except move her eyes. She also had accelerated hypertension, tachycardia, and generalized muscle rigidity. After ruling out any psychiatric or neurologic etiologies, suspicion for a cortisol secreting tumor was raised. A dexamethasone suppression test was performed, and was positive along with an undetectable adrenocorticotropic hormone level. Finally, after sufficient α and β blockade, the patient underwent laparoscopic tumor removal. The pathology report showed a low grade stage IV adrenocortical carcinoma with metastasis to the liver, which was also confirmed by a PET scan. She was started on treatment and at 3 month follow up, her symptoms were well controlled with less frequent psychotic episodes and complete resolution of catatonia. She is being treated with chemotherapy, which she is tolerating well, and has
returned to her routine lifestyle.

Conclusion: Through this case we aim to alert physicians about clinical presentation of ACC with emphasis on avoidance of anchoring bias. The patient was treated for pheochromocytoma initially due to the initial suspicion, until she developed catatonia, which made us investigate further. A low threshold must be maintained for investigation of such an adrenal tumor to ensure prompt treatment in order to prevent early mortality.

Abstract #144

METASTATIC BREAST CANCER: A RARE CAUSE OF ADRENAL CRISIS

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Case Presentation: Metastases to the adrenal glands are common in patients with malignancy but adrenal crisis is rare. Lung and breast cancer usually metastasize to the adrenal glands, however, these rarely cause any overt clinical symptoms. A 58 year old woman with breast cancer presented to the emergency department with complaints of uncontrollable left leg twitching and weakness of the left leg. Physical examination was remarkable for hyperpigmentation of the dorsum of both hands, minimal left lower extremity edema and decreased strength of the left lower extremity. There was concern for a new metastatic lesion to the brain. A head CT scan revealed a lesion in the right frontal region. There was suspicion for a focal seizure, and she was loaded with dilantin. She was later noted to be diaphoretic, less responsive and hypotensive. Laboratory results revealed hyponatremia (126 mmol/L) and hyperkalemia (6.5 mmol/L). ECG did not show ischemic changes or changes consistent with hyperkalemia. She developed hypoglycemia after receiving 10 units of insulin with dextrose. Fingerstick blood glucose was 55, and she was given an ampule of D50. Adrenal insufficiency was suspected because of the presentation of hypotension, hyponatremia and hyperkalemia despite normal renal function. She received 10 mg of IV dexamethasone. A random cortisol level drawn at that time was low (2.7 mcg/dL). She was started on dexamethasone and fludrocortisone. ACTH level drawn the next day was not suppressed at 29 pg/mL (reference range: 4.2 to 42.9 pg/mL). Cortisol levels remained low at 30 and 60 minutes post-cosyntropin stimulation. A diagnosis of primary adrenal insufficiency was made. Imaging studies including a CT scan of the chest, abdomen and pelvis revealed bilateral adrenal masses, with densities not consistent with adrenal adenomas. The patient continued to improve, and vital signs stabilized. Radiation treatment was planned for the brain lesion. She was discharged home with a regimen of dexamethasone and fludrocortisone, with arrangements for close follow up monitoring as outpatient.

Conclusion: We describe a case of a patient with breast cancer which metastasized to bilateral adrenal glands leading to adrenal crisis. It is important to have a high index of suspicion for adrenal insufficiency, especially in patients with metastatic lung or breast cancer, as its presentation can easily be missed.

Abstract #145

ADRENAL CRISIS AS THE INITIAL PRESENTATION OF ADRENOMYELONEUROPATHY

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Objective: Adrenoleukodystrophy (ALD) is a fatal X-linked genetic disease characterized by progressive neurologic deterioration due to demyelination of the cerebral white matter. It is caused by mutation of the ABCD1 gene leading to accumulation of very long chain fatty acids in different organs. Adrenomyeloneuropathy (AMN) is a phenotypic variant of ALD which is seen in adult males whose primary manifestation is spinal cord dysfunction with cerebral involvement seen in only 6% of the patients at the time of diagnosis. Most of the patients with ALD/AMN develop Addison’s disease but only 10% of them can present only with adrenal insufficiency. Most of the patients who present with Addison’s disease only develop symptoms of AMN later in life.

Case Presentation: A 21-year-old man was admitted for altered mental status and was found to be in septic shock requiring intubation. He remained hypotensive despite IV fluids, vasopressors and antibiotic resuscitation. Serum cortisol was found to be very low and he clinically improved after the addition of high dose hydrocortisone which was tapered based on clinical status. He reported that since childhood he had darker skin than his parents and he admitted to having increased fatigue over the last few years. Repeat outpatient testing confirmed primary adrenal insufficiency with ACTH level of 2790 pg/ml and cortisol less than 1 mcg/dl. Adrenal and 21-hydroxylase antibodies were negative. Very long chain fatty acids were elevated and subsequent genetic testing was positive for a hemizygous missense mutation of the ABCD1 gene. Physical exam is now positive for hyperpigmentation and a mildly stiff gait. MRI of the brain shows subtle abnormal T2/FLAIR in the periventricular parietal lobes with contiguous extension through the splenium of the
Pheochromocytoma (PCC) is a rare catecholamine secreting neuroendocrine tumor that arises from chromaffin cells of the adrenal gland. The annual incidence is 3-8 cases per million within the United States. Patients often present with the triad of diaphoresis, palpitations, and headache; however, other presentations may include tremors, anxiety, abdominal pain, and hypertension. Case Presentation: A 29-year-old male with no significant past medical history presented complaining of a one week history of sharp abdominal pain radiating from the umbilicus to the back. On presentation, the patient was hypertensive with a blood pressure of 259/160. Subsequent CT scan of his chest and abdomen revealed a right adrenal mass concerning for PCC; however, lab studies revealed a potassium of 2.7 mmol/L which initially suggested hyperaldosteronism due to an adrenal adenoma. The patient remained persistently hypokalemic despite aggressive repletion of potassium. Further work up revealed normal cortisol, ACTH, and aldosterone levels. Plasma and urine normetanephrines were significantly elevated at 3776 pg/mL and 3645mcg/24h respectively, which prompted the diagnosis of PCC. The patient was treated initially with alpha-blockade and then beta-blockade was added prior to surgery. Pathology revealed a benign PCC. Conclusion: Patients with PCC can have atypical presentations. The case we encountered presented as abdominal pain, hypertension, and hypokalemia suggestive of an aldosterone secreting adrenal adenoma. Subsequent studies however, revealed PCC as the diagnosis. This
case brings to light catecholamine-induced refractory hypokalemia. The pathophysiology of PCC-induced hypokalemia is uncertain and further research is needed to determine the correlation.
SUBOPTIMAL GLYCEMIC LEVELS IN A PATIENT WITH TYPE 1 DIABETES. THE IMPACT OF DIABETES DISTRESS AND PSYCHOSOCIAL FACTORS ON DIABETES SELF-MANAGEMENT

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Case Presentation: Suboptimal glycemic levels are common for patients with diabetes mellitus. In 2013 the National Committee for Quality Assurance reported that 45.6% of patients with Medicaid had an A1c greater than 9%. Diabetes distress and psychosocial factors have a sizable impact on glycemic levels, yet unfortunately, they are often overlooked and undertreated. Diabetes distress, is the combined emotional, physician related, regimen related and interpersonal stressors related to living with diabetes. The prevalence of diabetes distress is reported to be 18-45% in patients with diabetes. High levels of diabetes distress are associated with suboptimal glycemic levels, poor self-care, low diabetes self-efficacy and poor quality of life even after controlling for clinical depression.

We are presenting a typical patient with diabetes and diabetes distress leading to poor glycemic levels. Our patient is a 52-year-old woman with type 1 diabetes, diagnosed at age 20. Over the past 10 years her A1c has ranged between 6.9 to 12.5%, most recently 9.5%. Medical history includes retinopathy, hyperlipidemia, obesity, anxiety, and depression. Her last Beck Depression Inventory (BDI) score was 5 indicating no clinically meaningful depressive symptoms, while she scored a mean 3.06 on the Diabetes Distress Scale-17 (DDS) indicating the highest levels of diabetes distress. DDS subscale mean scores were as follows; emotional burden 4.6, regimen-related distress 4.4, physician-related distress 1, and interpersonal distress 1.

Discussion: Diabetes distress and depression are distinct clinical entities that can affect patients with diabetes in unique but interrelated ways. Our patient demonstrates the negative core beliefs associated with depression without clinically significant depression (BDI score), however we were able to capture her emotional and regimen related distress using the DDS.

In December 2016, the ADA published the first position statement to specifically address the issue of psychosocial care for people with diabetes. The ADA has recommended that psychosocial care be integrated into the medical care of all people with diabetes with the goals of optimizing health outcomes and health-related quality of life. The ADA has recommended screening for symptoms of diabetes distress, depression, anxiety and eating disorders.

Conclusion: We have described a typical patient with type 1 diabetes and diabetes distress leading to suboptimal glycemic levels. Depression and diabetes distress can and should be screened for using self report assessments such as BDI and DDS. Endocrinologists play a critical role in diagnosis and initial therapy of psychosocial issues related to diabetes.

PROLONGED KETOSIS IN A PATIENT WITH EUGLYCEMIC DIABETIC KETOACIDOSIS SECONDARY TO DAPAGLIFLOZIN

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Objective: Since approval of sodium-glucose co-transporter 2 (SGLT2) inhibitors by the FDA for use in type 2 diabetes (T2DM) there have been several reported cases of euglycemic diabetic ketoacidosis (euDKA) in patients using this class of medications. We present a case in which ketonemia and glucosuria persisted well beyond the expected effect of Dapagliflozin.

Methods: History, clinical features, and biochemical investigations were analyzed.

Case Presentation: A 50-year-old African American female with a history of type 2 diabetes since the age of 35 presented with 10 days of constipation and fatigue with reduced oral intake for 3 days prior to admission. Due to her reduced oral intake, she stopped taking her antihyperglycemic agents 2 days prior to admission – Metformin 500 mg twice daily and Dapagliflozin 10 mg daily. On initial assessment in the ER she was noted to be acidic with an elevated anion gap and beta hydroxybutyrate, severe hypokalemia, and hypophosphatemia. Due to reduction in blood glucose and improvement in anion gap with continued hypokalemia, an insulin drip was not initially started and she was instead placed on sliding scale insulin. On day 6 of her admission, at which time the patient had been off Dapagliflozin for 8 days, Endocrinology was consulted due to rise in anion gap and persistent beta hydroxybutyrate elevation. Despite blood glucose levels of 100-180 the patient’s urine glucose level was noted to be >1000 at that time. A diagnosis of euDKA was made and an insulin drip was started along with Dextrose infusion. The anion gap gradually improved over the next 3 days as did the beta hydroxybutyrate. She was discharged on Glargine 10 units daily.

Discussion: Reduced serum glucose, reduced insulin doses, increased glucagon release, and reduced clearance of ketone bodies are possible contributors to euDKA in patient’s on SGLT2 inhibitors. Many cases of euDKA attributed to the above causes have been reported in the literature. Unique in our patient is that despite a good oral intake and discontinuation of Dapagliflozin for 8 days prior, glucosuria and ketonemia persisted.
**Conclusion:** Based on our experiences with this case, we posit that the clinical effects of Dapagliflozin persist much longer than the reported half-life of 12.9 hours would suggest. Patients on SGLT2 inhibitors should be educated about the need to discontinue these medications and start basal insulin during times of acute illness to avoid entering a ketogenic state. We suggest that holding SGLT2 inhibitors at least one week prior to a planned procedure with initiation of basal insulin perioperatively seems to be the safest course.

**Abstract #202**

**LIMITATIONS TO THE USE OF MARKERS OF LONG-TERM GLUCOSE CONTROL IN THE MANAGEMENT OF DIABETES: LESSONS LEARNED FROM A PATIENT WITH NEW ONSET OF HYPOGLYCEMIA**

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**Objective:** Diabetes management is guided by information provided by markers of long-term glucose control. Hemoglobin A1c (HbA1c) is used to diagnose diabetes and evaluate the effectiveness of therapy. Fructosamine is useful when a shorter follow-up period is being evaluated or when factors that interfere with HbA1c interpretation are present. However, there are limitations to the interpretation of HbA1c and fructosamine levels. This case reminds providers on the limitations of both HbA1c and fructosamine levels.

**Case Presentation:** A 48 year old male with uncontrolled diabetes with macro and microvascular complications was readmitted to the hospital for new onset of hypoglycemia with an HbA1c of 5.7%. A few days prior, the patient was discharged from the hospital after presenting with hematochezia. He was found to have anemia of chronic disease and hemolysis. During the initial admission, prior to receiving 2 units of packed red blood cells (RBCs), his HbA1c was 10.4%. During both hospitalizations the patient was consistently hyperglycemic (average of 190 mg/dL). Given hypoglycemia, lack of home glucose monitoring, history of transfusion and hemolysis, a fructosamine level was obtained and found to be 257 umol/L (normal 200-285 umol/L). However, given patient’s overt proteinuria and hypoalbuminemia, fructosamine levels were deemed inappropriate for evaluation of glucose control. A decision was made to manage patient’s diabetes based on glucose monitoring alone and his insulin doses were increased.

**Discussion:** Management of diabetes may be complicated when markers of long-term glucose control cannot be used to adjust therapy. HbA1c is formed when RBCs enter the circulation and become glycosylated at a rate dependent on blood glucose concentration. Our patient had various factors that interfered with the interpretation of HbA1c levels, including acute blood loss and hemolytic anemia, both of which increase RBC turnover. Further, the blood transfusion he received markedly modified his HbA1c within days of the first measurement. Other proteins, such as fructosamine, undergo glycation and may be used as markers of average blood glucose concentration. However, fructosamine is dependent on the half-life of albumin. The presence of proteinuria and hypoalbuminemia in our patient significantly altered his fructosamine level and precluded its use as a measure of ambient glucose control.

**Conclusion:** Clinicians should be aware of factors that interfere with the accuracy of HbA1c and fructosamine levels as measures of glucose control. Patients’ clinical history and glucose monitoring may take precedence when HbA1c or fructosamine yield inconsistent results.

**Abstract #203**

**SUSPECTED TYPE B INSULIN RESISTANCE SYNDROME IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Objective:** Type B insulin resistance syndrome (TBIR) is an autoimmune disorder in which autoantibodies are produced against insulin receptors resulting in glucose abnormalities, most commonly hyperglycemia from severe insulin resistance. Our objective is to document a case of suspected TBIR in a patient with Systemic Lupus Erythematosus (SLE).

**Case Presentation:** A 29 year old female with Type 2 Diabetes Mellitus (DM) presented to an oral surgeon for evaluation of mouth ulcers for 7 months. She was given topical steroids and told to follow up. At her next visit, she was sent to the hospital for tachycardia and 40 pounds weight loss. She had a prolonged hospitalization for diabetic ketoacidosis, severe insulin resistance, a new diagnosis of SLE and secondary adrenal insufficiency from topical steroids. Her physical examination was significant for her weight-41 kg, height-142 cm, BMI 20.2 and prominent skin darkening around the eyes and neck, suspicious for Addison’s disease. She had been treated with multiple oral agents for DM with Hemoglobin A1c 10.1% however during the hospital course, she had required exceedingly high doses of insulin (insulin drip up to 19 units per hour). Glutamic acid decarboxylase and islet cell antibodies were
negative and C-peptide was present, ruling out Type 1 DM. Adrenocorticotrophic hormone was low at 19, which ruled out Addison's disease, making her skin hyperpigmentation more consistent with acanthosis nigricans. For evaluation of her mouth ulcers, she was found to have SLE. Based on case reports of association of TBIR and SLE, TBIR was suspected and insulin receptor antibodies were sent. She was treated with intravenous immunoglobulin for 5 days however her high insulin requirements did not decrease. She was eventually discharged with insulin glargine 60 units twice daily, insulin lispro 52 units with each meal, and hydroxychloroquine for SLE. 1 month after discharge, Metformin was added yet her insulin requirements did not decrease. 2 months after discharge, she was tapered off hydrocortisone with normal cortisol. 7 months after discharge, her insulin requirements drastically decreased after episodes of hypoglycemia. Unfortunately, we were unable to obtain the results of her insulin receptor antibodies due to lab error, so TBIR was never confirmed.

**Discussion:** TBIR is rare, with only several cases reported in the literature. It is associated with autoimmune diseases, the majority with SLE. Given her severe insulin resistance and SLE, we strongly suspect she had Type B insulin resistance syndrome. Her SLE treatment may have led to the remission of her TBIR 7 months after her initial presentation.

**Conclusion:** To present a rare case of SLE and Type B Insulin Resistance syndrome.

**Abstract #204**

**TYPE 2 DIABETES MELLITUS IN PATIENTS WITH BLOOM SYNDROME: A CASE SERIES**

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**Objective:** To demonstrate the pathophysiology and management of type 2 diabetes mellitus (T2DM) in patients with Bloom syndrome (BS)

**Methods:** BS is an autosomal recessive disorder characterized by chromosomal instability and severe pre-natal and post-natal growth retardation. The germline mutation (BLM gene) fosters cellular aging and increases risk of cancer, causing death in the 2nd or 3rd decade of life. Patients are frequently predisposed to T2DM (18% of 272 patients in BS registry). A1c is falsely low due to pancytopenia and SMBG readings are best for T2DM management. Newer chemotherapeutic agents have lowered mortality but there is scarce data on managing T2DM with a better survival rate.

**Case Presentation:** Case 1: 23-year-old male with BS presented for T2DM management. Past medical history included hypogammaglobulinemia (HG), hypertension (HTN), and hypertriglycerideremia. Home medications were intravenous immunoglobulin (IVIG) every 6 weeks, glucophage, enalapril, and fenofibrate. He was 40.45 kg, 4’9” tall with a BMI of 19 kg/m2. Glycosylated hemoglobin A1c (A1c) was 6.4%.

He developed acute myeloid leukemia (AML) requiring inpatient chemotherapy. He was discharged on prednisone, metformin 1000 mg twice daily, lantus 36 units daily, and humalog 26 units with each meal. He underwent remission and prednisone and insulin were discontinued. He was only on metformin and A1c was 4.9% discordant with self-monitored blood glucose (SMBG) readings near 150 mg/dl. Five months later, he had a relapse of AML requiring chemotherapy, insulin, and prednisone. To date, he is repeatedly hospitalized for neutropenic fevers. Insulin doses are adjusted based on SMBG for persistent discordance in A1c due to pancytopenia.

Case 2: 20-year-old female with BS, acute lymphoblastic leukemia in remission, presented for management of T2DM, hypothyroidism, and secondary adrenal insufficiency. She also had HG, HTN, and breast cancer. Home medications were IVIG every 6 months, metformin 500/850 mg daily, levothyroxine (LT4) 50 mcg daily, hydrocortisone (HC) 2.5 mg only for stressful states. She was 48.54 kg, 4’5” tall with a BMI of 23 kg/m2. Her A1c was 6.1%, thyroid stimulating hormone 1.86 uIU/L and morning cortisol 33.2 ug/dl. She was advised to continue metformin, LT4, stop HC, and follow-up in 3 months.

**Discussion:** Patients with BS are burdened with high morbidity and mortality. The correlation of obesity and insulin resistance is extensively studied. The mechanism of insulin resistance in patients with BS is postulated to stem from possible underlying genetic defects in lean individuals. A1c is falsely low due to pancytopenia and SMBG readings are best for T2DM management. Newer chemotherapeutic agents have lowered mortality but there is scarce data on managing T2DM with a better survival rate.

**Conclusion:** This case series provides an opportunity to understand and treat the complexities of T2DM in patients with Bloom syndrome.
Abstract #205

**SHARED MEDICAL VISITS FOR SPANISH-SPEAKING PATIENTS WITH DIABETES: PEAKS AND PITFALLS**

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UNMC

**Objective:** Type 2 diabetes (T2DM) is an expanding epidemic, and is pervasive in the Hispanic community. T2DM is a challenging chronic disease; shared medical visits (SMVs) have been shown to improve outcomes, self-management behaviors, and patient and provider satisfaction. A meta-analysis found that SMVs dropped hemoglobin A1c (A1c) one-third to half as much as an oral hypoglycemic agent.

This original prospective mixed-methods study utilized the SMV model with aims to improve A1c, improve surveillance for diabetic complications and depression, and identify barriers to care for Spanish-speaking patients with T2DM.

**Methods:** During quarterly SMVs, patients met with a social worker, pharmacist, psychiatrist, internist, endocrinologist, and diabetic educator, all in Spanish. A personalized approach was used to set goals, reduce stress, and find ways to provide financial and community support. Diabetic education and medication regimen modification occurred in a group setting. Follow up phone calls were made to monitor progress, encourage, and modify regimen.

**Results:** Despite aggressive recruitment tactics, only seven patients have participated in SMVs thus far, which does not provide sufficient power to assess for statistical significance. To date, three patients have attended two visits, and average hemoglobin A1c did improve from 9.6% to 8.1%. PHQ-9 depression scores improved from 5 to 3. Data will be available from consecutive future visits. The group celebrated individual successes and the foundation was laid for future program development. Screening for neuropathy, nephropathy, and hyperlipidemia and administration of flu shot were performed in 100% of patients.

**Discussion:** Challenges to the success of the SMVs provided insight into the barriers of care for Spanish-speaking patients. Time constraints, cultural stigmas, modes of communication, access to and knowledge of available resources for support and supplies, and financial difficulties were all obstacles to care for this patient population.

While not measurable statistically, the emotional support that patients received from the group was obvious. Patients remark about the overwhelming support they feel from the group and the benefit of shared experience. Providers were energized by the group dynamic and team approach that identified barriers and solved problems in real time.

**Conclusion:** While the size of the study does not allow for statistical significance of objective data, initial data is encouraging and worthwhile insight was gained into the needs of these patients. This knowledge forms a foundation for future care of both shared and individual patients, and hastens the progress toward the goal to reduce health care disparities.

Abstract #207

**PILOT TELEHEALTH STUDY IN PATIENTS WITH DIABETES IMPROVED HBA1C BUT WITH SEVERAL TECHNOLOGICAL CHALLENGES**

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**Objective:** Telehealth can be used to remotely monitor and manage patients with chronic disease to reduce the cost of care, manage risks, and increase access to providers. Through a partnership between our hospital, a tablet supplier and a software company, a 3 month remote patient monitoring feasibility study was launched targeting diabetic patients.

**Methods:** Patients were recruited from the Endocrine Clinic based on eligibility criteria: age > 18 years with diabetes mellitus. Exclusion factors included lack of regular high broadband access to internet and living outside the state. Participating patients were provided a tablet with VideoDoc care management software with a glucometer and test strips that linked to the tablet. Providers received a WebCam. Providers and patients met through a face-to-face eVisit weekly during the 3 month pilot. Key measurements focused on feasibility and patient and provider experience. HbA1c and POC glucose levels and testing frequency were also monitored. Patients and providers were asked to complete a satisfaction survey and participate in a focus group at study completion.

**Results:** A total of 10 patients were recruited with ages ranging from 24 to 61 years. Pre-pilot HbA1c ranged from 7.1-14.6 % with mean of 10.2% (reference: 4-6%). Seven patients completed the study and 6 had a reduction in HbA1C (mean reduction of 2.1%). Three patients withdrew due to operational concerns. Frequency of blood sugar testing increased for a majority of patients by 1-2 more tests per day. Post-pilot focus groups felt that remote monitoring was convenient and enhanced patient-provider interaction; however there were several technological issues with software updates and patients not being able to upload their blood sugars, which often led to visits being conducted over the phone rather than by video. A common theme was that there needed to be more technical support available and more training on the software. Overall, it
was perceived that the video conference provided no added benefit over a phone call, rather it was increased patient contact time that improved outcomes.

**Discussion:** This telehealth pilot which allowed virtual communication with providers on a weekly basis improved HbA1c and led to increased patient and provider satisfaction, but at the expense of frequent technological challenges.

**Conclusion:** Telehealth can be a useful tool in chronic disease management and improve patient outcomes, especially as we move towards population health management; however, it will be important for future pilots to streamline the software and provide comprehensive technical support. It may also be prudent to allow patients to use their own electronic devices with which they are more familiar.

**Abstract #208**

**RISK FACTORS FOR RECURRENT DIABETIC KETOACIDOSIS IN A COMMUNITY HOSPITAL**

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UTHSC

**Objective:** To describe factors associated with recurrent diabetic ketoacidosis (DKA) in a community hospital in Memphis.

**Methods:** We identified all patients admitted with the diagnosis of DKA to a community hospital in Memphis, TN, from January 2013 to September 2015. Patients with multiple admissions were identified and compared to patients who only one admission for DKA. The unadjusted association between each of the variables and DKA were determined using chi-square tests for categorical variables and t-tests for continuous variables. Logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for all categorical variables. Multivariable logistic regression was used to determine predictors of recurrent DKA.

**Results:** A total of 116 patients accounted for 349 admissions during the 33-month period of study. Of the 116 patients with DKA, 58 patients had only one episode and the remainder had multiple admissions. Unadjusted results suggested that patients with lower body mass index (BMI), mean body weight, and higher anion gap values were more likely to have recurrent DKA. But in multivariable analysis BMI and polypharmacy were the strongest predictors of recurrent DKA.

**Discussion:** Low BMI and polypharmacy are easily quantifiable in day-to-day clinical practice. Our study provides the clinician simple and easily available markers for patients at high risk for recurrent DKA. If confirmed in other data sets and different populations, these markers might help direct interventions towards high risk patients to reduce morbidity and mortality.

**Conclusion:** Demographic variables especially BMI and polypharmacy could potentially aid in identifying subjects at high risk of recurrent DKA.

**Abstract #209**

**A RARE CASE OF INSULIN ALLERGIES IN A PREGNANT PATIENT**

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Northwell University

**Objective:** To document a rare case of insulin allergies in a pregnant patient with Type 2 Diabetes Mellitus.

**Case Presentation:** A 36 year old 28 week pregnant female with a history of Type 2 Diabetes Mellitus (DM) was evaluated in the endocrinology clinic for DM management. She was diagnosed with DM 8 years ago and was treated with Metformin 1,000 mg extended release. After pregnancy, her glucose was uncontrolled so Glyburide 6.25 mg twice daily was added however her glucose was still high. She was then switched to insulin detemir and insulin aspart. About one week after she started insulin detemir, she noticed itchy, red and blotchy hives around the site of her injection. She did not notice any reactions to insulin aspart. Even when she changed the sites of her insulin detemir injections, she would get hives at the new sites. Due to her reaction, insulin detemir was discontinued and she was started on regular human insulin. With regular human insulin, she developed hives two days after throughout her entire body. She was then switched to insulin aspart and still noticed hives throughout her body. Prior to her pregnancy, she never had any hives with any medications. The hives were concerning because they left a hyperpigmented mark, which may be indicative of a vasculitis process, however the vasculitis workup was later negative. Physical examination was significant for acanthosis nigricans, however no rash was seen on the initial visit. She underwent percutaneous skin test and intradermal allergic testing and was found to have a strong Type 1 Immunoglobulin-E mediated reaction to insulin detemir, and delayed reactions to regular human insulin and human aspart. She tested negative to insulin glulisine, insulin lispro and insulin glargine. She was then hospitalized for an insulin challenge test with insulin lispro. She was given insulin lispro and observed for 48 hours for an acute or delayed reaction, and had no complications. The patient was placed on a V-Go insulin pump using insulin lispro and tolerated that well, and was discharged home with the V-Go insulin pump. She maintained good glycemic control during the rest of her pregnancy.
Discussion: Allergic reactions are rare in pregnant females due to altered immune reactions during pregnancy. There are only two cases reported in the literature. Our patient demonstrated local reactions to different kinds of insulin, including insulin detemir, regular human insulin and insulin aspart. After being monitored in a hospital setting, she responded well to insulin lispro.

Conclusion: We report an uncommon case of allergic reaction to different kinds of insulin in a pregnant patient that was successfully managed after an inpatient insulin challenge.

Abstract #210

NEW ONSET TYPE 1 DIABETES AFTER DOUBLE IMMUNOTHERAPY FOR NEUROENDOCRINE LUNG CANCER

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Objective: The new immunotherapies for cancer have increasingly been described to be associated with endocrine dysfunction. Some of these side effects can lead to life-threatening conditions, such as adrenal insufficiency or diabetic ketoacidosis (DKA). Due to the increasing oncological use of these immunotherapies, it is crucial for healthcare providers to be aware of these potential effects to prevent adverse events.

Case Presentation: We describe a case of a 61 y/o caucasian male who presented with DKA after 5 biweekly treatments with nivolumab and Ipilimumab for large cell neuroendocrine lung cancer. Prior to his 6th treatment, he complained of fatigue for 2 weeks and polyuria and polydipsia for 2-3 days. He was found to have DKA with glucose 569 mg/dL and A1c 7.2%. He was initially assumed to have autoimmune T1D because of his family history of T1D. Laboratory testing showed an undetectable c-peptide level and inappropriately low insulin level. He was started on insulin and his requirements were low with a basal need of 0.2 units/kg/day and bolus of 0.15-0.25 units/kg/day. Despite his insulin deficiency, all 5 antibodies associated with T1D (GAD65, ICA, IAA, IA2 & ZnT8) were absent. Insulin requirements decreased slightly 10 weeks after the diagnosis but he has not regained insulin secretory function. His family history suggests higher susceptibility to develop T1D but HLA typing had not been performed on the affected family members.

Discussion: Immune checkpoint inhibitors have been associated with endocrine related adverse effects. Specifically, the antibodies targeting the programmed-cell death-1 (PD-1) immune checkpoint, pembrolizumab and nivolumab, have been reported to induce the development of T1D. These reports have been rare and are usually classic autoimmune T1D. Fulminant T1D without ketoacidosis or autoantibodies has been previously described with nivolumab. Diabetes has also been reported with ipilimumab, which blocks cytotoxic T-lymphocyte antigen 4, an immune checkpoint molecule, to augment anti-tumor T-cell responses. The unique features of this case include fulminant T1D presenting with DKA and complete insulin deficiency with persistent absence of beta-cell function that developed in the presence of combination therapy with nivolumab and Ipilimumab.

Conclusion: Anti-PD-1 therapy can cause rapid onset of complete insulin deficiency, possibly because of inappropriate activation of T cells. Similarly, antibody therapy against CTLA-4 can also induce diabetes mellitus. The use of these immunotherapies is increasing and thus clinicians need to be aware of this rare but serious adverse event and plan for frequent glucose testing and monitoring of symptoms.

Abstract #212

ANTI - PROGRAMMED CELL DEATH PROTEIN - 1 ANTIBODY MEDIATED FULMINANT TYPE 1 DIABETES

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Objective: To review the clinical presentation and diagnostic challenges of anti programmed cell death protein 1 (anti-PD-1) antibody mediated Fulminant Type 1 Diabetes (FT1D).

Case Presentation: A 54 year old Japanese female was diagnosed with thymic cancer in 2013 and underwent robotic resection of the tumor. She had recurrence of her thymic cancer with distant metastasis in 08/2014 and was treated with a tyrosine kinase inhibitor which was discontinued due to severe neutropenia. Thereafter she was enrolled in a research protocol (01- C- 0129) in 09/2015 and underwent therapy with pembrolizumab, an anti-PD-1 antibody. Weekly labs revealed evidence of hepatitis and pancreatitis with amylase –149(<85)U/L, Lipase -763(<85)U/L, AST-128(<40)U/L, ALT- 128(<56)U/L and glucose -337(64-128)mg/dl, consequently anti-PD-1 Ab therapy was discontinued on 11/25/2015. Patient was admitted to the hospital on 12/05/15 with nausea, weakness and dyspnea. Labs showed Glucose- 739 mg/dl, β- hydroxybutyrate –0.7(0-0.5), Bicarb- 24(20 - 26)mmol/L, AG- 108(8 -14) mmol/L, Cl- 91(98-109), K-4.4 (3.3 - 5.0)mmol/L, Na-125(136 - 144)mmol/L, PH- 7.30 (7.35- 7.45), ALT-88,
ABSTRACTS – Diabetes Mellitus/Prediabetes

AST-102 and Lipase –180. A1C was 9.5 %. GAD- 65, IA2, ZnT- 8 antibodies and IgG4 were unremarkable. She was treated for DKA, discharged on insulin therapy and was advised to follow up at our endocrine clinic for further management of her newly diagnosed diabetes.

**Discussion:** Fulminant type 1 diabetes is characterized by a markedly rapid and almost complete destruction of pancreatic β-cell leading to absolute insulin deficiency. It is more prevalent in Japanese population and account for 15%–20% of Japanese T1D. FT1D has been associated with viral infections (EBV, HHV-6, HSV and coxsackie B3 virus), medications, autoimmune diseases, pregnancy and genetic factors (HLA/DRB1- DQBI). Recently therapy with monoclonal antibodies have been proposed as a cause of FT1D. It can present with or without ketoacidosis at onset. Mean A1c level is reported as 6.4% at the time of presentation. GAD- 65, IA-2 and ZnT- 8 Ab are usually unremarkable, as in our patient. Short term corticosteroids have been proposed in treatment of FT1D with evidence of other autoimmune diseases. Insulin remains the mainstay therapy. Beta cell functioning may or may not return after discontinuing the medication depending upon the degree of injury.

**Conclusion:** The evidence accumulated to data suggests that anti-PD-1 antibody treatment is associated with FT1D. Beta cell functioning may or may not return after discontinuing the medication depending upon the degree of injury. Short term Corticosteroid therapy may be beneficial in some cases of FT1D, however intensive insulin therapy remains the mainstay treatment.

**Abstract #213**

**IMPACT OF AN INPATIENT DIABETES CONSULTING SERVICE ON POST DISCHARGE GLYCEMIC CONTROL**

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**Objective:** There is an increasing prevalence of diabetes mellitus worldwide with an increased health care cost associated with the diagnosis. There is limited data on the efficacy of a dedicated inpatient diabetes mellitus consulting team in improving glycemic control, hypoglycemia and readmission.

**Methods:** We performed a retrospective chart review of all adult, diabetic patients admitted to the St. Mary’s Hospital, Rochester MN between January-April 2014. Patients were divided into two groups: the diabetes consulting group (DC) and the no consultation group (NC - no consultation with the diabetes consulting service within 12 months of admission). Patients admitted for less than 48 hours were excluded. The primary outcome was a reduction in the HbA1c 3 months post discharge. Secondary outcomes were post discharge HbA1c levels at 6 and 12 months, frequency of hypoglycemia as measured by a follow up mailed survey and readmission over 12 months. 774 charts were screened. 435 patients were excluded based on the predefined exclusion criteria.

**Results:** 339 patients (237 DC and 102 NC) were included. DC patients were younger (60±15 vs 68±14 years, p<0.01), admitted to the surgical service more frequently (32% vs 16%, p<0.01) and more likely to have type 1 diabetes mellitus (11% vs 2%, p<0.01). Hypoglycemia was addressed consistently in the DC group (94% vs 48%, p<0.001) with the DC group more likely to report preadmission severe hypoglycemia (5.5% vs 3%, p<0.01) and have insulin listed on their admission medications (60% vs 37%, p<0.01). Admission HbA1c was higher in the DC group (7.8±1.8 vs 7.1±1.8%, p<0.001) with the DC group achieving a statistically significant drop in HbA1c at 3 months post discharge (7.4±1.6 vs 7.8±1.8, p<0.001). This was not seen in the NC group (7.1±1.5 vs 7.1±1.8%, p=0.8). This improvement however was lost at 6 and 12 months. There was no difference in readmission rates between groups (DC 1.3±1.7 vs NC 1.3±1.9, p=0.7). 28% (94) of patients returned their survey (74 DC group and 20 NC group). There were no differences in reported frequency of hypoglycemic events, fear of hypoglycemia, anxiety or overall health status.

**Discussion:** The advice of the diabetes consulting service was more likely to be sought by surgical teams, for type 1 diabetic patients and patients with worse control of their diabetes mellitus. The DC service resulted in improvement in glycemic control at 3 months however this was not sustained. While low response rate may contribute to response bias, improved hyperglycemia did not appear to negatively impact the frequency and fear of hypoglycemia.

**Conclusion:** Inpatient diabetes consultation temporarily helps improvement in glycemic control post discharge.
Abstract #214

INSULIN DRIP AT >450 UNITS/HOUR, DRUG-DRUG INTERACTION OR PLUMBING PROBLEM? AN INTERESTING CASE OF NOREPINEPHRINE (LEVOPHED) INTERFERING WITH INSULIN.

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Objective: Troubleshooting causes of hyperglycemia despite being on high doses of intravenous-insulin. Medication administration-errors occur frequently and hospital-based direct observational studies have shown these rates to be around 19–27%. Insulin and vasopressors are the most commonly-used medications in critically-ill patients. It has been shown that many vasopressors are incompatible with regular-insulin if given in the same intravenous-line.

Case Presentation: We present a case of 62 year-old female with history of diabetes type-2, hypertension and dyslipidemia who was brought to the hospital after she had witnessed cardiac-arrest and received CPR after which she had spontaneous return of circulation. Initial laboratory-workup showed anion-gap, bicarbonate-level and serum beta-hydroxy-butyrate to be within reference-range ruling out DKA. Her serum-glucose was high at 578mg/dl. She was started on intravenous regular-insulin as per ICU hyperglycemia-protocol. She was also requiring vasopressors for blood-pressure support. Endocrinology consult was called when her insulin-dose was escalated to >450 units/hour and her blood-sugars were still ranging over 500mg/dl. On a lighter note, plumbing (tubings and pumps) was checked first, which was functioning properly. She had multiple intravenous-drugs going through two central-lines including a right-femoral central-venous catheter and a right internal-jugular central venous-catheter. Insulin-drip was going through the same right internal-jugular line as norepinephrine and vasopressin. Drug-drug interaction check showed that norepinephrine is incompatible with insulin in same line as it causes insulin to be ineffective. We ordered the insulin-drip to be started in a separate peripheral-line. Insulin drip was started again at 6 units/hour as per hyperglycemia-protocol based on current blood-sugars. Blood sugars stabilized at 14 units/hour of insulin on the new drip.

Discussion: There is scant published literature on compatibility of IV insulin with other drugs although it has been established that insulin is incompatible with norepinephrine, dobutamine, dopamine, magnesium, phenytoin, methylprednisolone and ranitidine. These drugs should not be given via the same IV line as insulin. Several studies indicate that infusion of pressor-doses of norepinephrine causes resistance to insulin action. Another study by Marangou et al. showed that insulin-mediated glucose disposal, was reduced by 70% in the norepinephrine-infused subjects.

Conclusion: This case report illustrates the importance of monitoring drug-drug interactions, medication errors and adverse drug events especially in ICU settings where multiple drugs are being used at the same time.

Abstract #215

COMPARISON OF A COMPUTER-BASED INTRA VENOUS INSULIN PROTOCOL WITH STANDARD PAPER PROTOCOL IN TERMS OF SAFETY AND EFFICACY IN MANAGEMENT OF DKA PATIENTS IN COMMUNITY HOSPITALS: A PILOT STUDY

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Objective: To compare the safety profile in terms of hypoglycemia and overall efficacy of a computer-based insulin-dosing software program (Endotool®) with the a paper based protocol

Methods: Patients admitted with DKA to 6 community hospitals in Eastern North Carolina between 12/2014 and 4/2016 were identified retrospectively. 40 and 42 consecutive patients treated with standard paper protocol (PP) and with software program (SP) were included in the paper arm and software arm respectively. Pertinent clinical and demographic variables were collected by chart review and analyzed to compare the outcomes.

Results: Among the PP patients (n=40, 45% female) 70% were Type 1 DM, mean baseline values were: age 38 years, BMI 27.14, HbA1c 10.96, 1st serum glucose 582, venous pH 7.22, anion gap 25.10. Among the SP patients (n=42, 52% female), 62% had Type 1 DM, mean baseline values were: BMI 25.72, HbA1c 11.28, 1st serum glucose 536, venous pH 7.25, anion gap 25.18. There was no statistically significant difference between the two groups’ baseline variables. The mean time to resolution of DKA (AG <12) was not statistically significant between the two groups (20.85 hrs vs 20.53 hrs; p>0.05). There were no hypoglycemic events in the SP group during the insulin infusion, but there were 4 patient-episodes of hypoglycemia in the PP group (RR=5.2, p=0.28, NNT= 20). The mean total time on insulin infusion was significantly higher for
the SP group (18.8 hrs vs 30.1 hrs, p=0.004).

Discussion: Literature has shown both safety and efficacy of computer-based insulin infusion protocols among hospitalized patients for hyperglycemia in various settings (i.e. post surgery, MICU, ER) but to the best of our knowledge, there is no published literature on safety and efficacy of computer-based insulin infusion protocols in hospitalized DKA patients. The difference in incidence of hypoglycemia between the two groups indicates that SP is a safer approach for managing insulin infusions for DKA patients. Also the SP appears to be non-inferior to the PP.

Conclusion: A computer-based insulin-dosing software program for treatment of patients with DKA appears to be safer and no less efficacious than a standard paper protocol. Although a higher initial cost is associated with implementing the infrastructure, fewer negative clinical outcomes prove benefit of its use even in small community hospitals. Larger prospective and multicenter studies are needed to validate these findings.

Abstract #216

A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS IN USE OF GLP1 RECEPTOR AGONISTS IN TYPE 1 DIABETES MELLITUS

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Objective: Glucagon like peptide-1 receptor agonists (GLP-1RA) are listed as investigational agent in treatment of type 1 diabetes mellitus (T1DM). Few randomized controlled trials (RCTs) are published using GLP-1RA in T1DM. The aim of this study is to do meta-analysis of efficacy and safety of GLP-1RA in all RCTs in T1DM.

Methods: We searched PUBMED, EMBASE, and Cochrane CENTRAL for RCTs on use of GLP-1RA in T1DM. Meta-analysis was performed using random-effects model. The change in HbA1c, basal and bolus insulin, body weight and adverse events were the main outcomes.

Results: We included 3 RCTs with liraglutide versus placebo with total of 212 patients. Compared to placebo, liraglutide significantly reduced HbA1c by -0.29%(3.16 mmol/mol) (95% CI, -0.52 to -0.06; P=0.01; I2=0%); reduced daily bolus insulin by -4.39 units (95% CI, -6.28 to -2.49; p=0.0001; I2=0%), daily basal insulin by -2.55 units (95% CI, -4.87 to -0.22; p=0.03; I2=0%) and body weight by -4.56 kg (95% CI, -5.42 to -3.7; p<0.0001; I2=0%) after 12 weeks of treatment. Compared to placebo, liraglutide significantly increased the risk of nausea (odds ratio: 6.55, 95% CI: 2.32 to 18.48, P=0.0004, I2=53%) but did not increase vomiting (odds ratio: 1.67, 95% CI: 0.34 to 8.13, P=0.63, I2=41%).

Discussion: This is the first meta-analysis of use of GLP-1RA in T1DM. This meta-analysis showed that the liraglutide had significant effect on lowering HbA1c by 0.29% in T1DM when compared to placebo after 12 weeks of treatment. This is a small but a significant reduction in HbA1c. Since T1DM do not have functional Beta cells, liraglutide decreases HbA1c by appetite suppression, reducing post-prandial glucagon surge and possibly by its insulin sensitizing effects. It is very likely that post-prandial suppression of glucagon by GLP-1RA is a key factor in controlling hyperglycemia in T1DM. Although true, it is not widely appreciated that when hyperglycemia is unaccompanied by increase in insulin, it stimulates rather than suppresses glucagon secretion. This paradoxical increase in glucagon could be an important factor in the exaggerated post-prandial hyperglycemia in T1DM and GLP-1RA have a therapeutic advantage to mitigate this paradoxical increase in glucagon in T1DM. Their weight loss potential makes them even more attractive as one third of patients with T1DM are obese.

Conclusion: This meta-analysis concludes that liraglutide as compared to placebo causes a significant decrease in bolus insulin, basal insulin and body weight as well as a moderate decrease in HbA1c, in patients with T1DM after 12 weeks of treatment with a relatively good safety profile.

Abstract #217

OPTIMIZING BLOOD GLUCOSE MANAGEMENT FOR 18F-FDG PET: A MULTIDISCIPLINARY APPROACH TO DEVELOPING A PROTOCOL

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National Institutes for Health

Objective: 18F-FDG PET studies are invaluable tools in establishing the diagnosis and following the disease course of many conditions. Careful management of patients’ diets and blood glucose (BG) is essential for the correct interpretation of the imaging results, especially in patients with diabetes. Uncontrolled hyperglycemia in patients scheduled for 18F-FDG PET studies can result in cancelled or repeated tests, leading to increased radiation exposure, delay of treatment decisions, higher cost and
wasted resources. We collaborated with multidisciplinary teams to optimize the process of BG management in diabetic patients undergoing 18F-FDG-PET studies at our Clinical Center with aims to 1) assess the BG management for optimal preparation of 18F-FDG-PET studies, and 2) describe the process of protocol development to manage BG in order to achieve euglycemia.

Methods: As part of this quality improvement project, we collaborated with nursing, the inpatient BG management service, endocrinology, internal medicine, oncology, and nuclear medicine teams. Following the Institute for Healthcare Improvement Project Roadmap, input was obtained from all involved patient care teams on existing problems and standard operating procedures. Data on proportion of 18F-FDG-PET studies that were cancelled or re-scheduled due to blood glucose disruptions were obtained. Using a Cause-and-Effect diagram, three main areas of improvement in blood glucose management were identified: 1) lack of a standardized protocol for patients with diabetes undergoing 18F-FDG PET, 2) need for appropriate diet and blood glucose management orders and, 3) education of staff regarding the appropriate management to establish euglycemia before FDG-PET studies.

Results: The action plan included: 1) collaborative input on development of a standardized protocol, 2) incorporation of automated diet and consult orders in the electronic medical record system, and 3) in-service training of nursing, medical and nuclear medicine staff on the protocol. Data on the impact of these changes including compliance with the protocol and outcomes on blood glucose excursions and rescheduled 18F-FDG-PET studies will be presented.

Discussion: Use of an organized roadmap to specify goals and collect data from multiple teams can be a challenging process. Using a Cause-and-Effect diagram can identify the areas requiring improvement and can guide changes for improvement, which can then be further refined.

Conclusion: Blood glucose optimization in patients with diabetes scheduled for 18F-FDG-PET studies can help obtain accurate imaging results for safer, cost-effective and efficient patient care.

Abstract #218

AN UNUSUAL CASE OF INSULIN RESISTANCE TYPE B AND ITS SUCCESSFUL TREATMENT WITH COMBINATION IMMUNOTHERAPY

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National Institutes for Health

Objective: Type B insulin resistance, a rare disease caused by autoantibodies against the insulin receptor, has high morbidity and mortality which makes recognition and appropriate management of this condition imperative. Type B insulin resistance is typically characterized by diabetes that is resistant to high doses of insulin. Predominantly seen in African American females, it usually presents between 40-50 years of life. We report the successful treatment of a patient with type B insulin resistance with rituximab, cyclophosphamide, and prednisone.

Case Presentation: A 60-year-old female with was diagnosed with diabetes in January 2015 after she presented with hyperglycemia, polyuria, polydipsia, and polyphagia. She reported weight loss of 50 lbs in 2 months and widespread acanthosis nigricans on her face, axillae, neck, and thighs. Her glucose levels stayed above 400 mg/dl almost daily and her HbA1c reached 15% in spite of increasing insulin requirements and multiple hospital admissions. In October 2015, she had a month-long ICU admission where her total daily dose of insulin exceeded 7000 units. Due to her classic clinical presentation, including abrupt onset of hyperglycemia, hyperinsulinemia, severe insulin resistance, dramatic weight loss, and severe acanthosis nigricans, she was diagnosed with insulin resistance type B. The presence of insulin receptor antibodies was confirmed, and she was started on antibody depletion therapy with Rituximab (a monoclonal anti-CD20 antibody), cyclophosphamide, and pulsed steroids in November 2015. She required two cycles of chemotherapy over the next few months and tolerated it well. Her HbA1c decreased from 12.5% in December 2015 to 5.6% in September 2016 (reference: 4.8-5.6%), fasting serum insulin decreased from >1000 mcU/mL to 8 mcU/mL. Cyclophosphamide was titrated during therapy to avoid neutropenia (a common side effect), and she was transitioned to Azathioprine for maintenance in June 2016. Her anti-diabetic therapy was discontinued in April 2016 to avoid hypoglycemia and by September 2016, the patient’s acanthosis nigricans resolved completely and she was normoglycemic.

Conclusion: In this patient with dramatic and sudden onset of type B insulin resistance, treatment with rituximab,
cyclophosphamide, and pulse steroids was successful in inducing a complete remission. It is essential to recognize different causes for hyperglycemia and hyperinsulinemia for appropriate management of rare conditions like insulin resistance type B to reduce morbidity and mortality in affected patients.

Abstract #219

EVIDENCE OF INSULITIS IN SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 5 (STAT5) KNOCKOUT MICE

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Results: Studies suggested that STAT5/JAK (the Janus Kinase) signaling have important roles in β-cell compensatory growth during natural courses such as gestation and obesity and in the defense against β-cell stress factors. Previously we reported impaired glucose homeostasis in 8-week old male STAT5 knockout (SKO) mice. In this study, we confirmed our previous findings in male 16-week SKO mice: in comparison to their wild-type (WT) littermate controls, SKO mice showed glucose intolerance, impaired glucose-stimulated insulin secretion (GSIS) from isolated islets, but similar insulin tolerance performance. To further investigate apoptotic death of islet cells as potential mechanism, we performed TUNEL (Terminal Deoxynucleotidyl Transferase Mediated dUTP Nick End Labeling) assays in pancreatic tissues, but found no difference in islet-associated apoptosis between male SKO mice and WT controls. However, strikingly, immunohistochemistry and Hematoxylin & Eosin staining data demonstrated that insulitis changes were evident in ~30% of tested formalin-fixed paraffin-embedded pancreatic tissues from 8-16 weeks-old male SKO mice but none in WT controls. In the line of similar findings, increased numbers of CD3 and F4/80-positive cells were found in pancreatic tissues from SKO mice.

Conclusion: Our findings indicated that STAT5 signaling is important in maintaining normal β-cell function and glucose homeostasis. The observed insulitis changes in SKO mice are not completely unexpected, since important roles of STAT5 have been implicated in T-cell homeostasis. However, it is unclear at this time whether insulitis is directly associated with β-cell dysfunction in our SKO mouse model and further investigation is warranted.

Abstract #220

AS SWEET OUTCOME: SEVERE HYPERGLYCEMIA MIMICKING STROKE WITH RESOLUTION AFTER INSULIN DRIP

Warren Lee, MD MHS, Alexander Lloyd, MD, Brenna Conroy, MD, Fnu Abhishek, MD

UPMC Mercy

Case Presentation: 54-year-old woman with a medical history significant for hypertension and type 2 diabetes with neuropathy presented with acute-onset left-sided weakness. On admission, she had decreased left-sided blink to threat, right-sided gaze deviation, left hemineglect, left facial droop, dysarthria, decreased left facial sensation, drift in the left upper and lower extremity, and an upgoing left toe. Her initial NIHSS score was 15 and ASPECTS was 8. She was diagnosed with right middle cerebral artery stroke based on symptoms. Initial labs on presentation were significant for a serum blood glucose of 727 mg/dL. The patient was not given tPA because she had arrived to the hospital five hours after being last seen well. The patient had a CT scan without contrast of her head, which showed no bleed or ischemia. Cerebral angiography was performed five hours after symptom onset and showed no large vessel occlusion. MRI of the brain showed possible ischemia of the central pons, but no acute infarct. The hospital’s stroke team made note at the time that this was possibly due to significant hyperglycemia, but no clinical correlation with her presenting symptoms was made. EEG was also obtained out of concern for seizure with postictal state. EEG did not show epileptiform discharges or other abnormalities. TTE with bubble study was negative for PFO or thrombus. Carotid dopplers were negative for large vessel occlusions or high grade stenosis.

An insulin drip was started at 5 units per hour. Her neuro exam subsequently improved with gradual, but complete, resolution of her symptoms once her blood glucose declined below 300 mg/dL 24 hours after her symptoms started.

Discussion: Hyperglycemia is well known to cause varied neurological symptoms, typically in the setting of non-ketotic hyperglycemia. Multiple documented cases of hemiballism, hemichorea, delirium and partial or generalized seizures are listed in the literature, but there has only been one other documented case to our knowledge of hyperglycemia causing stroke-like symptoms that follow a specific, ischemic distribution.

Conclusion: This case provides evidence that severe hyperglycemia may uncommonly lead to symptoms closely mimicking ischemic stroke and that resultant metabolic derangements may lead to MRI changes mimicking...
ischemia in areas inconsistent with presentation. It also serves as a reminder of the essential role blood glucose testing plays in the workup of stroke symptoms, regardless of how convincing the presentation.

Abstract #221

NO PATIENT LEFT BEHIND: PATTERNS IN DIABETES EDUCATION REFERRAL IN PRIMARY CARE AND ENDOCRINE CLINICS AND EFFECTS ON HBA1C

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Objective: Diabetes management should be a team approach and referrals for diabetes self-management education (DSME) and diabetes self-management support (DSMS) should be the basis of initial management. The indolent nature of the disease makes patient education paramount in understanding how to properly manage and prevent complications of diabetes. Our primary outcome in this Quality Improvement project was examining the rate of utilization of our certified diabetes educators (CDE) between our academic primary care and endocrine clinics for people with uncontrolled type 1 or type 2 diabetes. Our secondary outcome was comparing changes in HbA1c between patients who received diabetes education and those who did not at 6 and 12 month follow-ups after initial CDE visit.

Methods: Data were obtained from a large, university-affiliated patient data registry using the electronic medical record to identify all patients with diabetes at two academic outpatient clinics: a primary care clinic and an endocrine clinic. All patients (age 18–80 years) with a hemoglobin A1c >8% and seen by a physician at least once during 2013 to 2015 were included. Patients receiving steroids, hemodialysis therapy, pregnant, or undergoing bariatric surgery during the study interval were excluded.

Results: Of the 138 total patients, 79 were part of the primary care clinic and 59 were part of the endocrine clinic. All patients (age 18–80 years) with a hemoglobin A1c >8% and seen by a physician at least once during 2013 to 2015 were included. Patients receiving steroids, hemodialysis therapy, pregnant, or undergoing bariatric surgery during the study interval were excluded.

Results: Of the 138 total patients, 79 were part of the primary care clinic and 59 were part of the endocrine clinic. Of the primary care patients, 51.9% were given referrals for DSME but only 21.6% followed up with a CDE. In comparison, 52.5% of the patients from the endocrine clinic were given a referral for DSME, however, only 30.5% saw one. These differences in referral or visit rates between clinics were not statistically different. For the secondary outcome, individuals who saw a CDE had a mean difference (SD) of -1.23 (2.94) between baseline A1c and A1c at 6 months. For all patients who did not see a CDE, the mean difference at 6 months was -0.546 (1.97). When comparing A1c from baseline to 12-month follow-up, the mean difference for those who saw a CDE was -1.17 (2.85) compared to -0.837 (2.04) for those who did not see a CDE. Differences were statistically significant.

Discussion: DSME and DSMS provided by certified diabetes educators are under utilized at both of our academic primary care and endocrine clinics, but patients who attended had a greater decrease in HbA1c.

Conclusion: We aim to raise provider awareness to services offered by CDEs and facilitate identification and referral of individuals with uncontrolled diabetes. We hope to increase the utilization of CDE services to enhance interdisciplinary management approach of individuals with uncontrolled diabetes.

Abstract #222

AN ASSESSMENT OF DIAGNOSTIC CRITERIA FOR DIABETIC KETOACIDOSIS

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Objective: American Diabetes Association (ADA) diagnostic criteria for diabetic ketoacidosis (DKA) include the triad of ketonuria, hyperglycemia (glucose ≥250 mg/dl) and a serum bicarbonate (HCO3-) ≤18 meq/l. However, serum HCO3- is not specific for DKA, and ADA recommendations on laboratory testing for diabetes state that urine ketone testing should not be used for diagnosing DKA in view of its qualitative nature and its inability to detect the dominant ketone body anion in DKA, beta-hydroxybutyrate (βOHB). Because of these limitations, we previously suggested that an admission βOHB ≥3.8 mmol/l could be used in place of these criteria to diagnose DKA.

Methods: In the present study, we reviewed records from adult DKA admissions for the years 2012-2016 to assess the sensitivity and specificity of the ADA criteria, using βOHB ≥3.8 mmol/l to define DKA.

Results: Trace or negative ketonuria was considered to be inconsistent with a DKA diagnosis, whereas small, moderate or large ketones were considered to be consistent with DKA. Records were reviewed on 224 people with DKA and 151 individuals with diabetes but not DKA (βOHB <3.8). Among DKA patients, HCO3- was >18 meq/l in 17%, consistent with previous reports. Urine ketones were negative to trace in 21%, and glucose was <250 mg/dl in 4%. Urine ketones and HCO3- were both negative for DKA in 7%. Among individuals who did not have DKA, 17% had small to large urine ketones, 18% had a HCO3- ≤18 meq/l, and 4% had both. Thus, 35% of patients who had DKA as defined by βOHB lacked one or
more of the ADA diagnostic laboratory criteria, and 31% who did not have DKA fulfilled the criteria for DKA with respect to HCO₃-, ketonuria, or both.

**Discussion:** When patients with diabetes who are admitted to the hospital are characterized as having DKA or not having DKA based on the admission βOHB, there is substantial discordance with ADA diagnostic criteria. Specifically, HCO₃- and urine ketones were often at odds with the βOHB results. This is not surprising, considering the limitations of the urine ketone test and the fact that a serum HCO₃- ≤18 meq/l is not specific for DKA. These results argue in favor of the use of serum βOHB for the purpose of diagnosing DKA, at least in hospitals that have sufficient DKA admissions to justify test availability.

**Conclusion:** The BOHB measurement should not supersede clinical judgment in the care of DKA patients, but it does add diagnostic rigor.

**Abstract #223**

**NEWLY DIAGNOSED INSULIN DEPENDENT DIABETIC NEPHROPATHY: DO WE NEED DIFFERENT CRITERIA FOR SCREENING AND DIAGNOSIS OF DIABETES IN SOUTH EAST-ASIANS?**

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**Objective:** More studies are required to define if the threshold for diagnosis of diabetes needs to be lowered in South East-Asians

**Methods:** Case and review of the literature

**Case Presentation:** 27 year-old Sri Lankan woman with no prior history of diabetes mellitus or renal disease, presented with a markedly elevated Hemoglobin A1c and renal insufficiency. For two years she has been treated with Enalapril for hypertension, and recently she has been taking Amoxicillin and Advil 800mg every four hours for a neck abscess for one week. Of note, she had an unintentional 30 pound weight loss associated with polyuria and polydipsia over the last 6 months. Both parents have insulin dependent diabetes mellitus. Her vitals revealed BP 141/85mmHg, HR 111beats/min, weight 135lbs and BMI 23.6 kg/m2. Her exam was notable for periorbital edema, a 4.4cm left lateral soft neck mass, and bilateral ankle swelling, but no evidence of acanthosis or Cushing’s appearance.

The results of her laboratory were notable for a Hemoglobin A1c 17.4, Cr 2.73, Protein to Creatinine ratio of 17g, LDL 294, HDL 49. C-peptide 3.3, Glutamic Acid Decarboxylase <5 and Insulin Antibody <0.4. Her transthoracic echo was normal.

Renal pathology showed severe tubulointerstitial chronic inflammation with near-total loss of tubules and minimal fibrosis as well as glomerulosclerosis consistent with advanced diabetic nephropathy.

**Discussion:** Diabetic kidney disease (DKD) takes many years to develop. In some people the filtering function of the kidneys is actually higher than normal in the first few years of their diagnosis. Kidney damage rarely occurs in the first 10 years of diabetes and usually 15 to 25 years will pass before kidney failure occurs. Severe DKD documented by biopsy in this patient with newly diagnosed diabetes is almost unheard of.

There is a rising incidence of type 2 diabetes in the South East-Asia (SEA) population. Currently there are more than 72 million adults with diabetes and it is expected to exceed 123 million in 2035. Also alarming is the fact that 24.3 million people have been diagnosed to have impaired glucose tolerance.

We need to further study if the process of kidney damage is accelerated and if what is considered the threshold for diagnosing diabetes in the Caucasian population may be too high for the SEA population. This case illustrates the need for better understanding of this subgroup of patients.

**Conclusion:** Research has shown that the conventional cut off points for obesity do not correspond to comparable metabolic risk in all ethnicities; it has already been proposed to decrease the BMI cut off points for Asians. This case raises the question if we should also consider lowering the threshold for diabetes in South East-Asians.

**Abstract #224**

**EUGLYCEMIC DKA IN MODY PATIENT: EMPAGLIFLOZIN TO BLAME**

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**Objective:** Diabetic ketoacidosis (DKA) occurs when the body’s requirements for insulin are higher than the insulin available for use, resulting in lipolysis, ketogenesis, and ketoacidosis. DKA is classically associated with Type 1 diabetes mellitus (DM), but can occur in any patient with diabetes. Euglycemic DKA is defined by ketosis, metabolic acidosis, and a blood glucose level less than 200 mg/dl. Euglycemic DKA is concerning as it can be easily misdiagnosed and mistreated. Few cases have demonstrated a possible relationship between empagliflozin and euglycemic DKA. Empagliflozin is a sodium glucose co-transporter (SLGT-2) inhibitor in the proximal convoluted tubule of the kidney to reduce reabsorbed filtered glucose, resulting in decreased serum glucose levels.
Case Presentation: 42 year old female with mature onset diabetes of the young (MODY) type 2 presented to the emergency room with complaints of nausea, vomiting and epigastric abdominal pain worsening over four days. She was diagnosed with gestational DM at age 34 and post-partum was unsuccessfully treated with a variety of oral medications. She underwent testing which revealed a glucokinase mutation consistent with MODY type 2. Recently, she was changed from empagliflozin to a combination of empagliflozin-linagliptin in addition to a diet of less than 60 grams of carbohydrates per day. Imaging was unrevealing, and she was diagnosed with gastroenteritis. On admission, her serum glucose was 106 mg/dL, potassium was 4.6 mmol/L, bicarbonate was 21 mmol/L, anion gap was 14, and lipase was normal. Urinalysis revealed glucose of 500 mg/dL, ketones > 160 mg/dL, and specific gravity >1.030. Venous blood gas revealed metabolic acidosis. Beta hydroxybutyrate was 2.71 mmol/L. The patient was diagnosed with euglycemic DKA. Endocrinology discontinued empagliflozin, emphasizing that the only treatment required for MODY type 2 is diet restriction. Her symptoms improved, labs normalized, and she was discharged.

Conclusion: This case demonstrates a deadly combination of inappropriate SGLT-2 inhibitor use causing decreased serum glucose levels in a MODY type 2 patient resulting in euglycemic DKA. MODY type 2 results from a defective glucokinase enzyme, therefore increased serum glucose levels are required to trigger insulin secretion. These patients often present with mild fasting hyperglycemia, which is required to stimulate insulin secretion. In this case, empagliflozin resulted in decreased serum glucose and increased glucosuria. As a result, the body’s demands for insulin were higher than the amount of insulin being secreted due to defective glucokinase enzyme, inducing DKA.

Abstract #225

EMPAGLIFLOZIN INDUCED ACUTE RENAL FAILURE WITH DETRUSOR INSTABILITY AND BLADDER OUTFLOW OBSTRUCTION; A CASE REPORT

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Objective: The sodium–glucose co-transporter(SGLT)2 inhibitors are newer anti-diabetes agents that inhibit renal glucose reabsorption and promote glucosuria. They have been associated with acute renal failure, related to pre-renal etiology. This case highlights the importance of confounding etiologies that complicate the presentation of acute renal failure with this drug.

Case Presentation: 57 year old male with history of diabetes mellitus and hyperlipidemia, presented with acute renal failure. He had started Empagliflozin 1 month before the presentation. He reported increasing frequency of urination up to 30-35 times day and nocturia. The urinary flow was “fair”. He was taken off the medication 1 week prior due to these side effects, with no improvement in the frequency. Initial admission examination was normal, except for mild edema. Laboratory investigations showed acute increase in creatinine from 1.1 to 4.3 and decrease in GFR from >60 to 8, hyperkalemia (6.1mEq/L), and decreased bicarbonate (15mEq/L). CT scan of his abdomen showed bilateral moderate hydronephrosis and bladder distension. He was started on IV fluids. He was also started on tamsulosin by urology. Foley catheter was also placed on admission.

During his admission he improved slowly and the renal functions slowly improved to creatinine of 2.1 and GFR around 35. CT scan repeated in 1 week also showed mild hydronephrosis improved from before with bladder wall thickening and mild prostatic enlargement. Electrolytes normalized at discharge. He was started on basal bolus insulin regime in the hospital and discharged on insulin as well.

On his 1 week follow up his renal functions has stabilized at creatinine around 2 and GFR around 35. He has improvement in his frequency, urgency and incontinence after discontinuing the medication.

Conclusion: Although SGLT2 inhibitors have been associated with acute renal failure, related to pre-renal insults and dehydration but mechanisms behind detrusor instability or bladder wall thickening is not established. EMPA-REG OUTCOME study characterized the effects of empagliflozin on several safety issues, including; breast cancer, bladder cancer, lung cancer, and melanoma. But the numbers were very small to assess an attributable risk with Empagliflozin.

The GFR limitations have been well established to consider before initiating the medication. The case highlights that there is a need to entertain the post renal etiology of acute renal failure as well like Prostate enlargement and bladder wall thickening. SGLT2 inhibitors have an important role in diabetes control, with upto 2.1% improvement in hemoglobin A1c with metformin compared to 1.2% with metformin alone.
Abstract #226

BARRIERS TO CARE AND MEDICATION PRACTICES FOR TYPE 2 DIABETIC PATIENTS IN A STUDENT-RUN CLINIC IN MONTCLAIR, CALIFORNIA

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Objective: The purpose of this study is to assess medication practices at a student-run clinic for uninsured patients with type 2 diabetes (T2DM) and to identify barriers to their care.

Methods: A retrospective chart review was done at a clinic for uninsured patients where 39 T2DM patients received care. Charts were used to assess demographics, HbA1c, medications, lifestyle changes, compliance, and barriers to care at 3 visits: initial, a visit within the past 2 years, and the most recent visit.

Results: Of the 39 patients included, 64.1% were female, 94.9% were Hispanic and average age was 53.9 years (SD=9.6). The average patient had diabetes for 7.1 years, and had been receiving care at the clinic for 3.78 years. The average A1c was 7.76 at the most recent visit.

Regarding DM pharmacotherapy, during the initial visit, 38.5% used only metformin, 7.69% used both metformin and a sulfonylurea, and 8.57% used neither medication. Recommendations at the latest visit included 59.0% to continue their current regimen, 20.5% to increase the dose of their oral agent, and 10.3% to add an oral agent. Regarding the pharmacologic treatment recommendations, 89.7% completely accepted it, 5.1% accepted with compromise, and 5.1% refused treatment. At the most recent visit, the percentage using only metformin increased to 76.9%, using both metformin and a sulfonylurea increased to 30.8%, while 23.08% were on no medications. Although insulin was recommended to 7.9% of the patients, none were using insulin. No other diabetic medications were used. Only 15.4% were compliant with the recommended medications, with 84.6% noted to have at least one barrier to care. The self-reported barriers to noncompliance included 60.6% financial, 33.3% psychosocial, 15.4% lack of comprehension, and 10.3% occupational limitations.

Discussion: With a large proportion of patients reporting financial barriers, we note that agents other than metformin and sulfonylureas were not used. Another finding is noncompliance among this uninsured diabetic patient population. Though financial burden is inherent in the uninsured patient population, some reported psychosocial difficulties like lack of support at home, depression, and low motivation. Lack of comprehension and misunderstanding of medication administration contributed to a portion of the noncompliance. A unique complaint for the patients at the clinic was their occupation with certain professions prohibiting insulin use.

Conclusion: Diabetic patients at an uninsured student-run clinic in Montclair, California have multiple barriers to their care and a tendency toward use of a limited number of oral TDM2 agent use.

Abstract #227

IMPAIRED GLUCOSE HOMEOSTASIS WITH HYPERGLYCEMIA SECONDARY TO OPIOID OVERDOSE

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Objective: Opioid use is associated with impaired glucose homeostasis, weight gain, and metabolic syndrome. Preclinical and clinical literature shows that opioids create a metabolic state similar to diabetes mellitus by delaying onset of insulin secretion and increasing insulin resistance with consequent hyperglycemia and elevated HbA1c. We report a case of a patient with no history of diabetes mellitus who presented with acute hyperglycemia in the context of an opioid overdose.

Case Presentation: A previously healthy 23 year old female was found to be unresponsive next to a tray of heroin. Blood glucose was 440 mg/dL and she received 8 gm of naloxone. She remained lethargic and was transferred to our hospital. Upon arrival, she was hypotensive to 96/54 mmHg and had been receiving care at the clinic for 3.78 years. The average A1c was 7.76 at the most recent visit.

Regarding DM pharmacotherapy, during the initial visit, 38.5% used only metformin, 7.69% used both metformin and a sulfonylurea, and 8.57% used neither medication. Recommendations at the latest visit included 59.0% to continue their current regimen, 20.5% to increase the dose of their oral agent, and 10.3% to add an oral agent. Regarding the pharmacologic treatment recommendations, 89.7% completely accepted it, 5.1% accepted with compromise, and 5.1% refused treatment. At the most recent visit, the percentage using only metformin increased to 76.9%, using both metformin and a sulfonylurea increased to 30.8%, while 23.08% were on no medications. Although insulin was recommended to 7.9% of the patients, none were using insulin. No other diabetic medications were used. Only 15.4% were compliant with the recommended medications, with 84.6% noted to have at least one barrier to care. The self-reported barriers to noncompliance included 60.6% financial, 33.3% psychosocial, 15.4% lack of comprehension, and 10.3% occupational limitations.

Discussion: With a large proportion of patients reporting financial barriers, we note that agents other than metformin and sulfonylureas were not used. Another finding is noncompliance among this uninsured diabetic patient population. Though financial burden is inherent in the
fraction of 25-30%. Repeat blood glucose was 318 mg/dL which dropped over 6 h to the range of 80-110 mg/dL with no use of glucose lowering agents. BMI was 22.1 kg/m², no family history of diabetes mellitus and HbA1c was only 5.4%. She was not on steroids, thiazide, or any sympathomimetic.

Discussion: Through centrally and peripherally located opiate receptors; opioids interact with the endocrine system and dysregulate glucose homeostasis. To our knowledge, this is the first human case of demonstrated resolution of hyperglycemia after treatment of opioid overdose. It is unclear whether her cocaine use contributed to hyperglycemia; however, signs and symptoms of cocaine intoxication were not present.

Conclusion: It is important to recognize impaired glucose homeostasis in the context of opiate use. Further studies are needed to guide the management of hyperglycemia and insulin resistance in this patient population.

Abstract #228

ISLET CELL TRANSPLANT: SUCCESSFUL SURVIVAL THROUGH PREGNANCY

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Objective: Islet cell transplantation for patients with type 1 diabetes mellitus (DM1) has been performed approximately 750 times throughout the world in the last ten years. In research trials transplantation has been used to correct incapacitating recurrent hypoglycemia. Pregnant women with pre-existing DM require strict glycemic control to prevent diabetic related complications including congenital malformations and macrosomia. Physiologic changes during pregnancy cause beta-cell proliferation and increased beta-cell mass to match the increased metabolic demands of pregnancy, which is a potential challenge for a patient with an islet cell transplant.

Case Presentation: A 33 year old G2 P1 with past medical history of DM1 and islet cell transplant is currently carrying her second pregnancy without complications. Diagnosed with DM1 at age 15, she utilized an insulin pump for many years. Her diabetes was complicated by severe hypoglycemic unawareness and she underwent a successful islet cell transplant in March 2011. She was insulin independent for 3 years post-transplant. In June 2014, she presented with her first pregnancy at 5 weeks gestation and her HbA1c was 5.7%. During her first pregnancy, she required 10 units of insulin detemir two times daily without pre-prandial insulin. Her HbA1c at 36 weeks was 5.9%. At 38 weeks, she had a cesarean section for breech positioning and abnormal fetal heart rate tracings and delivered a female 21 inches long, weight 7lbs 8oz and Apgar scores 8,9. There was no neonatal hypoglycemia, however left hydronephrosis was noted. Detemir insulin was discontinued on the day of delivery. She remained normoglycemic and insulin-independent post-partum. In July 2016, the patient was found to be eight weeks pregnant with an estimated due date of 2/27/17. Her HbA1C on presentation was 5.4% from February 2016. Her most recent HbA1C at 18 weeks is 5.6%. She is currently requiring 11 units glargine two times daily without pre-prandial insulin. Current ultrasounds show normal fetal anatomy and growth without complications.

Conclusion: This case report is the first to outline the clinical course of a patient with islet cell transplantation who has been pregnant twice. To date, she has only required low dose basal insulin to maintain optimal glycemic control and she was insulin free after her first pregnancy. It is currently unknown how pregnancy ultimately affects transplanted islet cell function in the long term.

Abstract #229

WAYS TO IMPROVE SCREENING OF DIABETIC NEPHROPATHY AMONG PATIENTS WITH DIABETES MELLITUS - A QUALITY IMPROVEMENT (QI) PROJECT

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Objective: As a chronic disease with multiple complications, Diabetes Mellitus (DM) needs close attention in primary care settings. Due to short time office visits, optimal goals may not be achieved. We conducted a QI project in our clinic to achieve appropriate goals for diabetic nephropathy. American Diabetes Association (ADA) guidelines published in January 2016 were used in this study.

Methods: In the pre-intervention phase, we reviewed electronic charts of 100 patients out of 389 diabetic patients seen by Internal Medicine (IM) residents randomly. All patients had either type I or II DM and were above 18 years old and were seen by IM residents between January 1st till the end of July 2016. Patients with last A1C below 6.4 who were not actively treated for diabetes were excluded. A smart phrase was created in electronic medical record (EMR) system and shared with residents. The questions were designed to determine whether the patients were on ACEI/ARB, were seen by nephrologists, had chronic kidney disease stage 4 or 5 or they had urine test to check for proteinuria in the preceding year. Residents were asked to mention their plans for the patients who were not up to date with screening. In the post-intervention phase, data
from 70 patients seen by residents between October 3rd and November 7th, 2016 were analyzed.

**Results:** Review of 100 patients (4 with DMI, 96 with DMII) in the pre-intervention group showed that only one patient in DMI was screened for nephropathy. Out of 96 patients with DMII, 21% were not up to date with diabetic nephropathy care. Overall goals of care were addressed among 78% of this group. In the post-intervention group, DM nephropathy screening compliance improved from 87% to 96%. Percentage of ordering urine test for albuminuria increased from 47% to 81%. Starting either ACEI or ARB increased from 53% to 64%.

**Discussion:** Diabetic nephropathy is the leading cause of CKD in the U.S. Diabetes as a chronic disease with multiple complications needs close attention in primary care settings. There have been few studies in the past regarding diabetes goals of care. Due to multiple parameters for DM monitoring and short office visits, adequate goals of care may be lacking. By making a smart phrase in EMR to encourage the residents to actively participate and by sending reminders, our QI project improved diabetes nephropathy care in IM clinic.

**Conclusion:** This project was undertaken to increase the awareness of an easy and available intervention to improve diabetic nephropathy screening rates. Our study was an example of a QI project which could be easily implemented in primary care clinics. Similar interventions are encouraged in the future to advance other aspects of diabetic’s care.

**Abstract #230**

**A SHOT IN THE DARK: FALSE POSITIVE POSITRON EMISSION TOMOGRAPHY RESULTS WITH ONCE WEEKLY EXENATIDE AND 18-FLUORO-2- DEOXYGLUCOSE**

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**Objective:** To present a case of increased cutaneous 18-fluoro-2-deoxyglucose (FDG) uptake on Positron Emission Tomography (PET) caused by use of once weekly Exenatide (Bydureon), an extended-release GLP-1 agonist.

**Case Presentation:** A 55 year old female with a past medical history of type II diabetes mellitus, hypertension, and osteoporosis was recently diagnosed with breast cancer. Her diabetes regimen included Metformin ER 500 mg twice daily and Bydureon 2 mg weekly. Her most recent hemoglobin A1C was 7.0. As a part of her cancer staging, she underwent a PET/CT scan. Images revealed multiple sites of increased FDG uptake in the lower abdominal wall consistent with hyper-metabolic activity, corresponding with sub-centimeter skin and subcutaneous soft tissue masses. These correlated with subcutaneous injections of Bydureon.

**Discussion:** Bydureon has been shown to decrease hemoglobin A1C levels, decrease postprandial and fasting blood glucose levels, and result in weight loss. It consists of a 2-mg injection administered subcutaneously every seven days. Documented adverse effects include gastrointestinal effects, hypoglycemia, pancreatitis, injection-site reactions, headache, and antibody development. The difference between once weekly and once daily formulations is the microsphere of medical-grade poly-(d,l-lactide-co-glycolide), allowing a slower release of the medication. FDG is the most commonly used radionuclide for PET scanning. It is well known that rheumatoid nodules, fungal granulomas, infections, brown adipose tissue, thyroid tissue, surgical procedures, and other types of inflammation can cause false positive PET scan results. Hyperglycemia leads to decreases in intracellular FDG uptake, and can cause false negative PET results.

To our knowledge, there is no documentation of such uptake of FDG by Bydureon since its release in 2012. Although the mechanisms behind this are unknown, we suspect it is related to its GLP-1 agonist activity and/or hypoglycemia.

**Conclusion:** Bydureon has shown great stride in treating type II diabetes, and it is important to be aware of the possibility of a false-positive PET scan. Additionally, research has been conducted for radiotracers with GLP-1 agonist activity to help identify difficult to diagnose insulinomas, and the question arises whether this may be an application of Bydureon in the future.

**Abstract #231**

**ASSESSING INSULIN INJECTION TECHNIQUE AS A METHOD FOR IMPROVING GLUCOSE CONTROL IN AN ACADEMIC SETTING**

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University of Washington

**Objective:** Correct insulin injection technique is critical in diabetes management. We present 3 cases where detection and correction of errors in injection technique improved glucose control in patients with type 2 diabetes (T2DM).

**Case Presentation:** Case 1: 56yo man with cirrhosis, hepatic encephalopathy and T2DM previously controlled on oral agents (A1c 6.4%), presented to ED with a glucose
ABSTRACTS – Diabetes Mellitus/Prediabetes

Case 1: 58yo man with type 2 diabetes mellitus (A1c 7.2%) on insulin pump, glargine 40 units and liraglutide 1.2mg. Despite increasing insulin from 10 to 91 units, self-monitoring of blood glucose (SMBG) showed persistent hyperglycemia (400-500 mg/dl). When reviewing injection technique, he had not been removing the needle cap prior to injection. Within 6 weeks of technique correction, SMBG showed glucoses in 150-200 mg/dl.

Case 2: 50yo woman with cognitive delay and uncontrolled T2DM (A1c 8.2%) on metformin 1g BID, glargine vial 40 units and liraglutide 1.2mg. Prandial insulin was added and vials were switched to pens for ease of use. A1c increased to 10.1% despite increasing daily insulin requirement from 40 to 303 units. Despite reported adherence, she was not filling prescriptions at the expected rate. On review of injection technique, instead of pressing the plunger to inject, she was dialing the plunger backwards. When switched back to vials, actual insulin requirement decreased to 30 units daily and A1c improved to 7.3%.

Case 3: 72yo non-English speaking woman referred by PCP for uncontrolled T2DM (A1c 9.3%) on glargine and short-acting insulin pens. Despite increasing insulin requirement from 100 to 138 units, and the addition of liraglutide daily, A1c did not improve. Professional 3-day continuous glucose monitor showed glucoses in the 300-400 mg/dL range without change in glucose as expected with insulin administration. Review of injection technique showed she was dialing pens to zero prior to injection. With technique correction, A1c improved to 7.2%.

Conclusion: Insulin administration is a multistep process with potential for error at each step. These cases demonstrate that simple technique errors can go unperceived even in experienced academic institutions. We emphasize the importance of reviewing technique 1) when insulin therapy is started in a patient without prior experience using insulin, 2) when changing method of insulin delivery (vial to pen) or 3) for patients with cognitive impairment or language barrier. Providers should suspect technique issues when there is persistent hyperglycemia despite insulin up-titration or when medication refills do not match with self-reported adherence.

Abstract #232

LOW SERUM TESTOSTERONE IS ASSOCIATED WITH ANAEMIA AMONG MEN WITH TYPE 2 DIABETES MELLITUS.

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Objective: Low testosterone has been reported to be common among men with type 2 diabetes mellitus. Asides from its association with hypogonadism and increased cardiovascular risk, low serum testosterone has been reported to be associated with anaemia among men with type 2 diabetes mellitus. We aimed to determine the relationship between serum testosterone levels and haemoglobin concentration among patients with type 2 diabetes.

Methods: In a cross-sectional design, sociodemographic and clinical characteristics were obtained among men with type 2 diabetes attending an outpatient clinic. Serum total testosterone was measured using ELISA and haemoglobin (Hb) concentration was measured by flowcytometry. The glomerular filtration rate (GFR) was also estimated from the serum creatinine. Testosterone levels lower than 10.4nmol/L was classified as low. Tests of association between testosterone and haemoglobin concentration were done.

Results: Forty-five men participated in the study. The mean ± SD age was 63 ± 11 years and the median (IQR) duration since diabetes diagnosis was 8 (3 - 15) years. The mean testosterone level was 14.8 ± 5.2 nmol/L and 24% of the subjects had low serum testosterone. There was a significant positive correlation between testosterone and Hb concentration (rho = 0.48, p = 0.001). The mean Hb concentration among subjects with low testosterone concentration was significantly lower than in those with normal testosterone levels (11.7 versus 13.2 g/dl; p = 0.004). Using linear regression analysis to control for age and GFR, serum testosterone remained independently associated with haemoglobin concentration.

Discussion: The low serum testosterone found among men with type 2 diabetes mellitus in this study is consistent with earlier reports. The association between testosterone levels and haemoglobin concentration found in this study was independent of age and renal function. Testosterone induces erythropoesis by increasing production of hematopoietic factors and increasing erythroid stem cell proliferation. Low serum testosterone likely contributes to anaemia that is found among men with type 2 diabetes mellitus.

Conclusion: Low testosterone is associated with anaemia among men with type 2 diabetes mellitus. The presence of lowosterone found among men with type 2 diabetes mellitus in this study is consistent with earlier reports. The association between testosterone levels and haemoglobin concentration found in this study was independent of age and renal function. Testosterone induces erythropoesis by increasing production of hematopoietic factors and increasing erythroid stem cell proliferation. Low serum testosterone likely contributes to anaemia that is found among men with type 2 diabetes mellitus.
of features of hypogonadism should trigger evaluation for anaemia in men with type 2 diabetes mellitus.

Abstract #233

PERFORMANCE OF GLYCASED HEMOGLOBIN (HBA1C) FOR DETECTING NEWLY DIAGNOSED DIABETES AND PRE DIABETES IN DIFFERENT ETHNICITIES OF PAKISTAN

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Objective: To calculate the mean HbA1c level in newly diagnosed diabetes mellitus (DM) patients of our population and to determine difference due to ethnicity.

Methods: A cross sectional study was conducted from July 2014-November 2015 at the Section of Chemical Pathology, Departments of Pathology & Laboratory Medicine and Medicine, AKUH. After approval from institution’s ethical review committee, all consecutive subjects with suspected of DM above 18 to 65 years, coming for oral glucose tolerance test (OGTT) were included in the study. The informed consent was taken after explaining procedure. Blood sample for OGTT were taken in sodium fluoride tube at baseline, two hours post glucose load (2-hr PG) and analyzed immediately. Additional 5ml blood sample was taken in EDTA for HbA1c and stored at -80°C until analysis. Data was analyzed using the Statistical Package for the Social Sciences (SPSS version 19.0 for Windows).

Results: Total 146 subjects who underwent OGTT testing for diagnosis of type 2 DM were included in this study. Amongst them majority were females (52%) and mean age of study participants was 44.9±13.2 years. Mean HbA1c of the study subjects was in prediabetic range (6.2±1.0). Positive correlation was observed between age and HbA1c (5.8±0.98 in <40yrs vs. 6.4±1.0 in >40yrs subjects; r 0.3, p<0.000*), while amongst genders; males had higher HbA1c than female (6.4±1 vs. 6.1±1; r 0.2, p<0.05).

HbA1c levels were significantly different amongst the ethnicities (p-value <0.03*) showing highest mean HbA1c, FPG and 2-hr PG levels in Sindhis. Comparison gave the following correlation coefficient, HbA1c was positively correlated with FPG (r=0.69**, p value <0.001) and 2-hr PG (r=0.61**, p value <0.001).

Discussion: Ethno-racial difference was observed in the present study with significantly high mean HbA1c levels in Sindhi population compared to other ethnicities. Aspects that may be responsible for this ethnicity differences and which should be further evaluated are anemia which can be common in some populations than others, difference in mean erythrocyte and other environmental factors. These findings advocate that HbA1c must be used with caution in different ethnicities and better in combination with other criteria when diagnosing diabetes.

Conclusion: The mean levels of HbA1c among Sindhi population are greater than that in other populations. Therefore, a single value of HbA1c ≥6.5% is not adequate to identify patients with impaired diabetes and early diabetes and we suggest that new cutoffs for HbA1c should be defined for our population.

Abstract #234

POSTPARTUM GLUCOSE TESTING AFTER GESTATIONAL DIABETES MELLITUS AND PATTERNS OF ABNORMAL GLUCOSE RESULTS

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Objective: To assess factors associated with postpartum glucose testing among women with gestational diabetes mellitus (GDM) and patterns of the results.

Methods: This study was a retrospective review of 85 women that were diagnosed as having GDM using 75g oral glucose tolerance test from 2006 to 2015 at a tertiary healthcare facility. Information concerning their screening and sociodemographic features within 6 to 12 weeks of delivery were collected using a proforma. The different patterns of their test results were assessed and analysed. Linear and logistic regression models were employed to evaluate the correlation between maternal age, parity, body mass index, mode of treatment and results of postpartum screening.

Results: Out of the 85 women with GDM, 34 of the women comprising 40% were tested during the 6 to 12 weeks postpartum period. The mean age of GDM mothers is 36yrs ± 2 SEM. Majority of GDM mothers 58.8% (50) had parity2-3 while 65.9% (56) had body mass index (BMI) ≥ 25kg/m². Majority of women that did not present for postpartum testing had dietary control. There was significant correlation between the use of insulin during pregnancy and testing between 6 to 12 weeks postpartum. Among the GDM mothers tested, 15.3% (13) had impaired glucose tolerance while 7.05% (6) of the GDM mothers were diagnosed to have diabetes mellitus. There was significant correlation between abnormal postpartum results and use of insulin therapy during pregnancy.

Discussion: Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Women with GDM are at increased risk of recurrence and future development
of type 2 diabetes mellitus, hence the need for postpartum screening and follow up. This study revealed that majority of women with GDM did not have postpartum screening as recommended. This is similar to other studies that found most women with GDM do not have standard re-testing at the end of postpartum period. Mothers who had insulin therapy comprised majority of subjects with postpartum diabetes mellitus. The drawback to follow up among GDM mothers may have been due to lack of communication after patients discharge. This can be improved with use of text messages and telephone calls which were not used for the subjects.

**Conclusion:** Women with GDM that required insulin during pregnancy are at higher risk of having diabetes mellitus in the postpartum period. Women with GDM should have a long term management plan from pregnancy period to prevent being lost during follow up

**Abstract #235**

**PREVALENCE AND CHARACTERISTICS OF LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA) IN A REGION OF INDIA**

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**Objective:** LADA is a subtype of diabetes defined by the presence of islet auto antibodies in the sera and lack of insulin requirement in the first 6 months of diagnosis. Due to heterogeneity of LADA, observations from one population cannot be assumed to be valid in others. We aimed to study the prevalence and characteristics of adult-onset autoimmune diabetes in a region of North India.

**Methods:** A total of 139 patients aged 30–70 years at diagnosis of diabetes with disease duration 6 months to 5 years were examined cross-sectionally. Clinical data were collected and glucose, HbA1c, lipid profile, creatinine, C-peptide and GAD-65 antibody (GADA) were measured in a fasting blood sample.

**Results:** Prevalence of LADA was 6.5% (9/139). GADA negative patients were diagnosed with type 2 diabetes (DM2). No patient was diagnosed with type 1 diabetes. LADA (n=9) and DM2 (n=130) patients were compared. LADA patients were younger (p = 0.045), had lower age at onset (p = 0.025), waist (p = 0.021), systolic blood pressure (SBP) (p = 0.033), triglycerides (p = 0.033), fasting C-peptide (FCP) (p = 0.009) and prevalence of metabolic syndrome (MS) (p = 0.003). LADA patients had also longer duration of diabetes (p = 0.045). Patients with GADA at-high titer (GADA-Hi, n=4) were compared with GADA at-low titer (GADA-Lo, n=5) group. Compared to GADA-Lo, all GADA-Hi patients were male (p = 0.048), had lower BMI (p = 0.040), waist (p = 0.026), FCP (p = 0.025) and MS (p = 0.048). Compared to DM2 patients, GADA-Hi patients were younger (p = 0.035), had lower age at onset (p = 0.020), BMI (p = 0.040), waist (p = 0.005), SBP (p = 0.003), triglycerides (p = 0.026), FCP (p = 0.001) and MS (p = 0.001). The rate of patients on insulin was higher in GADA-Hi compared to DM2 (p = 0.018). No difference was observed between DM2 and GADA-Lo patients.

**Discussion:** This study shows different clinical and metabolic profile of LADA patients compared to DM2 patients. GADA titer is an important parameter in defining the severity of the disease as patients with high GADA titer tend to have significant β-cell impairment. Earlier studies on Indians have shown varied results probably due to the different methodologies used. We adopted criteria suggested by Immunology of Diabetes Society and Action LADA group using a Diabetes Antibody Standardization Program validated method to measure GADA.

**Conclusion:** Our results indicate that LADA is prevalent form of adult-onset autoimmune diabetes and is not rare. Diagnosis of LADA should not be delayed as it may have therapeutic implications. In developing world, sometimes routine antibody testing is not cost effective. Thus, clinical and phenotypic features of LADA may help clinicians recognize patients for potential antibody screening.

**Abstract #236**

**FERRITIN AND SERUM IRON AS SURROGATE MARKERS OF POOR GLYCEMIC CONTROL AND MICROVASCULAR COMPLICATIONS IN TYPE-2 DIABETES MELLITUS**

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**Objective:** This study was designed to find the correlation of Iron indices with HbA1c levels and microvascular complications among patients with Type 2 DM

**Methods:** 100 T-2DM were studied. The mean Age of study group was 58.57 ± 3.17 years; whereas the mean age of Control group was 53.95 ± 4.43. The mean HbA1c of Study group was 9.46 ± 1.31; whereas the mean HbA1c of Control group was 6.42 ± 0.28. The duration of diabetes in Study group was 9.69 ± 2.69 years; whereas it is 5.26 ± 2.81 years in Control group. The mean Serum iron level in Study group was 155.08 ± 22.13 µg/dl; whereas it is 88.81 ± 38.04 µg/dl in Control group. The mean Serum ferritin level in Study group was 284.79 ± 50.06 ng/ml; whereas it is 181.31 ± 54.08 ng/ml in Control group. The mean
serum transferrin saturation in Study group was 30.25 ± 9.94; whereas it is 28.92 ± 6.03 in Control group

**Results:** Serum Ferritin and HbA1c:
Our study shows there is a significant positive correlation between serum ferritin level with HbA1c(r=0.43; p=0.001*)

Microvascular Complications: In the present study there is a significant positive correlation between Serum iron, Serum Ferritin levels and micro-vascular complications; Nephropathy, Retinopathy and Neuropathy(p=0.001). HbA1c and Duration of diabetes also correlated well with microvascular complications(p=0.001)

**Discussion:** In the present cross-sectional, comparative study we have found significant positive correlation between iron indices(serum iron,serum ferritin)and HbA1c levels in Study type 2 diabetes mellitus patients. We also found that these iron indices i.e.(serum iron, serum ferritin and Transferrin saturation) have significant correlation with micro-vascular complications in them.

**Conclusion:** We didn’t observe any significant correlation between transferrin saturation and HbA1clevels in the present study (p=0.62). We conclude that Serum ferritin and Serum iron may be used as surrogate markers of poor glycemic control and micro vascular complications in assistance with HbA1c.

**LIMITATIONS**
1. Sample size of the study is small, thereby preventing us from drawing strong conclusions.
2. The causal relationship between raised ferritin and Study diabetes mellitus is a matter of debate and require further exploration in establishing the authenticity of causal hypothesis.

Abstract #237

**DIABETIC KETOACIDOSIS IN TYPE 2 DIABETES: PROGNOSTIC FACTORS AND CHANGING TREND IN MORTALITY AT A TERTIARY CARE HOSPITAL.**

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Aga Khan University Hospital

**Objective:** To determine prognostic factors associated with increased mortality in type 2 diabetes patients admitted with diabetic ketoacidosis (DKA).

To compare mortality of type 2 diabetes patients admitted with DKA from July 2010 to February 2016 with mortality observed in same institute during period of 1991-1996.

**Methods:** Medical records of 279 patients admitted at Aga Khan University Hospital,Karachi with a diagnosis of DKA during the period of July 2010 to February 2016 were reviewed. A total of 128 patients fulfilling this criteria were included in the study.

**Results:** 118 patients had a history of type 2 diabetes mellitus whereas 10 patients had no history of diabetes or DKA. The mean age was 56.9 ± 12.4 years of which 53.1% (n=68) were males and 46.9% (n=60) were female. Out of total patients, 10 (7.8%) patients had severe DKA, 68 (53.12%) patients had moderate DKA and 50 (39.1%) had mild DKA. The mean age, duration of diabetes, hemoglobin, HbA1c, random blood sugar and BMI were not statistically significant in these groups (p>0.05). Mortality was seen in 2 patients with severe DKA, 8 patients moderate DKA patients and 6 patients with mild DKA. Age and creatinine contributes significantly in univariate analysis (HR 1.05 and HR 1.23, p<0.05). All variables used in univariate analysis were further analyzed for adjusted model. Advanced age, ICU stay were independent predictors (HR 1.06 and 5.85, p-value <0.05).

A greater frequency of type 2 diabetics (n=128) presented with DKA during July 2010 to February 2016 as compared to the study from same institute by Jabbar et al (n=57) in 1991-1996. Furthermore, marked reduction in mortality (12.5%) of type 2 diabetic patients admitted with DKA was observed during this period of July 2010 to February 2016 as compared to mortality observed in a study (21%) from same institute during period of 1991-1996. Factors relating to such improvement include inpatient endocrine consult service comprising of endocrine consultant, endocrine fellow, diabetic nurse, teaching of nursing staff, interns, residents by endocrine faculty on managing DKA patients, timely institution of insulin infusion protocols specially designed for managing DKA patients, and more patients now getting expert care.

**Conclusion:** Advanced age, ICU stay and deteriorating kidney function signify a poorer prognosis among type 2 diabetics with DKA. Although frequency of type 2 diabetic patients admitted with DKA has increased at our institute but there has been a considerable decrease in mortality owing to number of improvements in managing DKA patients and development of standardized protocols.
Abstract #238

IMPROVED SHORT TERM AND LONG TERM OUTCOMES OF EARLY INSULIN INITIATION IN TYPE 2 DIABETES OVER 10 YEARS

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Objective: Several studies have proven the benefits of early and aggressive intervention in lowering blood glucose and thereby reducing the risk of long-term complications. However, “clinical inertia” seen among physicians and “psychological insulin resistance” among patients has been recognized as predominant inhibiting factors towards timely initiation, or intensification of insulin therapy even when it is clinically indicated. By means of a retrospective analysis, we have tried to evaluate the benefits underlying early initiation of insulin therapy among type 2 diabetes mellitus (T2DM) patients attending our centre.

Methods: Electronic medical records of patients enrolled at our centre during Jan 2005 to Jan 2010 were extracted to identify patients who were detected with new onset T2DM (diabetes duration < 1 year) and subsequently initiated on insulin. Their follow-up data were analyzed retrospectively to investigate the benefits of early initiation of insulin therapy. Statistical analysis (Paired t-test) was done using GraphPad Prism version 6.01 for Windows.

Results: 57 patients were de-identified and had a mean age 2.93±1.185 years; mean HbA1c 10.90±2.15%; mean FBS 200.4±12.63mg/dL; mean PPBS 348.0±142.3mg/dL and mean BMI 26.42±4.07kg/m² at baseline. Total Daily Dose of Insulin (TDD) was found to be 21.67±14.61U. Upon analysis of the most recent follow-up data of these patients (as on October 2016), different clinical parameters were found to improve significantly from their baseline levels. Mean HbA1c was found to be 7.56±1.91% (p<0.0001); mean FBS 141.3±54.76mg/dL (p<0.0001); mean PPBS 159.0±40.26mg/dL (p<0.0186) and mean BMI 25.58±3.79kg/m² (p<0.0001). TDD required was found to remain stable (13.45±10.30U; p=0.0664) without requiring further escalated doses even with the progression of disease duration.

Discussion: Results reveal the advantages of early initiation of insulin in T2DM individuals. It aided in improving the clinical parameters of the patients which in turn can delay the development of diabetes associated complications. The escalation required in TDD usually observed with progression of the disease could also be avoided with this early intervention of insulin therapy.

Conclusion: Early insulin initiation in eligible candidates with T2DM lays a very strong foundation for future diabetes care. Early insulin initiation improves their clinical profile thereby delaying the onset of complications along with lower requirement of total insulin dosages which in turn will significantly bring down the cost of diabetes treatment.

Abstract #239

TREATMENT OUTCOMES WITH LIRAGLUTIDE IN NEW ONSET TYPE 2 DIABETES – A RETROSPECTIVE ANALYSIS

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Objective: Incretin mimetic Liraglutide (LIRA) is a very popular human GLP-1 in the treatment of type 2 diabetes(T2DM). By virtue of its action on the GLP-1 receptors located at vital organs thus delaying gastric emptying, reducing body weight and avoidance of hypoglycemia, this therapy could address the multiple etiopathogenesis of T2DM. Hence, LIRA should bring complete remission of T2DM in newly diagnosed patients provided the subjects are strictly followed up via a telemedicine integrated protocol for titration of injectables and metformin. We performed a retrospective analysis to assess the treatment outcomes of LIRA among these patients.

Methods: The electronic medical records of T2DM patients enrolled in our diabetes centre were extracted to de-identify patients who had been treated with LIRA. The inclusion criteria were new onset T2DM patients (diabetes duration < 1 year) who were initiated on LIRA+metformin or along with insulin. Those lost to follow up and discontinued LIRA due to GI side effects were excluded. A retrospective analysis of the follow-up data was conducted to evaluate the treatment outcomes of LIRA. Statistical analysis (Paired t-test) was done using GraphPad Prism version 6.01 for Windows.

Results: 71 patients were identified with mean age- 40.90±11.25years, males 76.06%, mean HbA1c 8.27±2.5%, mean FBS= 155.8±57.0mg/dL, mean PPBS 179.4±85.81 mg/dL, mean BMI 30.50±4.0kg/m², mean Body Weight (BW) 86.34±13.36kg and mean Waist Circumference (WC) 104.2±12.32cm. At 6 months, LIRA treatment brought out positive results in terms of improvements in various clinical parameters viz. HbA1c
was lowered to almost near normal levels of 5.96±0.35% (p<0.0001), FBS to 105.5±13.73mg/dL (p<0.0001), PPBS to 105.0±20.20mg/dL (p=0.0003), BMI to 28.99±3.85kg/m² (p<0.0001), BW to 81.82±12.34kg (p=0.0001) and WC to 98.08±8.94cm (p=0.0017).

Discussion: At 2 years, LIRA therapy resulted in complete remission of diabetes in 74% of subjects, requiring no medications for the treatment of diabetes. LIRA+metformin with or without insulin in new onset T2D when administered via a telemedicine integrated protocol, and when tapered and discontinued over a period of 6-8 months resulted in complete remission of diabetes in significant number of patients.

Conclusion: LIRA was well tolerated and resulted in significant improvement in glycemic parameters along with significant reductions in BW, BMI and WC. This observation calls for RCTS in a wider population which will have a significant impact as a cost effective option for treating new onset diabetes.

Abstract #240

DIABETES AND CANCER AMONG VETERANS

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1. WJB Dorn VAMC, 2. Stratton VAMC

Objective: Objective of the study is to evaluate the prevalence of cancers among Veterans with type 2 diabetes. Methods: In a single center, retrospective chart review study using computerized patient records. After the IRB approval the study was carried out Albany VAMC. Using CPT codes and verification by review of clinical and laboratory information, the study was carried out. The information collected include the BMI, smoking status, duration of diabetes, medications used, other medical problems such as hypertension, atherosclerotic cardiovascular disease, various cancers; laboratory data included HbA1C, eGFR, Creatinine and lipid parameters. Case Presentation: The study identified 6,777 subjects with type 2 diabetes with a mean age of 61± 10 and BMI of 32.6 ± 6. Total of 1045 subjects identified with cancers, after exclusion of skin cancers. The most common cancers among Veterans with type 2 DM are prostate cancer, colon cancer, bladder cancer and Lung Cancer. These cancers correlated with BMI. No correlation with age or duration of diabetes or diabetes medications. Other cancers noted include renal cell cancer, hepatocellular cancer, pancreatic cancer, lymphomas and breast cancer.

Discussion: Prevalence of diabetes is almost three times more than general population. Based on the epidemiological data, joint consensus statement from American Diabetes Association and American Cancer Society states that prostate cancer is less common in subjects with diabetes. The current study noted higher prevalence of prostate cancer among subjects with type 2 diabetes among the list of cancers. In a recent Korean study, prevalence of prostate cancer increased with increase in BMI among subjects with diabetes. Limitations include small study group and very few women. In addition, the study did not include the PSA level, family history of prostate cancer. Next most common is Colon cancer, which is similar to the epidemiological data. Another interesting finding is that bladder cancer is significantly high and no association with therapeutic agents for diabetes.

Conclusion: In contrast to general belief, prostate cancer is common among Veterans with type 2 diabetes. It is worth looking into the causes why prostate and bladder cancers are so common among subjects with diabetes among Veterans using national database.

Abstract #241

CIRCULAR ROUTE TO DIAGNOSIS OF HEMOGLOBIN D: DISPROPORTIONATE A1C

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Objective: HbA1C (glycated hemoglobin) is used both for making the diagnosis of diabetes mellitus and assessing the degree of glycemic control. Also, HbA1C can be altered by age, race, presence of hemoglobinopathy, red cell turnover, and anemia. This case will demonstrate how an inappropriately elevated HbA1c led to the diagnosis of Hemoglobin D though not in the exact manner we expected. Case Presentation: A 58 year old Indian female came to the endocrine clinic after an episode of hypoglycemia on a low dose sulfonylurea medication. A 3 hour OGTT was performed. Fasting glucose off medication was 112 mg/dL, 1 hour 203, 2 hour 104, and 3 hour 66. HbA1C was recorded at 8.8%. Since the HbA1C seemed inappropriate for the degree of hyperglycemia, a hemoglobin electrophoresis was performed. Results showed Hemoglobin D 36.9 (N=0), Hemoglobin A 58.5 (N=96%). Patient was advised to initiate lifestyle modifications including nutritional consultation. No antidiabetic or hypoglycemic agents were prescribed.

Discussion: Hemoglobinopathies usually manifest themselves with a falsely low HbA1C. This case seemed to show an opposite result. Glycated hemoglobin can be used to calculate the average glucose level for the life of the red blood cell. Hemoglobinopathies lead to a shortened red blood cell survival length due to an increased tendency for hemolysis.
In some hemoglobinopathies, HbA1C cannot be calculated accurately on routine testing such as HPLC technique, leading to a falsely high value. In this case, subsequent specialized testing confirmed the erroneous reading.  

**Conclusion:** Medical conditions with decreased red cell survival and hemolysis usually lead to a spuriously low HbA1C. In northwestern India, Hemoglobin D is a common variant, after Hemoglobin S and Hemoglobin C. A discordant HbA1C relative to blood glucose should lead to consideration of a hemoglobinopathy, among multiple considerations. However, a falsely high HbA1C can occur instead of the expected low value as described here.

**Abstract #242**

**THE IMPACT OF UTILIZING A NOVEL INSULIN DELIVERY DEVICE IN PATIENTS WITH TYPE 2 DIABETES**

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**Objective:** Advancements in insulin delivery technology have improved quality of life, adherence and glycemic control in patients administering insulin. This study was conducted to evaluate the clinical impact of a novel wearable insulin delivery device in patients with type 2 diabetes administering insulin.

**Methods:** This retrospective analysis utilized electronic medical records to identify patients switched from insulin delivery by an insulin syringe or insulin pen to insulin delivered by V-Go® a wearable insulin delivery device. Patients meeting predetermined criteria were included. A1C, weight, and insulin dosing were collected at baseline and for up to two follow-up visits using V-Go. Data were analyzed based on all patients and stratified for patients administering ≥ 2 insulin injections/day at baseline.

**Results:** A1C results were available for 103 patients after a mean of 15 weeks and for 84 patients after a mean of 34 weeks using V-Go. Patients administering ≥ 2 insulin injections/day prior to switching to V-Go comprised 85% of the population. Overall baseline demographics were age 59 years, weight 101 kg, and diabetes duration 14 years. Mean baseline A1C for all patients as well as for those administering ≥ 2 insulin injections/day was 9.6%. Significant A1C reductions at both time points were observed across all analyses (p<0.001). Mean changes [95% CI] from baseline for 15 and 34 weeks were as follows: all patients (-1.4% [-1.7 to 1.0%], -1.4% [-1.8 to -1.1%]), patients administering ≥ 2 insulin injections/day (-1.3% [-1.7 to -0.9%], -1.4% [-1.8 to -1.0%]). Patients previously administering ≥ 2 insulin injections/day experienced significant reductions in TDD (72 to 60 and 63 U/day; p=0.007) from baseline to 15 and 34 weeks, respectively. A small change in weight (+2 kg; p<0.001) was observed.

**Discussion:** Insulin is one of the most potent agents available to treat diabetes; however, when adherence is suboptimal, glycemic control is negatively impacted. Inconvenience, complexity and anxiety to inject have all been cited as adherence barriers. Addressing these barriers through advancements in insulin delivery has proven beneficial to clinical outcomes. V-Go offers a simple and discreet way to deliver basal-prandial insulin. In this analysis, switching to V-Go resulted in significant and sustained A1C reductions across the entire patient population and significant reductions in TDD for patients administering ≥ 2 insulin injections/day. The small change in weight is not believed to be clinically relevant.

**Conclusion:** V-Go offers a novel option to deliver basal-prandial insulin and in this analysis proved to be an effective and efficient advancement for insulin delivery in patients with type 2 diabetes.

**Abstract #243**

**UTILIZATION OF GLARGINE U300 IN CLINICAL PRACTICE TO IMPROVE GLYCEMIC CONTROL**

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**Objective:** Common basal insulins for patients with poorly controlled diabetes (DM) have been detemir or glargine U100. There are now several types of basal insulins on the market that claim to improve glycemic control in patients over the standard of two basal insulin regimens. Glargine U300 is a long-acting basal insulin glargine concentration which has reported to provide more consistent basal coverage and lower glycemic variability than standard insulin analogues. Our institution began to utilize glargine U300 in an attempt to optimize glycemic control in patients that are poorly controlled with standard basal regimens.

**Methods:** We retrospectively reviewed the results of one T1DM and four T2DM patients who were treated with basal glargine U100 or detemir for glycemic control. The patients were switched to glargine U300 per prescription labeling without any initial adjustment in preexisting pre-prandial insulin or antihyperglyemics. The patients’ chart was retrospectively reviewed and hemoglobin A1C, weight, and BMI was tracked at baseline and at 3 months.

**Case Presentation:** The patients’ hemoglobin A1C
reduction ranged between 1.6% - 3% in T2DM and 0.7% in T1DM patients at 3 months. The patients' BMI and weight was overall unchanged at 3 months in both groups. Of the T2DM patients, one was able to reduce their pre-prandial insulin requirements by 41% and one patient was able to discontinue pre-prandial insulin. The T1DM patient was also able to reduce their prandial insulin requirement by 30%. Two of the patients who had hypoglycemic episodes prior to glargine U300 had resolution of hypoglycemia. All of the patients subjectively reported improved well-being and compliance with glargine U300 insulin.

**Discussion:** Our series of five patients demonstrated a reduction in hemoglobin A1c and pre-prandial insulin requirements with transition of basal insulin to glargine U300. These real world results show that glargine U300 improves glycemic control with a possible reduction in hypoglycemic events.

**Conclusion:** Clinicians should consider transition to longer acting basal insulin such as glargine U300 in patients with uncontrolled hemoglobin A1c on multi-dose insulin regimen.

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**Abstract #244**

A RANDOMIZED, CONTROLLED, PILOT STUDY TO EVALUATE THE EFFECTS OF CULTURALLY-TAILORED PROGRAMS FOR DIABETES PREVENTION IN THE LOCAL KOREAN COMMUNITY

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**Objective:** The prevalence of diabetes mellitus (DM) among Korean Americans is higher than the prevalence among non-Hispanic whites, although in national research, DM rates among Korean Americans often are low or unreported. In a pilot study, we evaluated the effect of culturally-tailored programs for DM prevention in the Korean community using a randomized controlled trial to improve health behaviors and clinical measures in at-risk individuals.

**Methods:** Through a local Korean health fair in the spring of 2015, 29 participants were recruited for the study and randomized to a control and intervention group, with one participant excluded due to previous diagnosis of DM. The mean age of the participants was 61, with 100% being born in Korea, with Korean as the primary language, and on average, having lived in the US for 18 years. At baseline, there were no significant differences in age, height (Ht), weight (Wt), body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), TG, HDL, HbA1c in both groups. All participants received an introductory lecture on prediabetes and DM prevention and were invited back at 6 months for clinical reassessment and bloodwork. Participants in the intervention group were invited to attend 5 additional seminars which included a talk, interactive question and answer sessions and small group exercises.

**Results:** There were no significant differences at 6 months between the control and intervention group for the primary endpoints of Wt, BMI, and HbA1c. There were no significant differences at 6 months for secondary endpoints as well for WC, HDL, SBP, DBP, PHQ9 (depression survey) scores, GAD 7 (anxiety survey), IPAQ (physical activity survey), and DM knowledge. In assessing dietary intake goals, there were also no significant differences in the proportion of study participants who achieved a goal of dietary fat intake <30%, saturated fat intake <10%, and fiber >15g/1000 calories.

**Discussion:** Due to a small sample size, and loss of study participants to follow-up, no significant differences were noted in this study.

**Conclusion:** In this pilot study, a culturally-tailored program for DM prevention in the Korean community using a randomized controlled trial was feasible, though no significant differences were found between the control and intervention group for primary endpoints of Wt, BMI, and HbA1c. Larger scale recruitment and retention efforts may yield beneficial effects on DM prevention in this at-risk Korean-American population.

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**Abstract #245**

MULTIMODAL APPROACH TO DIABETES CARE UTILIZING GROUP VISITS, TELEMEDICINE INTERVENTION AND CONSUMER ACCELEROMETER BASED TRACKING TECHNOLOGY

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**Objective:** The goal is to assess the effects of a group intervention from a multidisciplinary team on HbA1c and energy expenditure, measured via accelerometer motion tracking. Secondary objectives include assessment of blood pressure, triglycerides, weight, and self-reported physical health.

**Methods:** A search of the database was performed with the following inclusion criteria: age >18 years, HbA1c >8.5%, and diabetes mellitus type 2. 12 patients were randomly selected from this patient pool to participate in the study. A control group was also randomly selected and received the current standard of care. Study patients
attend 6 diabetic education sessions following the standards set by the AADE. These include an overview of type 2 diabetes, a discussion of complications associated with diabetes, physical activity guidelines, nutrition management, a review of oral and injectable medications, stress management, and goal setting. Sessions are conducted by a care team consisting of physicians, residents, pharmacists, and diabetic educators. Patient blood pressure, weight, energy expenditure extrapolated, HbA1c, and blood work are collected routinely. On the first and last visits, patients complete surveys including the Diabetes Attitude Questionnaire, the Summary of Diabetes Self-Care Activities, the Adherence to Diabetes Medicine (ARMS-D), and the PHQ-9 for depression screening, administered by a practitioner.

Results: The average HbA1c of the group on their first session was 9.85%. Patients’ HbA1c’s decreased by an average 10.3% by their fourth session approximately 3 months later. On the first visit, the average blood pressure of the entire group was 154/81 mmHg. When asked to rate their ability to fit diabetes into their lives in a positive manner, the average rating was 3.87 (using a scale of 1 to 7, with 1 being not at all comfortable and 7 being very comfortable). When asked to rate their own understanding of diabetes and its treatment on a scale of 1 to 7, the average rating was 4.3.

Discussion: While still halfway through the six-month intervention, the study has reached its primary objective of substantially lowering HbA1c. The results also clearly indicate that most patients began the study uncontrolled (per the ADA guidelines) for both blood pressure and HbA1c. Patient survey results indicated rather low self-confidence about managing diabetes.

Conclusion: Once the study is completed and further statistical analysis is reviewed, we are confident that interdisciplinary team-based care will be proven a superior model compared with the traditional standard of care for uncontrolled diabetes. As evidenced by the decrease in HbA1c by session four, we are still very much on target to reach our goals.

Abstract #246

IMPACT OF INSURANCE FORMULARY AND MANUFACTURER COUPONS MEASURED BY DIABETES SUPPORT SOFTWARE

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Objective: The progressive nature of Type 2 Diabetes Mellitus often requires combination therapy. Cost considerations provide patients and physicians with difficult decisions balancing efficacy, side effects, and complexity with cost of prescriptions. Impact of cost, with and without use of manufacturer’s coupons, will be considered using a cost sensitive decision support tool.

Methods: Path, a clinical decision support tool for Type 2 Diabetes, was developed based on patient impact of efficacy, cost, implementation difficulty, comorbidities, and side effects. Monthly patient cost is calculated through access of the insurance formularies of November 2016. Value of renewable manufacturer coupons were utilized where appropriate.

Chart review of patients with A1c > 7 seen during a 30 day period of time was performed. Abstracted information was placed into a multivariable decision engine. Three cost scenarios were run for drug optimization. The control scenario was run without consideration to cost of regimen. A second scenario considered implementation without use of manufacturer coupons (CPN-). A third scenario made coupons available for each appropriate patient (CPN+). Outcomes were measured for cost, projected A1c, number of medications, and a composite score representing side effects, weight impact, and adherence difficulty.

Results: Mean manufacturer cost of the control regimen was $331. Mean projected A1c was 6.2. Composite score was measured at 93.7 of 100. Mean number of medications was 3.4 per patient. Mean patient cost in CPN- was $82. Mean projected A1c was 6.5. Composite score was measured at 82.2 of 100. Mean number of medications was 3.2 per patient. Mean patient cost in CPN+ was $51. Mean projected A1c was 6.3. Composite score was measured at 89.4 of 100. Mean number of medications was 3.1 per patient.

Differences were observed between A1c of control and CPN- scenarios (p < 0.001). No difference was seen between A1c in control vs CPN- (p = 0.050) or CPN+ vs CPN- (p = 0.053). No significant difference was observed in number of medications in each scenario. Composite score and cost showed significant difference across groups (all p < 0.001).

Conclusion: Software decision support can provide valuable economic analysis with regard to cost of therapy.
Manufacturer coupons allow for similar intervention patterns to unlimited cost scenarios with limited cost to patient but high total cost. Insured patients not using coupons achieve similar A1c goals at higher patient cost but lower total cost. Composite side effect/adherence score and cost showed the largest differences between cost scenarios. Physicians have conflicting incentives for community verses individual benefit.

Abstract #247

INSULIN RESISTANCE IN ADULT TYPE 1 DIABETICS: AN INCREASING PROBLEM WITH MORE SEVERE LIVER DISEASE THAN TYPE 2 DIABETICS

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Objective: NAFLD is characteristic of insulin resistance (IR) in diabetes type 2 (DM2) but not noninsulin resistant type 1 (DM1); however, coexisting IR and DM1 (IRDM1) are increasingly recognized. Here we compare IR effects on NAFLD in DM1 and DM2.

Methods: NAFLD severity was quantified by analyzing Tc-99m-sulfur colloid liver SPECT from a Siemens e.cam with SCINTRON software. A sensitive fractal parameter, F, combined effects of best (Sb) and worst (Sw) liver function. F was calibrated by liver biopsy and ultrasound and normalized (Fn) for effects of liver and spleen size, BMI, BSA and ECF.

Case Presentation: In 14 near normal patients F 1.54+-0.20 was similar to uniform activity phantoms. Among 823 patients with liver SPECT, age 52+-15 years, 43 (5.2%) had DM1 and 25 (58.1%) of these, including 3 (12%) with LADA, also had IR, using > 50 units insulin/day. Fn for patients with IR alone was similar to DM2 with HbA1c < 9.5%. Excluding patients with liver disease risks other than IR or DM2, Fn for IRDM1 was > Fn for DM2: in near normal (3.73+-0.13) > (2.56+-0.45); in NAFL (7.13+-0.99) > (4.48+-0.46); in NASH (10.54+-1.22) > (7.15+-0.69) and in fibrosis (12.84+-0.32) > (10.83+-1.71); p < 0.03.

Patients with IRDM1 had HbA1c (8.1+-1.7)% > (6.8+-1.2)% in DM2 or IR (p < 0.02). Patients with either DM2 or IRDM1 who had uncontrolled HbA1c (11.2+-1.5)% had similar Fn (9.2+-2.9). Decreasing HbA1c to normal in 4 months did not change Fn in IRDM1; however, among 221 DM2 patients with follow-up studies of 4 to 48 months, Fn improved in 92 (41.6%), was unchanged in 78 (35.3%) and worsened in 51 (23.1%). DM2 patients with hepatic metastasis had significantly (p < 0.003) increased Fn (20.5+-4.7).

Discussion: The fractal parameter, F the sum of absolute values of Sb and Sw, reflects overall liver function inhomogeneity; greater values indicate worse function. Normal patients or phantoms with uniform activity had similar Sb (0.61+-0.05) and Sw - (0.93+-0.01). Not surprisingly, such control Sb and Sw are nonzero and unequal without image attenuation correction or log plot weighting factors. Since the BMI of IRDM1 and DM2 patients was taken account of in normalizing Fn, attenuation is not likely causing greater Fn in IRDM1 than DM2. Prior studies suggest greater diabetic complications in patients with worse NAFLD. Higher Fn in IRDM1 likely indicates a high risk category, and patients with hepatic metastasis and even higher Fn are at even higher risk.

Conclusion: Liver dysfunction in increasingly recognized IRDM1 is more severe than in DM2 or DM1 without IR, but similarly exacerbated in IRDM1 or DM2 patients who have uncontrolled HbA1c.

Abstract #248

ACHIEVEMENT OF GLYCEMIC TARGETS IN PATIENTS WITH UNCONTROLLED TYPE 2 DIABETES WHEN SWITCHING TO A WEARABLE INSULIN DELIVERY DEVICE FOR INSULIN DELIVERY

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Objective: It is recognized that even moderate A1C reductions can provide both short and long-term clinical and economic benefits in patients with long-standing uncontrolled diabetes, despite insulin therapy. The primary objective of this retrospective analysis was to evaluate the % of patients with uncontrolled type 2 diabetes that achieved an A1C < 8% and/or a reduction in A1C of ≥ 1% after being switched from conventional insulin delivery (syringe or pen device) to V-Go® a 24-hour wearable insulin delivery device.

Methods: An electronic medical records database was queried to identify patients prescribed insulin with an A1C > 8%. Patients meeting predetermined criteria and switched to V-Go for insulin delivery were included. Evaluations of A1C (%), change in A1C and insulin total daily dose (TDD) were conducted based on the first documented A1C result > 30 days post V-Go initiation compared to baseline.

Results: Eighty-nine patients were evaluated. The mean age was 59 ± 12 yrs, weight 101 ± 21 kg, duration of
diabetes 14 ± 7 yrs, A1C 9.9 ± 1.4% and TDD 66 ± 32 U/day (range 10 to 200 U/day). At baseline the majority of patients (84%) administered ≥ 2 insulin injections/day. After a mean duration of 15 ± 6 weeks using V-Go for insulin delivery, 71% of patients achieved an A1C < 8% and/or a reduction in A1C of ≥ 1%. Mean insulin TDD requirements were reduced from baseline across the patient population.

Discussion: The achievement of stringent A1C goals is low in patients with advanced type 2 diabetes administering insulin ± additional glucose lowering agents. Evidence from a large medical claims database supports that only 20% of patients prescribed insulin have an A1C < 7.0% and over 30% of patients have A1C levels ≥ 9%. Contributing to this problem is the progression and complexity of diabetes over time; however, non-adherence to prescribed insulin regimens also contributes to poor glycemic control. In this study, switching patients to V-Go resulted in the majority of patients achieving established glycemic targets while benefitting from a decrease in insulin requirements in a relatively short time period. We attribute this success to improved insulin adherence as well as to insulin being continuously infused and readily available for bolus dosing.

Conclusion: Therapeutic options for patients with uncontrolled diabetes despite insulin therapy are limited. New and novel ways to improve insulin adherence and delivery may offer a solution for these patients. Switching to V-Go in patients with uncontrolled diabetes resulted in the achievement of clinically meaningful glycemic targets and required less total insulin than prior insulin regimens.

Abstract #249

THE VARIABILITY IN NIGHTTIME INSULIN DELIVERY AND GLUCOSE LEVELS WITH A HYBRID CLOSED-LOOP SYSTEM IN A PIVOTAL TRIAL

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Objective: The MiniMed® 670G hybrid closed-loop (HCL) system was previously shown to be safe, reduce mean A1C, increase sensor glucose (SG) time-in-target, and decrease hypoglycemia (percentage of SG ≤50 mg/dL and ≤70 mg/dL) in 124 adolescents and adults with type 1 diabetes. SG time-in-target (percentage of SG >70-180 mg/dL) and insulin delivery metrics, from 10:00 pm to 7:00 am, were evaluated in the same individuals during the HCL pivotal trial.

Methods: An initial 2-week run-in phase without HCL control enabled was compared to a 3-month in-home study phase with HCL control enabled, in 30 adolescents (14-21 years) and 94 adults (22-75 years). The run-in phase had basal rates pre-set by the patient and health care provider. The study phase had variable basal rates ranging from 0 units to an individualized insulin limit, determined daily, which were automatically adjusted every 5 minutes based on SG levels.

Results: The mean nighttime insulin delivered for all subjects was 9.0±4.7 units during run-in versus 9.4±5.9 units during the study phase (p=0.04). The mean standard deviation (SD) and coefficient of variation (CV) of insulin delivered per night for run-in were 0.3±0.4 units and 3.1±5.1%, respectively, versus 2.4±1.6 units and 25.3±5.0%, respectively, for the study phase (p<0.001 for both comparisons). There was an almost 3-fold increase in the nighttime maximum interquartile range (IQR) of insulin delivered during HCL control, compared to that during run-in (0.55 versus 1.58 units/hr, p<0.001). During the 9-hour overnight span, the HCL algorithm suspended insulin a mean of 95±81 minutes and delivered insulin at the maximum limit a mean of 147±107 minutes. For the remainder of 298 minutes, it delivered insulin between
Abstract #250

LIRAGLUTIDE ACUTELY SUPPRESSES GLUCAGON, LIPOLYSIS AND KETOGENESIS IN TYPE 1 DIABETES

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Objective: In view of the occurrence of diabetic ketoacidosis associated with the use of SGLT2 inhibitors in patients with type 1 diabetes (T1DM) and absence of this complication in patients treated with liraglutide in spite of reductions in insulin doses, we investigated the effect of liraglutide on ketogenesis.

Methods: Twenty six patients with inadequately controlled T1DM (age: 43.8±3.9 years; HbA1c:7.7±0.3%, BMI:31.8±1.8Kg/m2), treated with CSII were randomly divided into two groups of 13 patients each. After an overnight fast, patients were injected with either liraglutide 1.8mg or with placebo. They were maintained on their basal insulin infusion and were followed up for 5 hours.

Results: The patients injected with placebo maintained their glucose and glucagon concentrations without an increase but there was a significant increase in FFA (from 0.35±0.06 to 0.49±0.07Mm), acetoacetate (from 0.41±0.04 to 0.68±0.10mM) and β-hydoxybutyrate (from 0.29±0.06 to 0.57±0.19mM) and ghrelin (from 288±28 to 362±35pg/ml) concentrations (p<0.05 for all). In contrast, liraglutide significantly suppressed glucose (from 173±21 to 135±18mg/dl) and glucagon (from 91±15 to 72±13pg/ml) concentrations, reduced the increases in FFA (by 39±14%), and totally prevented the increase in ghrelin, acetoacetate and β-hydroxybutyrate concentrations. There was no significant change in hormone sensitive lipase or in lipoprotein lipase plasma levels in either group.

Discussion: Our data show clearly that while the peripheral insulin concentrations in inadequately controlled T1DM was sufficient for maintaining steady glucose concentrations, though at an elevated level, do not provide enough insulin to prevent the increase in concentrations of ghrelin, FFA, acetoacetate and β-hydroxybutyrate. These changes are prevented by single a dose of liraglutide.

Conclusion: We conclude that acute treatment with liraglutide suppresses ghrelin, glucagon, lipolysis and ketogenesis. These observations are relevant to the use of liraglutide in the management of T1DM.

Abstract #251

VALUE OF CHRONIC DISEASE REGISTRY IN EVALUATING PREDICTORS FOR DIABETES-RELATED CLINICAL INERTIA.

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Objective: Use Electronic Diabetes Registry to identify predictors for uncontrolled glycosylated hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL_C) and mean arterial blood pressure (MAP) in diabetics.

Methods: A retrospective, records-based, cross-sectional study was conducted using data sets from unique 44055 electronic medical records (EMR) of patients presenting at a U.S. metropolitan healthcare system. Using an dynamic EMR-based clinical-decision-support tool, patients with diagnosis of Diabetes Mellitus have been enrolled into an electronic diabetes registry since 2012. We pulled pertinent clinical, laboratory & therapeutic data items that might relate to diabetes care since their enrollment up to October 2016. The last HbA1c, LDL_C & MAP were used as surrogate measures for diabetes related clinical inertia. We studied variables that might contribute to clinical inertia including patient, provider or system related factors. Statistical analyses included multivariate regression. The analyses were done for the whole group & for the subgroups based on HbA1c at enrollment.

Results: Pertinent factors related to clinical inertia included A) Patient related factors; Age & Gender at enrollment had significant impact on last HbA1c, LDL_C and MAP with higher values present in younger male population. Generally, The higher the HbA1c at enrollment, the higher the last HbA1c, LDL_C, and MAP (P<0.01). Having urine microalbumin/creatinine ration < 30 was associated with lower last HbA1c, LDL_C & MAP (P<0.01) compared to higher ratios. Patients on insulin were associated with higher last HbA1c (P<0.01) compared to those who are
not. As expected being on statin was associated with better Last LDL_C and better last MAP (P<0.01) but but with higher last HbA1c (P<0.01) when the enrollment HbA1c is less than 8%. B) Provider related factors Frequent and recent endocrinology visits predicted better HbA1c & better LDL_C regardless of HbA1c at enrollment (p<0.01). Frequent primary care visits were associated with significant improvement in HbA1c only when A1c at enrollment is between 8-9% (p<0.05). C) System Related factors Having a provider affiliated with the healthcare system was associated with lower last HbA1c mainly when the enrollment A1c was more than 9% (P<0.01). Having no access to personal health record was associated with higher HbA1c when enrollment HbA1c is more than 9%.

Conclusion: Chronic Disease Registries can help to identify predictors for suboptimal care in patient with diabetes. HbA1c at enrollment into the registry, frequent endocrinology visits, better titration of insulin regimens and having access to Personal Health Records would have significant impact on diabetes care.

Abstract #252

EFFECTS OF CANAGLIFLOZIN VERSUS GLIMEPIRIDE ON ADIPOKINES, INFLAMMATORY BIOMARKERS, AND CHEMOKINES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: Type 2 diabetes mellitus (T2DM) and obesity are pro-inflammatory states that are associated with an increased risk of cardiovascular disease (CVD). Canagliflozin (CANA), a sodium glucose co-transporter 2 (SGLT2) inhibitor, demonstrated superiority in lowering A1C versus glimepiride (GLIM) and greater body weight reduction via loss of fat mass in a 52-week, Phase 3 trial of patients with T2DM on metformin. This post hoc analysis assessed the effects of CANA versus GLIM on select adipokines, inflammatory markers, and chemokines that have been associated with impaired adipose tissue function, insulin resistance, and CVD.

Methods: Serum samples were from randomly selected patients receiving CANA 300 mg (n=100) or GLIM (n=100) in the overall study. Change from baseline to Week 52 in serum leptin, adiponectin, CRP, PAI-1, VCAM-1, and MCP-1 was measured using a multiplex assay (Myriad RBM). Change in serum IL-6 and TNFα was measured with ultra high-sensitivity assays (Simoa-Quanterix). Change in leptin, adiponectin, and IL-6 was correlated with change in A1C, body weight, and lipids (HDL-C, LDL-C, triglycerides) within each group.

Results: At Week 52, the least squares mean (LSM) change in A1C was –0.99% with CANA and –0.91% with GLIM (BL=7.7-7.8%). LSM change in body weight was –4.1 kg with CANA and 0.7 kg with GLIM (BL=90-91 kg). At Week 52, serum leptin was decreased 26% with CANA versus GLIM (LSM change, –1.65 vs 2.14 ng/mL; difference [95% CI] of –3.80 ng/mL [–5.74, –1.85]). Serum adiponectin was increased 17% with CANA versus GLIM (LSM change, 0.74 vs –0.02 μg/mL; difference [95% CI] of 0.75 μg/mL [0.45, 1.06]). There was a 23% reduction in median serum IL-6 (–0.3 vs 0.2 pg/mL; difference [95% CI] of –0.5 [–0.7, –0.2]) and a 9% increase in median serum TNFα (0.1 vs –0.1 pg/mL; difference [95% CI] of 0.2 pg/mL [0.0, 0.3]) with CANA versus GLIM. No between-group differences were observed with CRP, PAI-1, VCAM-1, or MCP-1. Change in leptin was correlated with change in body weight (r ≥0.35) only; change in adiponectin and IL-6 was not correlated with change in A1C, body weight, or lipids.

Conclusion: CANA 300 mg demonstrated reductions in serum leptin and IL-6, and an increase in adiponectin versus GLIM in patients with T2DM; CANA was also associated with a small increase in TNFα and had neutral effects on other biomarkers. The CANA-related changes in leptin, adiponectin, and IL-6 were independent of glycemic benefit, and the changes in adiponectin and IL-6 were independent of weight loss in this analysis. These collective results suggest that CANA may improve adipose tissue function, which may have positive effects on cardiometabolic health.
META-SYNTHESIS AND TRENDS IN PUBLICATION ON EVIDENCE BASED MEDICINE FOR TENELIGLIPTIN: A YEAR IN REVIEW

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Objective: Recently, popularity and use of teneligliptin in treatment of type 2 diabetes mellitus have increased with the parallel rise in the publications for teneligliptin with the highest number published in last one year with 23 documents. The objective of this bibliometric study is to assess the global scientific production analysis across the global biomedical literature in last one year and explore the developing trend in qualitative and quantitative perspectives

Methods: We explored the global publication database across the Cochrane medical library and the medline-pubmed from August 2015 till November 2016 by using the MeSH term ‘Teneligliptin’. These included human evidences (clinical trials and case reports), reviews, experimental medicine

Results: The meta synthesis resulted in an integrated output for the insights into the different but inter-related studies and generated new insights and understanding from the recent publications. Out of 23 publications 12 studies involved human intervention (2 publications for the case reports and 10 clinical studies). The average impact factor of journals were 3.37 (1.23-6.36). Predominantly, 64% (16/23) of the studies have been published from Japan as the country of origin including human studies (10) and experimental (6). Cumulatively, 697 patients across 12 human studies and case reports have been evaluated under the teneligliptin group across the varied trials including comparative arm with Sitagliptin. Patients included were drug naïve, gliptin naïve, and were ongoing therapy with metformin. The endpoints beyond glycemic improvement included biomarker evaluation for the reduction in renal and vascular oxidative stress, early phase of insulin release, improvement in insulin resistance, cytoprotective actions like improvement in left ventricular diastolic function and endothelial function, improvement in hemodialysis for antiatherothrombotic effect that may be beneficial in the primary prevention of cardiovascular disease. Indian experimental research from Hyderabad explores the differentiated high protein binding profile.

Discussion: Our meta synthetic analysis of recent publications for teneligliptin provide important insights to the ascending trend of scientific publications through the varied patient profiles evaluated under evidence based medicine setting.

Conclusion: This meta synthesis would deepen the understanding for the evolution of the published strength of evidence for teneligliptin with a potential to bridge the rapid transition from evidence to experience

UNDERSTANDING GAPS TO ENHANCE DIABETES CARE INTERACTION: QUESTIONNAIRE BASED EVALUATION OF DIABETES CARE PHYSICIANS

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Objective: We conducted a survey to understand the gaps in the perception and the reality to achieve better glycemic control at the level of the diabetes care physician and for the perceived understanding of the patient’s level of the knowledge

Methods: We conducted a one to one interface validated questionnaire based interview among 79 leading Diabetes Care Physicians (DCPs) attending a national medical educational forum, through a 10 point questions including 3 closed ended questions, through a interaction based on paper-pen approach. The average time per interaction, including the briefing the objective of this study was 12 minutes

Results: 81% (n=64) of the participants (DCPs) were male. 41 participants were senior medical fraternity age more than 50 years, with more than 2 decades of active clinical practice in diabetes care. (min age 23 yrs, max age 70 yrs). 35% (n=44) of DCPs report that at least 50 % of the patients understand the seriousness of having diabetes. 25 % (n= 31) perceive that at least 50 % of patients are aware and serious for increased risk of cardiovascular disease in diabetes. 40% (n=32) and 58 % (n=46) of DCPs agreed and strongly agreed, respectively that explaining consequences of uncontrolled diabetes is an effective way of managing diabetes. 42 either just agreed (n=14) or strongly agreed (n=28) that instilling fear in the mind of the patient helps achieve better glycaemic control. 37 either
agreed (n=29) or strongly agreed (n=8), were satisfied and contended with the quantum of effort excellence on part of the DCPs to consistently motivate patients to adopt lifestyle modification. 40 % (n=32), 54% (n=43),14% (n=11), 30% (n=24) perceive that atleast 50 % of the patients are adherent to the recommended exercise schedule, follow dietary advice, consult a qualified dietician and adhere to self-monitoring of glucose, respectively, as advised by the DCPs. The common barriers by the DCPs to achieve glycemic control included lack of education by patient, lack of diet and exercise control and the fear of insulin

Discussion: Understanding and applying the knowledge of diabetes care are both equally important to implement an effective diabetes care delivery model. Our study highlights that the effective communication between the people with diabetes and the healthcare professional is essential to implement an effective diabetes delivery model.

Conclusion: The perception analysis from the sample size is representative of the nationwide DCPs at the same time adds value to the quantitative methodology to address the issue from the qualitative perspective. It would be meaningful to incorporate communication with diabetes patient as an integral part of the medical curriculum

Abstract #255

GLIMEPIRIDE – BENCH TO BEDSIDE: NARRATIVE REVIEW OF THE TECHNOLOGICAL ADVANCEMENT UPDATE 2016

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Objective: The structure activity relationship of glimepiride provides unique binding affinity to the beta-cell sulfonylurea receptor, with preservation of cardioprotective responses to ischemia. The technological development for glimepiride formulation could provide incremental advancement to improvise patient care in diabetes.

Methods: We performed a comprehensive research of the literature till November 2016 on Pubmed, ScienceDirect and Google Scholar by using specific MeSH, Boolean operators and text key words including, Glimepiride AND Technology AND Formulation AND emulsion. Secondary references were also explored for analysis.

Results: The qualitative research across 26 studies reveal that glimepiride has been well explored through considerable empirical research published across the world specially, India. Various innovative and technologically advanced formulations by utilising techniques such as micro emulsification, nano vesicles, transdermal formulation, hydrotropy, self-nanoemulsifying drug delivery system. Recent kinetics and molecular docking study reveal acetylcholinesterase inhibitor property which may have implication for alzheimer’s disease as diabetes dual therapy. Innovative technologies under development include nnonization for the particle size reduction and stabilization of nanocrystals could have impact on the. Ethosomal formulation – vesicles for enhanced delivery could be considered a suitable glimepiride delivery through transdermal vehicle with possible reduction in side effects and controlling the drug release. Oral glucose tolerance test studies demonstrated plasma glucose levels were efficiently controlled in case of nanosuspension.

Discussion: Substantial glimepiride- drug development work has happened in over last two decades, with an accelerated development in last one decade. This could reduce the dose frequency and enhance compliance.

Conclusion: India stands a unique distinction for the maximal no. of publications of the validated technology development which could be further strengthened by demonstrating the clinical outcomes.

Abstract #256

EVIDENCE MAP OF GLIMEPIRIDE: RESULTS OF A BIBLIOMETRIC ANALYSIS FOR INDIA, CHINA AND THE WORLD DURING 1988-2016

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Objective: Glimepiride is a well-established anti-diabetic agent with substantial weight for the evidence based medicine ever since the first publication in 1988. We explore the continuum of published strength of evidences for glimepiride through a comparative analytical approach across the publications from the world, China and India.

Methods: The evidence map is based on the systematic review of the published evidences. We searched pubmed and Cochrane medical library electronic databases since inception to November 2016. The bubble plot graph methodology is used to depict the quantum and the level of the evidence. A systematic search was done using MeSH terms on PubMed. The rate of articles published per million population with diabetes across the world was calculated and then compared as a benchmark for India and China to develop an index score of publications

Results: Pubmed had 1117 articles cited for Glimepiride
of which 744 are human published evidences. Two thirds (750) of the publications appear in the last one decade of which 60% (443) have been published in last five years. India accounts for approximately 16.8% population of diabetics and contributes 8% of publications, compared to 6% contribution from China for publications on glimepiride. The indexed score from India and China was benchmarked against the global score for the parameters including the human studies, clinical trials, randomised clinical trials, reviews, meta analysis and case reports with the publication time lines for last 5 years and 10 years.

Discussion: The glimepiride evidence map provides an overview of the published strength of evidences, without taking into account whether these studies are positive, neutral or negative studies.

Conclusion: Our bibliometrics analysis demonstrates that India scores over China in several parameters with a scope to escalate the quantum with the higher level of evidences for glimepiride. The propensity score reflects that the evidence base for glimepiride is evolving in alignment with the geographical burden of diabetes.

Abstract #257

EFFICACY OF TENELIGLITPIN AS MONITORED WITH CONTINUOUS GLUCOSE MONITORING SYSTEM (CGMS) IN COMPARISON WITH STANDARD OF CARE IN INDIAN SETTING

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Bhatia, Jaslok & Br Candy Hosp

Objective: HbA1c provides information about a patient’s glucose exposure. Acute diurnal glucose oscillations and chronic sustained hyperglycaemia result in diabetic complication. Literature shows that patients with similar HbA1c values, can have dissimilar pattern of glucose peaks and nadirs throughout the 24 hours. In India, Sulphonylureas and Glitins are widely used as adjuvants to Metformin. Teneligliptin, well studied in Japanese and Korean patients for its HbA1c reduction and safety, was evaluated in this study for daily glucose control and variability pattern in Indian diabetic patients having different meal preferences, physique and metabolic rate compared to Asians and Westerners.

Methods: This is a single centre, prospective, open label, comparative study between Teneligliptin and Glimepiride in patients with type 2 diabetes recruited from outpatient clinic. 52 patients aged 30–79 years, with HbA1c above 7.0% and below 9.5% in spite of optimal metformin dose, diet and exercise, were divided into two groups to receive either as an adjuvant. Baseline parameters like post prandial and fasting glucose levels were noted and 14 days CGMS was conducted.

Case Presentation: After 14 days the mean fasting glucose level dropped by 15.2% and mean postprandial level dropped by 4.6% in Glimepiride group while in Teneligliptin group, mean fasting glucose level reduced by 9.6% and postprandial reduced by 13.6%. CGMS analyses showed 10.04% cases of Glimepiride had glucose level below 80mg/dl, the lowest recorded was 40mg/dl Vs that in Teneligliptin group was just 3.4%, with lowest glucose level of 73 mg/dl. Similarly the mean highest glucose excursion of 320 mg/dl was observed in Glimepiride arm, while in Teneligliptin it was 287mg/dl. The average glucose level and percentage of time in target were not significantly different among the groups.

Discussion: Teneligliptin has a half-life of around 24 hours with dual route of elimination. CGMS studies in other Asian population has shown significant reduction in glycemic excursion and improved proportion of time in euglycemia. CGMS has helped clinicians in understanding better, therapeutic efficacy vis-à-vis patient’s dietary habits and varied lifestyle, thereby ensuring treatment success. This study analysed efficacy of Teneligliptin Vs Glimepiride with CGMS, in an uncontrolled environment of real world in the outpatient set up, where patient’s compliance and good glucose control is absolute necessary to achieve glycemic target.

Conclusion: The study explored the benefits of teneligliptin beyond the regular glycemic parameters. Teneligliptin has shown better post prandial glucose control with less glucose excursion and lower incidence of hypoglycaemia Vs traditional standard of care in India.

Abstract #258

ENERGY INTAKE AND EXPENDITURE IN TYPE 2 DIABETIC SUBJECTS ATTENDING A TERTIARY CARE HOSPITAL IN BANGLADESH

Md. Fazlarabbi Khan, Md Faruque Pathan

BIRDEM

Objective: Increased body weight in type 2 diabetic patients leads to worse glycemic control and higher incidence of complications. The approach for reducing obesity among type 2 diabetic subjects is changing lifestyle through healthy dietary practice and increasing physical activity. This study was undertaken to measure energy intake and expenditure in a group of Bangladeshi type 2 diabetic subjects.

Methods: One hundred type 2 diabetic subjects (male 25%, female 75%, age 45±6 years, BMI 26±4, mean ±SD) were selected from the Out-Patient Department of BIRDEM
ABSTRACTS – Diabetes Mellitus/Prediabetes

ABSTRACTS – Diabetes Mellitus/Prediabetes
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Results: The daily energy intake \{median(range)\} of the subjects was 2137(1105-4775) kcal. In 72% of the subjects this intake was 300 kcal more than the recommended calories. The total daily energy intake (kcal/day) was higher in the Obese group \{median (range), kcal, 2747(1875-3620)\} compared to the Overweight group \{2216 (1327-4775)\} and Normal \{1960 (1105-3934)\} groups. The total daily energy expenditure (kcal/day) was also significantly lower in the Obese group \{median (range)kcal, 2449(1775-3124)\}, p<0.006) compared to the Overweight \{2175 (1985-2782)\} and Normal \{2060(1883-2495)\} groups. The median (range) duration of exercise of the subjects was >45 min/day. The physical exercise was adequate in duration only in 53% subjects. There was a significant negative correlation between daily energy expenditure and BMI (r= -0.374, p=0.0001).

Conclusion: Obesity in type 2 diabetes mellitus is clearly a function of positive energy balance and it should be managed by reducing intake of energy as well as increasing its expenditure.

CARDIOVASCULAR RISK FACTORS AMONG TYPE 2 DIABETIC SUBJECTS ATTENDING SELECTED DIABETES CARE FACILITIES IN BANGLADESH

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BIRDEM

Objective: Diabetes mellitus, hypertension, cigarette smoking, dyslipidemia, obesity and physical inactivity are traditional or conventional risk factors for cardiovascular diseases (CVD). To assess the proportion of cardiovascular risk factors among diabetic subjects attending different diabetes care centers at the capital city and at northern part of Bangladesh.

Methods: Under an analytical cross-sectional design 754 type 2 diabetic subjects (age >20 years) were selected. Sampling was done by selecting each alternative subjects attending the OPD of the Centers. Hypertension was defined as systolic blood pressure (SBP) > 140mmHg or diastolic blood pressure > 90 mmHg or being on treatment for a physician diagnosed hypertension. Obesity was defined as BMI > 27.5kg/m2 or waist circumference > 90 cm for men and > 80 cm for women. A patient was considered to have dyslipidemia in the presence of at least one of the following: high serum total cholesterol (>200mg/dl), high LDL-C (>100mg/dl), low HDL-C (<40mg/dl in men or < 50mg/dl in women) and high triglyceride level (>150mg/dl).

Results: Of the respondents 44% were male and 56% were females. The mean (±SD) age was 49 (±11.3) years, monthly income was US$ 398 (±375) and 66% lived in urban areas. Mean BMI was 25.4±(3.7) Kg/m2. Mean fasting serum glucose was 8.9(±3.8) mmol/l, SBP was 123(±15.4) mmHg and DBP was 79(±7.4) mmHg. The proportion of hypertension, overweight & obesity, waist circumference, dyslipidemia, physical inactivity, betel quid consumption and current smoking was 26%, 74.7%, 77.2%, 52.9%, 18.2%, 28.1% and 10.3% respectively. Among the 402 participants for whom all measurements were available, 1% had at least one of the six risk factors (hypertension, overweight & obesity, waist circumference, dyslipidemia, smoking and physical inactivity). Only 5% had two risk factors while 20% had 3 and 25% had 4 risk factors. On logistic regression no predictors were found to be associated with hypertension. Fasting blood glucose and waist circumference were more while semi urban diabetics were less likely to be obese (OR =2.1, 17.7 and 0.3 respectively). Male gender was predictors of dyslipidemia (OR=6.7) and waist circumference (OR=14.55).

Conclusion: Overweight & obesity, waist circumference and dyslipidemia are common while current smoking is uncommon among diabetic subjects. Fasting blood glucose, waist circumference and habitat are predictors of obesity. Diabetic males are more likely to develop central obesity and dyslipidemia. Focused attention is needed for screening and management of these risk factors.

Abstract #259

Abstract #260

TYPE 1 DIABETES IN A NIGERIAN FAMILY- A CASE REPORT OF OCCURRENCE IN THREE OUT OF FOUR SIBLINGS

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Case Presentation: Introduction

Majority of type 1 diabetes is an autoimmune disease (type 1A) characterized by the destruction of insulin-producing beta-cells in the pancreas. The lifetime risk in siblings of type 1 diabetic probands in Nigeria is rare. It is extremely rare for type 1 diabetes to develop in three or four siblings within a family. Here we report a Nigerian family
ABSTRACTS – Diabetes Mellitus/Prediabetes

in which type 1 diabetes occurred in three siblings among four siblings in which neither the father nor the mother has diabetes. Remarkably, all the three siblings were positive for anti-islet cell antibodies, GAD and IA-A2.

Patients History
There were four siblings (3 males & 1 female) born to a couple without diagnosis of diabetes. The eldest child (male) was diagnosed of diabetes at the age of 15, the third child (female) at the age of 11 and the fourth child (male) diagnosed at the age of 9. All of them had markedly reduced serum C-peptide levels with high levels of GAD and IA-A2 antibodies. We could not perform genetic analysis of HLA-DR, DQ and CTLA4 in the siblings as well as the parents; hence haplotypes could not be characterized.

Conclusion: Although the occurrence of T1DM in proband siblings is uncommon, screening for diabetes among siblings should be encouraged.

Abstract #261

TO STUDY THE PREVALENCE OF COMORBID DEPRESSION AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS IN BANGLADESH

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Objective: Diabetes Mellitus (DM) is the most prevalent, non-communicable and chronic disease. Bangladesh is in the world’s top 10 in terms of highest number of people with DM. Depression is an important global public health problem. Coexistence of Diabetes and depression is associated with poor symptom control, increased suffering, decreased quality of life. The aim of this study was to determine the prevalence of comorbid depression among patients with type 2 diabetes mellitus in Bangladesh.

Methods: This cross-sectional study was conducted at outpatient private practice chamber of AL Kamy Hospital, Feni, Bangladesh. The study was carried out over a period of three months (1st July, 2016 to 30th September, 2016). Diabetic patients visiting the hospital between the ages of 40-80 years were included in the study. Participants were assessed for depression by Bangla translated version of Patient Health Questionnaire-9 (PHQ-9) and demographic, social, clinical variables also assessed after obtaining informed written consent.

Results: A total of 100 participants were included in this study. 59% were males. Mean age of the respondent was 51.21 ± 14.63 years. The prevalence of depression among type 2 Diabetic patients in this study was 14 %. Female patients are prone to develop depression (mean score 9.67 ) comparing with male patients (mean score 4.38). This study also showed that there is a positive correlation between duration of diabetes and depression score. Patients on insulin with or without oral hypoglycaemic agents (OHA) are prone to develop depression in comparison with patients on OHA only. Patients with higher level of education were more likely to develop depression (OR 4.46, 95% CI: 1.19 - 7.48). Those with complications of Diabetes were more likely to have depression compared to those without complication (OR 2.61, 95% CI : 1.06 - 5.91).

Discussion: The relationship between depression and diabetes has been argued to be essentially bi-directional. The prevalence of depression in type 2 diabetics in this study was 14%. Engum et al. conducted a population study find the prevalence 19.0%. In this study female patients are prone to develop depression similar to study conducted by Katon et al. in USA. This study showed a positive relation between duration of diabetes and depression that is consistent a study conducted by Khizran et al. in Pakistan at 2015.

Conclusion: Depression is significantly associated with diabetes from incidence to mortality. It may thus be recommended that all patients with diabetes should be screened for depression and treat depressive symptoms if present.

Abstract #262

PREVALENCE OF GLYCAEMIC CONTROL DURING FOLLOW UP IN MEXICAN DIABETIC PATIENTS

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Objective: To evaluate how frequent diabetic population in our city fulfills the criteria of glucose control according to American Diabetes Association criteria and how frequent they stay into the glycemic goal during their follow up.

Methods: From our database of patients attending our laboratory we selected results of diabetic patients with at least 3 years of follow up and ≥ 3 determinations of HbA1c each year. With this results we studied how frequently they meet the criteria of glucose control (HbA1c < 7%), and how frequently they have this result during 3 years period (group 1: no determination < 7%, group 2: at least 1 determination < 7% to 49% of determinations < 7%, group 3: 50% to 99% of determinations < 7% and group
4: 100% of determinations < 7%). We also compare age, fasting glucose, creatinine and number of determinations between groups.

**Results:** 257 patients fulfill the inclusion criteria (54.9% women, mean follow up 1240±241 days, mean HbA1c determinations per patient 14± 5 (95%CI 13 to 14). Frequency of groups: 1: 20.2%, 2: 41.2%, 3: 30.4% and 4: 8.2%. Mean percent of HbA1c determination <7% in the total group was 41% (95% CI 36 to 45%) We found a statistically significant difference in HbA1c and glucose levels between groups but not in number of determinations, age and creatinine level. No difference was found between basal and final HbA1c determination (7.87±2 vs 7.64±2).

**Conclusion:** We describe for the first time which patterns of glycemic control could be identify in Mexican diabetic patients and the very low frequency of patients that reach the Hba1c goal and stay in that level during time.

**Abstract #263**

**EVALUATION AND UTILITY OF A NOVEL GLUCOSE MONITORING SYSTEM IN INDIAN ADULTS WITH TYPE 2 DIABETES MELLITUS**

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**Objective:** Glycemic variability is a strong predictor of hypoglycemia and is also correlated with poor glycemic control is probably the most compelling reason to identify and to work to minimize glycemic variability. Flash glucose monitoring is a novel glucose sensing technique that estimates interstitial glucose levels for up to 14 days and does not require any calibration.

**Methods:** The FreeStyle Libre Pro(TM) sensor was utilised in 112 patients for 14 days. We did a real-world evaluation from the registry database from July 2015 till October 2016. Wilcoxon signed rank test and Mann-Whitney test through the GraphPad Prism 7 were applied for the statistical analysis. 26 patients were excluded from the analysis as the data was non-evaluable.

**Results:** The glycemic variability data was evaluated in 86 patients. Mean duration of diabetes was 13.66 years (SD 9.26 ±1.12, min 0, max 50 yrs; 95% CI 11.41-15.9, p < 0.0001). Mean age was 57.61 years (SD 9.26 ±1.12, min 0, max 50 yrs; 95% CI 11.41-15.9, p<0.0001). The HbA1c reductions before (mean 8.5 ± 2.2, Min 31, max 81 yrs; 95% CI 54.95-60.27, p < 0.0001). The HbA1c reductions before (mean 8.5 ± 2.2, Min 31, max 81 yrs; 95% CI 54.95-60.27, p < 0.0001). The HbA1c reductions before (mean 8.5 ± 2.2, Min 31, max 81 yrs; 95% CI 54.95-60.27, p < 0.0001). The HbA1c reductions before (mean 8.5 ± 2.2, Min 31, max 81 yrs; 95% CI 54.95-60.27, p < 0.0001). The comparative reductions in HbA1c in patient group <60 & > 60 yrs did not achieve statistical significance (p=0.7898, NS). The modifications in the therapeutics included the change in the timing of the drug administration, drug choice, dose and diet modifications exclusively in 25, 39,51, 71 patients respectively. 16 patients had all four components of change. High glycemic load was commonly observed even after 2 hours of the first meal which reflects the typical Indian pattern of glycemic overload.

**Discussion:** FreeStyle Libre Pro(TM) is a unique tool to achieve a better glycemic control with more accurate real time assessment of the glycemic variability which has enabled a better therapeutic decision making. The appropriate intervention to modulate the post breakfast glycemic spikes has been an important contributor for the effective management of the glycemic spikes.

**Conclusion:** The utility of the novel FreeStyle Libre Pro(TM) translates into a physician led and patient enabled empowerment tool which helps physicians customise the therapy and empowers patients through the visual snapshots to sensitively adapt to the prescribed regimen.

**Abstract #264**

**THE PREVALENCE OF DIABETIC NEUROPATHY, PAINFUL DIABETIC NEUROPATHY AND THE AT RISK DIABETIC FOOT IN QATAR**

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**Objective:** To define the prevalence of Diabetic Peripheral Neuropathy (DPN), painful diabetic neuropathy (PDN) and the at risk diabetic foot in 2 out of the 3 National Diabetes Centres in Qatar.

**Methods:** 712 people with Type-1 & Type-2 diabetes recruited from Alwakra Hospital and Hamad General Hospital underwent assessment for DPN & PDN using the Neurothesiometer and the DN4 questionnaire, respectively.

**Results:** The average age, duration of diabetes, systolic BP, BMI, Hba1c were: 52.2 ± 0.49, 10.8 ± 0.32 years, 132.6 ± 1.26 mmHg, 32.2 ± 0.52 kg/m2 and 8.3 ± 0.11 %, respectively. The prevalence of DPN and PDN were 31% and 36%, respectively. However, 4 in 5 adults with DPN and 9 in 10 adults with PDN were undiagnosed. One in ten adults with diabetes were at high risk for diabetic foot ulceration (VPT >25) and had not been diagnosed. Patients with DPN were significantly older (57.1 ± 0.73 v 49.8 ± 0.62, p<0.0001), had a longer duration of diabetes (14.34 ±
0.57 ± 0.36, p<0.0001), higher systolic blood pressure (139.8 ± 2.25 v 129.2 ± 1.46, p=0.001) and higher creatinine (118.6 ± 16.76 v 70.9 ± 2, p=0.007), but no difference in HbA1c (8.6 ± 0.21 v 8.2 ± 0.13), vitamin D (23.7 ± 1.7 v 23.3 ± 0.9) or B12 (344.7 ± 39.17 v 322 ± 21.3).

**Conclusion:** The overall prevalence of DPN, PDN and those at risk of foot ulceration in Qatar are comparable to that reported in Europe and the US. However, an alarmingly low proportion of patients are diagnosed and treated for DPN and PDN. There is a need for a systematic screening for DPN and PDN in Qatar. Age, duration of diabetes, blood pressure and high creatinine are risk factors for DPN.

**Abstract #265**

**NECK CIRCUMFERENCE TO HEIGHT RATIO IS A RELIABLE PREDICTOR OF LIVER STIFFNESS AND NON-ALCOHOLIC FATTY LIVER DISEASE IN INDIANS WITH PREDIABETES**

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**Objective:** Non-alcoholic fatty liver disease (NAFLD) and dysglycemia are public health challenges in India. There is urgent need for anthropometric surrogates for NAFLD screening. This study evaluated neck circumference (NC) and neck-height ratio (NHtR) as predictors of liver stiffness measure (LSM) in individuals with prediabetes (IPD), as compared to body mass index (BMI), waist circumference and waist-hip ratio (WHR).

**Methods:** 188 IPD from 1130 screened individuals underwent anthropometry, ultrasonography, Fibroscan® for liver stiffness (LSM), dyslipidemia, insulin resistance (IR) and fetuin-A assessment.

**Results:** Hypertension, hypertriglyceridemia, low HDL-C, metabolic syndrome (MetS), NAFLD and significant liver stiffness (SLS) (LSM>8.5kPa) were observed in 53.7%, 31.4%, 71.3%, 73.9%, 24.5% and 11.2% IPD respectively. IPD with NAFLD had significantly higher BMI, NC, NHtR, glycated haemoglobin, triglycerides, fatty liver index (FLI) and LSM. IPD in highest NHtR quartile had significantly higher BMI, hypertension, MetS, fasting glucose, glycated hemoglobin, HOMA-IR, NAFLD, LSM, SLS, and lower HDL-C. Stepwise forward linear regression revealed that NHtR, FLI and LDL-C were best predictors of LSM, at baseline (Model-1), after adjusting for age and sex (Model-2) and after adjusting model-2 plus systolic and diastolic blood pressure (Model-3). Fetuin-A was significant predictor of LSM (Model-2).

**Discussion:** A quarter of IPD in this study had USG evidence of NAFLD. Nearly half of IPD with NAFLD had significant liver stiffness in our study. In a Turkish study, prediabetes occurrence in NAFLD was associated with more severe portal inflammation and liver fibrosis. We showed that IPD in highest NHtR quartile had significantly worse glycemia, dyslipidemia, IR and elevated fetuin-A. Fetuin-A has been linked to systemic inflammation, adverse glycemic outcomes in prediabetes, NAFLD and advanced hepatic fibrosis. Our study also demonstrated fetuin-A to be a predictor of liver stiffness in prediabetes. In our study, FLI and LSM were significantly increased in patients in highest NHtR quartile, highlighting more severe NAFLD in them. In a cohort of 967 IPD, FLI>60 was associated with increased progression to T2DM. In our study, fetuin-A had a positive correlation with FLI, in accordance with a Chinese study.

**Conclusion:** NHtR is a good screening tool for community screening of NAFLD and liver stiffness in IPD.

**Abstract #266**

**A THREE-YEAR REVIEW OF DIABETIC KETOACIDOSIS IN PREGNANCY – CAUSES AND OUTCOMES**

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**Objective:** The incidence of diabetic ketoacidosis in pregnancy (DKP) is 0.5%-8.9% and the associated fetal mortality ranges from 9% to 36%. There are no studies to assess DKP performed after the approval of insulin analogues for use in diabetic pregnancy. The aims of this study were to evaluate the incidence, causes and outcomes of DKP. Also, to identify factors those were associated with favorable fetal and maternal outcomes.

**Methods:** A retrospective chart review of 20 DKP tertiary center admissions, out of 3679 diabetic pregnancies delivered between January 2012 and May 2015 was conducted. Maternal baseline characteristics, DKP causes and treatment, fetal and maternal outcomes and neonatal outcomes were recorded. Statistical analysis was carried out using the software SPSS 17.0. Two groups were compared,
group A, with successful DKP management and group B, where the baby was delivered or was an intrauterine fetal death (IUFD) during treatment. The chi square test was used to compare the 2 groups in relation to the possible risk factors or significant differences in presentation.

**Results:** Thirteen cases had type 1 diabetes and 6 had type 2 diabetes, including 2 patients with undiagnosed diabetes before DKP presentation. The commonest precipitating factors were vomiting (55%) and insulin non-compliance (45%). Plasma glucose was < 140 mg/dl in 20% of the patients. There was 1 fetal mortality (5%) while there was no maternal death. A comparison of the successfully treated 14 admissions (group A) versus 6 admissions with IUFD or emergency delivery (group B), showed significant difference only in the mean gestational age 21.8 ± 11.0 and 33.7 ± 4.6 weeks (P= 0.005).

**Discussion:** The incidence of DKP was 0.5%. Both types of diabetes were complicated by DKP. The fetal mortality was 5%. Our incidence of DKP was similar to the lowest reported in the literature while the fetal mortality was better which indicates an improvement of medical care with prompt diagnosis and management of DKP. Euglycemic DKP is not uncommon during pregnancy. No clinically modifiable significant differences between DKP patients with favorable versus poor outcome. This may be related to the small sample size, which was a relative limitation of our study. This study had the largest number of DKP patients reported in the literature who were managed only at one center.

**Conclusion:** DKP associated fetal mortality was better than previous reports. Antenatal diabetes screening, patient education and adherence to insulin regimen may prevent many cases. Physicians dealing with diabetic pregnancies should be aware of euglycemic DKP.

**Abstract #267**

**IMPACT OF SOCIOECONOMIC STATUS ON DIABETES RELATED KNOWLEDGE AMONGST DIABETIC PATIENTS IN A NIGERIAN TEACHING HOSPITAL.**

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**Objective:** Diabetes mellitus is a chronic metabolic disorder with increasing prevalence globally. Diabetes knowledge impacts positively on glycaemic control. We assessed the socioeconomic status in conjunction with awareness and knowledge of diabetes in patients attending a teaching hospital in South west Nigeria.

**Methods:** Cross sectional questionnaire based study at Lagos State University teaching hospital. 153 diabetic patients who consented. Age less than 18 and GDM excluded. 3 part questionnaire incorporating bio data, diabetes medical history, modified Diabetes Knowledge Test of the Michigan Diabetes Research Training Centre (MDRTC) and, physical examination.

**Results:** One hundred and fifty three subjects, 70% females and 30 % males. Mean age (SD) 62(12.08). Sixty-two percent had up to secondary school education. 10% were illiterate. 28% had university education. 52% earned N20, 000 ($62) or less per month. Average cost of medication per month is N10, 000 ($31). Mean duration of DM (SD) is 9.54(7.53) years. 80% on OADs. 20% on insulin either alone or in combination with OADs. 9% belong to DM association. 9% visit DM related website. University education is positively associated with visiting DM related sites p= 0.005 and self monitoring of blood glucose p=0.002. 70% receive diabetes education. Nurse delivered education in 47% of these cases. 64% do self monitoring of blood glucose. 87% knew what diabetes diet is. 51% had abnormal short term glycemic control based on ADA targets. Level of education positively associated with knowledge of significance of HbA1c, and treatment of low blood glucose p value 0.001, and 0.000 respectively. 70% of those on insulin did not have knowledge of intervention for hypoglycaemia. 86% had diabetes related complication.

**Discussion:** Majority of patients are in the low socioeconomic group, which may create challenge of adherence since healthcare in Nigeria mainly funded out of pocket by the patients, may also be responsible for abysmal indices of DM management. Nurses are more actively involved at delivering diabetes education which may account for the appreciable number who do SMBG. There appears to be limited knowledge of insulin amongst those on insulin therapy. The higher the educational status the better the knowledge exhibited about diabetes and components of management.

**Conclusion:** Diabetes awareness is still poor among our patients. There is need for targeted group education. Diabetes patients may need to be divided according to educational status during education sessions to ensure adequate assimilation of information.
Abstract #268

COMPARISON OF NEONATAL OUTCOME IN WOMEN WITH GESTATIONAL DIABETES ON DIFFERENT PHARMACOLOGICAL AGENTS DELIVERED AT TERM

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Objective: Though many studies have looked at the neonatal outcomes in patients with gestational diabetes on different medications, there is no consensus on the preferred drug for initiation of therapy. We aim to compare the neonatal outcome in a cohort of patients attending our service, to determine if one modality is superior to the other.

Methods: This study is a prospective observational study from 1-07-2015 to 31-04-2016. The data of all gestational diabetic patients referred to the Joint Diabetic Clinic, in a local secondary Hospital, who required pharmacological intervention were entered into an excel spreadsheet. This included their antenatal, intrapartum and postnatal details. P values calculated with Student’s t-test. Statistical significance if p< 0.05.

Results: The total number of patients studied was 107. There were 58 patients (54%) who were treated with Metformin only, their BMI at booking was 30Kg/m2, average HbA1c 5.69%. The average birth weight of the neonates of this group was 3287.78gm and there were 9 (15.51%) Neonatal ICU admissions. 17 patients were commenced on insulin, thier HbA1c was 5.78% and their booking BMI was 32. The average birth weight in this subgroup was 3409.24gm with 2 (11.76%) NICU admissions. 32 (29.90%) of our patients required Metformin and insulin. Their average weight at booking was 35, and thier HbA1c was 5.8%. In this subgroup, the average birth weight was 3494.56gm with 5(15.62%) requiring NICU admission. The least birth weight was observed in the subgroup with Metformin alone (54% of our patients), p<0.4. The subgroups with insulin showed a higher neonatal birth weight. The least NICU admissions were in the insulin only group.

Discussion: The least birth weight was observed in the subgroup with Metformin alone (54% of our patients), with the subgroups with insulin showed a higher neonatal birth weight. However, the least NICU admissions were seen in the insulin only group.

Conclusion: Whether the increase in birth weight seen in patients on insulin, is indicative of uncontrolled blood sugars or due to the direct effect of insulin as shown in some studies, requires further evaluation. Further analysis of the ongoing cohort is needed before we can recommend any one mode of treatment as the preferred choice in our setting.

Abstract #269

HEALTH-RELATED QUALITY OF LIFE USING EQ-5D IN PATIENTS WITH TYPE 2 DIABETES

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BIRDEM

Objective: Diabetes management requires a fundamental change in the patient's lifestyle and the one of the important outcome criteria in this view is quality of life. The aim of the study was to assess the health-related quality of life (HRQoL) and to examine the factors associated with HRQoL.

Methods: An analytical cross-sectional study was conducted among 500 type 2 diabetics (age>25 years and diabetes duration >1 year). Data were collected by a pre-tested, interviewer-administered questionnaire. HRQoL was assessed by an adapted and validated Bangla version of the EQ-5D (Euroqol Group, 2009) questionnaire.

Results: Among the patients 50.2% were females; mean ±SD age was 54.2(±11.2) years. Most of the patients (92.2%) belonged to middle to upper-middle age group;41% had completed high school and 50.8% were from lower-middle income family. Mean BMI was 26.1(±6.7)kg/m2 and about 78.8% were overweight or obese according to Asian BMI cut-off value. About 49.6% patients had no problem in mobility,71.8% in self-care and 52.4% in usual activities though 57.8% had some problem in pain/discomfort and 59.4% in anxiety/depression. The mean ±SD EQ VAS score was 65.4(±18.3). The EQ VAS score of the female patients was significantly lower than the male (60.4±17.6 vs 70.5±17.5, p<0.0001).

In binary logistic regression, age (OR 1.05; 95% CI 1.02 to 1.07), gender (OR 4.87; 95% CI 1.48 to 15.99), taking of OHA & insulin (OR 1.62; 95% CI 1.02 to 2.59) and lower-middle income group (OR 2.51; 95% CI 1.08 to 5.85) were significantly associated with mobility. Self-care was significantly related with age (OR 1.03; 95% CI 1.01 to 1.06), family history of DM (OR 0.43; 95% CI 0.26 to 0.73) and duration of DM (OR 1.05; 95% CI 1.01 to 1.08). Gender (OR 4.79; 95% CI 1.45 to 15.78), family history of DM (OR 0.46; 95% CI 0.28 to 0.74) and lower-middle income group (OR 2.67; 95% CI 1.13 to 6.29) had significant association with usual activities. Pain/discomfort was significantly associated with age (OR 1.05; 95% CI 1.02 to 1.07), taking of OHA & insulin (OR 1.75; 95% CI 1.04 to 2.93), lower-middle income (OR 2.89; 95% CI 1.25 to 6.64) and upper-middle income
group (OR 2.54; 95% CI 1.12 to 5.79). Higher education (OR 0.24; 95% CI 0.08 to 0.68) was significantly related to anxiety/depression.

**Conclusion:** Around half of the patients have no problem in mobility, usual activities and majority in self-care although more than half have some problem in pain/discomfort and anxiety/depression. Age, female gender, taking of medication, lower-middle & upper-middle income group, higher education, and family history of DM and duration of DM are important factors associated with HRQoL in patient with type 2 diabetes.

**Abstract #270**

**DIABETIC RETINOPATHY: RISK FACTORS AND ASSOCIATIONS**

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**Objective:** To find out risk factors for patients with diabetic retinopathy and to find out the relation between diabetic retinopathy and various associated factors.

**Methods:** This cross-sectional study investigated 50 diabetic patients with visual disturbance due to retinopathy of both sexes irrespective of duration of diabetes and age of onset of diabetes attending outpatient department of Endocrinology and department of Ophthalmology, Bangabandhu Sheikh Mujib Medical University.

**Results:** Age distribution of studied subjects, minimum age was 30 years and maximum was 80 years. Maximum 26 (52%) patients were above 60 years old. Retinopathy developed according to duration of diabetes was less than 10 years in 06(12%) patients, 10-15 years in 20(40%) patients and above 15 years was in 24 (48%) patients. Out of 50 patients NPDR 35(70%), PDR 15(30%). Distribution of best corrected visual acuity large number 18(36%) patients are 6/18 (36%), 10(20%) are 6/12, 10(20%) are 6/24. Less number 2 patients in each 4% BCV A are 6/9, <6/60. BCVA 6/36 and 6/60 4 patients in each 8%. Blood pressure 40% normotansive and 60% hypertensive. Biochemical parameter of these group serum creatinine normal 28(56%), elevated 22(44%) patients, serum total cholesterol normal 20(40%), elevated 30(60%), serum triglyceride normal 22(40%), elevated 28(56%), urinary albumin excretion normal 24(48%), elevated 26(52%) cases. Distribution of diabetic neuropathy and cardiovascular abnormality are autonomic neuropathy 12(24%), polyneuropathy 18(36%), elevated blood pressure 20(40%), abnormal ECG reading 18(36%) cases.

**Discussion:** In this study it was found that presence of retinopathy increases with increasing age. The lower the age of patient the lower the rate of retinopathy. It was evident that retinopathy increase with the increasing duration of diabetes and was more prevalent when diabetic status was uncontrolled. A significant percentage of patients (40%) were to have elevated blood pressure. Elevated serum total cholesterol and triglyceride was also observed in 60% and 56% cases of retinopathy respectively. Diabetic autonomic neuropathy was observed in 24% cases and polyneuropathy was observed in 36% cases. Cardiovascular abnormalities evidenced as abnormal ECG (electro-cardio graphic) reading observed in 36% cases and raised blood pressure was observed in 40% cases. In the current study 44% patients with retinopathy were suffering from diabetic nephropathy.

**Conclusion:** It is concluded that diabetic retinopathy has association with diabetic neuropathy diabetic nephropathy and cardiac abnormalities. Older age, long duration of diabetes, hypertension and dyslipidemia are some important risk factors for the development of diabetic retinopathy.

**Abstract #271**

**RELATIONSHIP BETWEEN BODY MASS INDEX AND GLYCAEMIC INDICES IN PREGNANCY**

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**Objective:** The increase in overweight and obesity prevalence observed in low- and middle-income countries such as Nigeria has been recognised as an important public health problem. Anthropometric indices such as pre-pregnancy weight and body mass index (BMI) has been shown to have some relationship with glycaemia in pregnancy. Increase in maternal pre-pregnancy body mass index (BMI) is associated with higher glycaemic indices-fasting blood glucose and post prandial levels with subsequent development of Gestational Diabetes Mellitus (GDM) . Diabetes complicating pregnancy is associated with adverse maternal and perinatal outcomes.

The aim of this study was to determine the relationship between pre-pregnancy BMI with glycaemic indices in pregnancy using the new World Health Organization Criteria(W.H.O)

**Methods:** A prospective study in which consenting antenatal attendees underwent an oral glucose tolerance test(OGTT) with a 75gram glucose load using the new W.H.O obtaining fasting of (5.1-6.9mmol/L) , 1hr (≥10.0mmol/L) and 2hr (8.5-11.0mmol/L) glucose values and associated body weight and BMI measured. Those with pregestational diabetes mellitus, those on drugs that affect glucose metabolism like steroids and those with multiple
pregnancies were excluded from the study. Pearson’s correlation was done to determine the relationship between OGTT indices and anthropometric indices

**Results:** There was a statistically significant positive correlation between OGTT indices and BMI implying that the higher the BMI, the higher the OGTT indices. The correlation coefficient (R) between BMI and fasting plasma glucose was R= 0.358 with a p value < 0.001 , one hour post OGTT was R=0.272 with a p value of 0.002 and two hours post OGTT R= 0.291 and p value of 0.001. These will be represented in tables and scatterplot.

**Discussion:** The strongest association was between increasing pre-pregnancy BMI and fasting blood glucose thus underscoring the new WHO criteria with FPG of 5.1mmol/l. Pregnant women with higher pre-pregnancy BMI have higher glycemic indices with the risk of developing GDM.

**Conclusion:** There was a strong relationship between increasing pre-pregnancy BMI and the three key glycaemic indices viz: FBG, 1HR, 2HR post OGTT, especially with the FPG in this Nigerian study. This shows that the increase in the pre-pregnancy BMI is associated with higher glycaemic indices and thus risk of developing GDM.

**Abstract #272**

**MANAGEMENT OF DIABETIC PERIPHERAL NEUROPATHY (DPN) USING LOW FREQUENCY PULSED ELECTRO MAGNETIC FIELD (LF - PEMF)**

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

**Methods:** A comparative observational study of 60 patients, male and female (1:1) aged 60 to 85 years. Enrollment criteria - known diabetics, HbA1c 7 to 9 and DPN of 1-5 years. Patients were randomized into 2 treatment groups G1 and G2. The study period was 4 weeks (w) with results assessed at baseline and bi-weekly follow-ups using diabetic neuropathy symptom (DNS) score.

G1: 30 patients with an established DPN were treated with PEMF therapy - frequency of 10Hz, thru two emitters of 20 mTesla and 6 mTesla, keeping north polarity was towards the body. A total of 15 sitting of 20 (10 + 10) minutes - one per day.

G2: 30 patients with an established DPN were continued on oral symptomatic treatment options like - amitriptyline, duloxetine, gabapentin, pregabalin and tramadol.

Patients in both the groups were on Vitamin B 12 + Alpha Liponic Acid which were continued.

**Case Presentation:** In G1 application of LF - PEMF therapy significantly facilitated the regression of the main clinical symptoms of DPN. Patient scores were more differentiated on DNS score. Complete relief in the symptoms of DPN was achieved in 4 patients at 2w which sustained at 4 patients at 4w. DNS score of 1 was achieved in 10 patients. DNS score of 2 was achieved in 18 patients at 2w which was sustained at 4w. Overall 32 patients had a relief of main clinical symptoms on the DNS score.

In G2 there was a mild regression of the main clinical symptoms of DPN. Complete relief in the symptoms of DPN on DNS score was achieved in 0 patients at 2w and in 1 patient at 4w. DNS score of 1 was achieved in 2 patients at 2w which increased to 3 patients at 4w. DNS score of 2 was achieved in 7 patients at 2w which was increased to 11 patients at 4w. Overall 14 patients had a relief of main clinical symptoms on the DNS score.

**Conclusion:** The present study provides convincing data regarding the effectiveness of LF - PEMF therapy, on patients with DPN symptoms. The usage of oral symptomatic drugs is limited due to the high frequency of adverse events, lack of evidence of long term efficacy and concern about dependence. Considering the benefits and safety, in comparison to oral symptomatic drugs, LF - PEMF can be used as an adjacent in the management of diabetic neuropathy cases. A bigger study is warranted to determine whether DPN can be modulated with LF - PEMF and how it can influence nerve regeneration. Limitations of this study include small sample size, short duration of treatment and non-availability of follow-up data.

Key words: LF – PEMF – low frequency pulsed electro magnetic field, DPN – diabetic polyneuropathy, DNS - diabetic neuropathy symptom, w – weeks.
Abstract #273

GENDER DIFFERENCE IN CARDIOMETABOLIC RISK PROFILE AND OTHER COMPLICATIONS IN TYPE 2 DIABETIC AT THE OBAFEMI AWOLOWO TEACHING HOSPITAL, ILE-IFE.

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Objective: This study determined gender specific differences in cardio-metabolic risk, microvascular and macrovascular complications in patients with type 2 diabetes.

Methods: This cross-sectional descriptive study involved four hundred type 2 diabetes patients, males and females, matched for age and disease duration who were consecutively recruited from the diabetes clinic of OAUTHC, Ile-Ife from May to December 2014. Relevant clinical information and physical examination data were obtained. Venous blood sample was collected for FBG, and 2HPP, HBA1c, total cholesterol, LDL-C, HDL-C, triglycerides and urine sample was collected for albumin. ECG was also done on the entire participant.

Results: Of the 400 patients with type 2 DM, 47.5% were males and 52.5% were females respectively. 85.7% of the females were post-menopausal. The mean age of the study population was 60.6 + 9.93 years. The mean duration of DM was 7.81 + 5.76.

Women had higher prevalence of hypertension and obesity than men p < 0.05. Mean total cholesterol was significantly higher in women p = 0.001 and more men were more likely to achieve LDL treatment goals than women (p < 0.05). More women attained glycaemic goals than men (2HPP and HBA1c) p < 0.05.

There were no gender differences in microvascular and macrovascular complications (p > 0.05) but women were more likely to develop moderate and severe diabetic retinopathy (p= 0.027) while men were more likely to develop the severe form of diabetic neuropathy (defined as > 2 abnormal tests plus symptoms); p = 0.011.

Logistic regression analysis showed that the use of antiplatelet drugs were more likely to be associated with a lower risk of microvascular complication in both men and women while diastolic blood pressure above 80mmHg increased the risks 2 times in men and 3 times in women (p < 0.05). Risk factors associated with macrovascular complications were poor glycaemic control (FBG above 7.2mmol/l and 2HPP above 10mmol/l) in men and total cholesterol above 5.2mmol/l in men and women.

Discussion: Obesity occurred more commonly among female patients compared to their male counterparts. This is similar to the findings of Fasanmade et al in Lagos and Bakari et al in Northern Nigeria and may be due to cultural practices that tend to limit physical exertion by females with resultant sedentary habits, and its attendant complications. There was significantly higher prevalence of hypertension in women.

Conclusion: There are notable gender variations in DM complications. A clearer understanding of the influence of sex differences may provide better clues to achieving optimal care for patients with Diabetes.

Abstract #274

SERUM VITAMIN B12 IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

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Objective: To observe serum vitamin B12 level in newly diagnosed Type 2 DM patients.

Methods: This observational cross-sectional study recruited 50 newly diagnosed cases of T2DM and 50 controls with normal glucose tolerance (NGT); all were Bangladeshi aging 30-45 years. Participants were interviewed and examined for clinical features of peripheral neuropathy. Serum vitamin B12 and HbA1c were measured for all. Serum vitamin B12 ≤200 pg/ml was labeled as deficiency, >200 to ≤300 pg/ml borderline deficiency and >300 pg/ml was labeled as normal. Data were analyzed using computer based SPSS program (version 22.0). P value ≤0.05 was considered significant.

Results: Both mean (492.46±28.82 vs. 346.48±19.65 pg/mL, mean±SEM; p=<0.001) and median (435.50 vs. 334.50 pg/mL) values of serum vitamin B12 were found to be higher in T2DM than those of controls. None of the diabetic subjects were found to be B12 deficient whereas 6 were borderline deficient; these frequencies were 7 and 11 respectively among the controls. There was no statistical difference of B12 level between male and female either in T2DM (473.04±41.59 vs. 511.88±40.39 pg/mL, mean±SEM; p=<0.001) and median (435.50 vs. 334.50 pg/mL) values of serum vitamin B12 were found to be higher in T2DM than those of controls. None of the diabetic subjects were found to be B12 deficient whereas 6 were borderline deficient; these frequencies were 7 and 11 respectively among the controls. There was no statistical difference of B12 level between male and female either in T2DM (473.04±41.59 vs. 511.88±40.39 pg/mL, mean±SEM; p=0.506) or in control group (334.47±19.07 vs. 372.00±46.69 pg/mL, mean±SEM; p=0.465). B12 level was higher (though not significant) in patients with clinically evident peripheral neuropathy (mean±SEM; 523.48±39.39 vs. 441.84±38.76 pg/mL, p=0.172). B12 level showed positive correlation with fasting plasma glucose (FPG, r=0.285, p=0.061) and HbA1c (r=0.287, p=0.092).
Discussion: Patients with DM were found to have decreased serum B12 level in several studies. Metformin has been implicated to be a cause of B12 deficiency in diabetic subjects, but B12 deficiency was found in newly diagnosed T2DM subjects and also in those who were not taking metformin. The present study clearly observed that newly detected T2DM subjects had higher serum vitamin B12 than those of NGT and the numbers of subjects with subnormal B12 level (deficient and borderline deficient) were higher in NGT group. Clinically B12 deficiency may mimic diabetic peripheral neuropathy (DPN) and B12 supplementation has shown to improve symptoms of DPN. It was interesting to observe that our study found higher levels of vitamin B12 in diabetic subjects with clinically suspected peripheral neuropathy than those without neuropathy. Some authors found obese subjects with or without DM to have lower serum B12. Our study found no significant correlation of B12 level with BMI either in T2DM or in controls though in both the cases the trend was inversely related.

Conclusion: Vitamin B12 is found sufficient in newly diagnosed Bangladeshi T2DM patients.

Abstract #275

CLINICAL PREDICTORS OF PROGRESSION TO INSULIN USE AMONG CHINESE PATIENTS WITH TYPE 2 DIABETES- THE HONG KONG DIABETES REGISTRY

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Objective: Factors that affect disease progression and glycaemic deterioration in type 2 diabetes are poorly understood, but may facilitate precision medicine in diabetes. In this study, we aim to identify factors predicting earlier need for insulin treatment among Chinese patients with type 2 diabetes (T2D).

Methods: We included 10,129 consecutive Chinese patients with diabetes who were enrolled into our registry between 1995-2007. We excluded patients with type 1 diabetes, those already on insulin treatment at baseline, or patients who required insulin within 1 year of follow-up. We identified all subjects who progressed to continuous insulin treatment during the follow-up period. We calculated time-to-insulin use for each patient. We performed Cox regression analysis to identify clinical predictors of progression to insulin use.

Results: Among 7,570 patients with T2D in our registry not requiring insulin at baseline, 2882 (38%) progressed to insulin treatment during a median follow-up period of 9.3 years (IQR 5.4-13.6). Subjects who progressed to insulin use during follow-up period were younger, had earlier onset of diabetes, longer duration of diabetes at time of recruitment and shorter duration of follow-up. Incident insulin-users had higher HbA1c, TG, LDL-cholesterol and lower HDL cholesterol at baseline, and were more likely to have sensory neuropathy, retinopathy, albuminuria, or CKD at baseline. On multivariate analysis, independent predictors of progression to insulin use included: age at diagnosis (HR 0.97 [CI 0.97-0.98]), smoking status, higher baseline HbA1c (HR 1.3 [1.30-1.35]), lower eGFR, presence of diabetic retinopathy (HR 1.68 [1.54-1.83]) and low BMI (<18.5kg/m2) (HR 1.71 [1.36-2.17]).

Discussion: In this large cohort of patients with T2D representative of real-life clinical practice, a significant proportion progressed to insulin use during follow-up. In addition to poor glycaemic control, young-onset diabetes was identified as an important predictor for disease progression to insulin use. Low BMI should alert clinicians regarding the earlier need for insulin. Limitations of the current study include clinical inertia and delay in commencement of insulin treatment. Additional analyses to define glycaemic deterioration and need for insulin using serial A1c and prescription data on oral medications are currently underway. Genome-wide association analyses to identify genetic factors associated with need for insulin is also being conducted.

Conclusion: Asian T2D patients with low baseline BMI, higher baseline HbA1c, younger age of diagnosis and impaired renal function are at increased risk of progression to insulin use.
Abstract #276

DISCORDANCE IN ENERGY EXPENDITURE AND GLUCOREGULATION BETWEEN NORMOGLYCEMIC SUBJECTS WITH AND WITHOUT PARENTAL DIABETES

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UTHSC

Objective: Resting energy expenditure (REE) plays a role in regulating body weight. This is important in obesity, insulin resistance (IR) and type 2 diabetes (T2DM). Available evidence indicates that REE may be an inherited trait and subjects with dysglycemia have higher REE than euglycemic individuals. This may represent an early abnormality in the pathogenesis of T2DM. Furthermore, T2DM exhibits remarkable heredity; therefore, we sought to determine the effect of parental diabetes on REE and glucoregulation in normoglycemic subjects.

Methods: A total of 176 subjects with (n=88) or without (n=88) parental T2DM were matched for age, gender, race, BMI, weight and waist circumference. Subjects underwent 75g OGTT after an overnight fast with sampling for glucose and Insulin at 0, 30 and 120 minutes. Insulin resistance (IR) and β-cell function were estimated using Homeostatic Model Assessment (HOMA-IR and HOMA-B respectively) and Insulinogenic and Disposition Indices were derived. REE was determined by indirect calorimetry using Cardio Coach 2 equipment and Lean body mass (LBM) using DEXA. Statistical analysis was done by student t- test and ANOVA.

Results: The mean REE (Kcal/Kg LBM) was lower in subjects with parental diabetes vs those without (31.04±6.85 vs 29.01±5.5; p=0.0312), and in African-Americans (AA) compared to European Americans (EA). In a 4-way comparison, AA with parental T2DM had the lowest REE/LBM (ANOV A, P< 0.0001).

Compared to subjects without parental diabetes, offspring of diabetic parents showed evidence of a lower REE, diminished insulin action and secretion. These metabolic alterations increase the risks for obesity, IR and T2DM.

Conclusion: Compared to subjects without parental history, normoglycemic offspring of T2DM parents showed evidence of a lower REE, diminished insulin action and secretion. These metabolic alterations increase the risks for obesity, IR and T2DM.

Abstract #277

THE BENEFITS OF THE I-PORT SYSTEM USAGE IN AN INSULIN DEPENDENT PATIENTS

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Objective: Insulin dependent diabetes mellitus (IDDM) had low adherence to insulin injection that result in poor glycemic control. I-port advance system is one of the newly advanced injection method allowing patient to take the multiple daily subcutaneous injections for three days without having to puncture skin for each insulin dose. Our aim is to evaluate the patient’s satisfaction, adherence, and outcome while using I-port advance and its impact on glycemic control.

Methods: A prospective study was conducted in IDDM. Baseline characteristics and Diabetes Treatment Satisfaction Questionnaire status (DTSQs) were collected at baseline and at the end of the follow up. All patients were trained to use the I-port advance injection system. We divided them into two groups, regular users of the I-port whom used it >3 months and irregular users whom used it <3 months. Both groups were asked about the local complications during the I-port use.

Results: A total of 55 patients, with 92.7% were T1D, mean age of 14.96+8.95 and 92.7% were on insulin pen. The mean duration of DM was 4.6+4.3 yrs, 45.5% reports non-compliance to insulin with 58.3% reporting forgetting to inject while fear of needle accounted for 9.1%, the mean HbA1c was 9.54+1.8%, and 59.3% had DM related hospitalization in the previous 3 months. 36.4% of the patients’ reports self-insulin inject while 41.8% report insulin inject by parent.

27 patients were regular users and 28 patients irregular user. At baseline and compared to the regular users, irregular users has shorter duration of I-port usage 0.6+0.35 vs 7.1+3.6m (p <0.001), have longer duration of DM 5.1 vs 4 yrs, were less likely to report non-compliance to insulin 40.7% vs 50% (p 0.338), has lower mean HbA1c of 9.2 vs 10.02 (p 0.056), were less likely to reports fear of needle 3.6% vs 14.8% (p 0.328), and more likely to self-inject insulin 48.1% vs 25.9% (p 0.038). There was no statistical difference in the mean (DTSQs) score or the mean glycemic control score between groups.

In regular users group only and compared to baseline, at the end of the follow up the mean HbA1c improved to
9.29+2.1 compared to 10.02+1.9 (p 0.187), DM related hospitalization in the previous 3 months reduced to 7.4% compared to 59.3% (p <0.001), and patients were less likely to report insulin non-compliance 11.1 compared to 50% (p 0.028) but there was no change in the DTSQ score.

Discussion: The most common local complication was scar 60% and the least common was swelling at the I-port site 5.5%.

Conclusion: Regular I-port usage improved compliance to insulin, decreased DM related hospitalization and hypoglycemia with non-significant 0.73% reduction in HbA1c.

Abstract #278

PREVALENCE OF DIABETES MELLITUS AMONG ADULT FILIPINO PATIENTS WITH THYROID DISEASE IN AN OUTPATIENT CLINIC IN CEBU CITY FROM 2004 - 2015

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Objective: Thyroid disorder (TD) has been associated with metabolic syndrome with an increase prevalence of diabetes and cardiovascular disease. It was noted that an abnormal thyroid function could have an impact on the diabetes control and increases the risk for diabetic complication. Due to the limited data in the Philippines, we determine the prevalence of diabetes among adult Filipino patients with thyroid disorders.

Methods: This is a retrospective cross sectional study of 870 randomly selected patients previously diagnosed with thyroid disease. Clinical data were obtained using an electronic medical search database. Anthropometric measures, BMI and laboratory parameters were reviewed. Patients with incomplete data were excluded. Only 487 patients were included in the final analysis. Data were analyzed using the IBM SPSS Software version 21 and Chi square test of independence with 2x2 Fisher exact test adjustment wherein a p-value of < 0.05 alpha was considered significant.

Results: The overall prevalence of diabetes among patients with thyroid disease was 60.2%. Prediabetes and diabetes were noted in 37.8% & 22.4% of patients presenting with thyroid disorder, respectively. The prevalence increased up to 88% for those with metabolic syndrome, which is prevalent among women (81%) and those aged 40 to 60 years old (63%).

Discussion: Our study showed that diabetes was prevalent among patients presenting with thyroid disorder, especially in those with metabolic syndrome. A significant number of patients (53.6%) presented with obesity on initial evaluation, which is believed to predispose individuals at risk for metabolic syndrome through insulin resistance, and in turn increases the risk for dyslipidemia, hypertension and increases their risk for cardiovascular disease.

Conclusion: Our study showed that diabetes was prevalent among patients presenting with thyroid disorder and further increase in those with metabolic syndrome. Screening for diabetes is therefore advised on all patients with thyroid disorder. Early diagnosis and treatment for diabetes and thyroid disorder in patients who remain asymptomatic can result in better long term outcome.

Abstract #279

DIABETES COMPLICATIONS AND CONTROL IN OBESE T1DM AND LEAN T1DM.

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Objective: Obesity has been an increasing problem in the most recent years, it contributes to glucose dysregulation and a large number of other medical complications. The incidence of type 1 diabetes (T1DM) has been also increasing worldwide and now we are seeing an increased number of overweight or obese patients with this particular disease. The aim of this study is to examine the effect of obesity in the rate of complications of diabetes, glycemic control and insulin requirements in a cohort of patients with T1DM in West Virginia where obesity is highly prevalent.

Methods: This is a retrospective observational cohort study that included patients with T1DM followed at an academic diabetes center. The whole cohort was included in the analysis to decrease the selection bias. The study cohort compromised 202 patients. Data regarding the duration of diabetes, glycemic control, insulin requirement, the prevalence of complication, blood pressure and lipid control were obtained.

Results: The mean age of our cohort was 43.79 (N 202 SD 17.59), the mean duration of DM was 23.91 years. There prevalence of obesity in our cohort was 24.26% (49). Duration of diabetes in obese patient was 24.79 years which was not statistically different from non-obese patient. HbA1c was better in obese group, mean 8.3% and higher in non-obese group (8.8%) but it was not statistically significant. There was no difference in blood pressure control in both groups. Obese participants were more likely to have been diagnosed with hypertension and dyslipidemia and received treatment for them. Compared to non obese patients, participants with BMI ≥30 were more likely to be using insulin pumps (77% VS 54% in non-obese) and also using higher doses of insulin (78.16...
units/day +SD 9 vs 39.40 units/day +SD 1.88); Adjuvant therapy was used in obese patients and metformin was the main choice (11% vs 0.66 % in non-obese). Patients with obesity used on average 17.3 units more of total daily dose of insulin when compared to non-obese. It remained unchanged with multivariable regression adjusted for age, gender, insulin method and GFR. There was no difference in retinopathy, neuropathy and nephropathy in both groups, there was no significant difference in cardiovascular disease, peripheral vascular disease or cerebrovascular disease either.

**Conclusion:** Our study showed that obese patients with T1DM do not appear to have more complications. The degree of glycemic control was not inferior to non-obese patients. Mean HbA1c was lower in the obese population and more obese patients used insulin pump delivery systems and adjuvant oral or injectable medications medication. Bariatric surgery was performed in 5 patients.

**Abstract #280**

**ACHIEVING AND MAINTAINING HBA1C TARGETS WITH EMPAGLIFLOZIN/LINAGLIPTIN SINGLE-PILL COMBINATION THERAPY IN TYPE 2 DIABETES**

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1. Boehringer Ingelheim Pharmaceuticals Inc., 2. Florida Hospital Diabetes Institute, 3. Boehringer Ingelheim GmbH & Co. KG

**Objective:** For type 2 diabetes (T2D), determining how treatments benefit certain patients and which patients will benefit from specific treatments would improve treatment success. In this study, among patients treated with the SGLT2/DPP-4 inhibitor single-pill combination (SPC) empagliflozin/linagliptin (EMPA/LINA) or empagliflozin and linagliptin monotherapies, we aimed to identify characteristics associated with achieving an HbA1c target of ≤7% at weeks 12 and maintaining target at week 52.

**Methods:** We pooled data from 2 Phase 3 studies (both registered as NCT01422876) in T2D patients who were treatment-naïve (study 1, n=677) or on background metformin (study 2, n=686). Patients were randomized to EMPA/LINA 25 mg/5 mg or 10 mg/5 mg, EMPA 25 mg or 10 mg, or LINA 5 mg. Target attainment groups were defined as patients at HbA1c target of ≤7% at weeks 12 and 52 (AT12&52), those at target at week 12 but above target at week 52 (AT12-only), and those with HbA1c above target at week 12 (ABT12). We used machine learning analysis (classification tree and random forest approaches) to estimate target categories using multivariate baseline characteristics without a priori selection. Descriptive analysis was also used to assess univariate associations between target categories and each baseline characteristic, eg HbA1c.

**Results:** The distribution of at-target categories in the SPC groups was significantly different from the monotherapy groups (χ² test, p<0.0001). The proportions of AT12&52 with EMPA/LINA 25 mg/5 mg, 10 mg/5 mg, EMPA 25 mg, EMPA 10 mg and LINA 5 mg were 43.3%, 45.9%, 31.1%, 30.5% and 21.8%, respectively. In addition, proportions AT12-only were 22.4%, 17.8%, 11.4%, 11.5% and 15.3%, respectively. Machine learning analyses identified baseline HbA1c and FPG as the strongest predictors of target attainment, while body weight, waist circumference, SBP, DBP etc did not contribute to the outcome in the final model. In the descriptive analysis, lower mean baseline HbA1c and FPG were both associated with achieving and maintaining HbA1c target (mean baseline values across treatment groups who were AT12&52: HbA1c 7.4–7.6%, FPG 137.9–145.7 mg/dL; AT12-only: HbA1c 7.5–7.8%, FPG 136.7–149.6 mg/dL; ABT12: HbA1c 8.3–8.5%, FPG 167.4–177.1 mg/dL).

**Discussion:** More patients treated with EMPA/LINA SPC reached HbA1c target at 12 weeks and maintained it through 52 weeks versus monotherapy treated patients. Baseline glucose control was associated with early HbA1c target attainment and maintenance.

**Conclusion:** EMPA/LINA SPC was associated with a greater proportion of HbA1c attainment and maintenance from 12 to 52 weeks. Only baseline HbA1c and FPG predicted goal attainment and maintenance, among baseline characteristics assessed.

**Abstract #281**

**PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND TYPE 2 DIABETES MELLITUS COMPPLICATED BY NEUROPATHY ARE AT HIGHER RISK OF HAVING COMPLICATIONS FROM GASTROESOPHAGEAL REFLUX DISEASE**

*Padma Chamarthy, MD, Hadie Razjouyan, MD, Kheng-Jim Lim, MD, Xiangbing Wang, MD, Sita Chokhavatia, MD*

Rutgers

**Objective:** For type 2 diabetes (T2D), determining how treatments benefit certain patients and which patients will benefit from specific treatments would improve treatment success. In this study, among patients treated with the SGLT2/DPP-4 inhibitor single-pill combination (SPC) empagliflozin/linagliptin (EMPA/LINA) or empagliflozin and linagliptin monotherapies, we aimed to identify characteristics associated with achieving an HbA1c target of ≤7% at weeks 12 and maintaining target at week 52.

**Methods:** We pooled data from 2 Phase 3 studies (both registered as NCT01422876) in T2D patients who were treatment-naïve (study 1, n=677) or on background metformin (study 2, n=686). Patients were randomized to EMPA/LINA 25 mg/5 mg or 10 mg/5 mg, EMPA 25 mg or 10 mg, or LINA 5 mg. Target attainment groups were defined as patients at HbA1c target of ≤7% at weeks 12 and 52 (AT12&52), those at target at week 12 but above target at week 52 (AT12-only), and those with HbA1c above target at week 12 (ABT12). We used machine learning analysis (classification tree and random forest approaches) to estimate target categories using multivariate baseline characteristics without a priori selection. Descriptive analysis was also used to assess univariate associations between target categories and each baseline characteristic, eg HbA1c.

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**Discussion:** More patients treated with EMPA/LINA SPC reached HbA1c target at 12 weeks and maintained it through 52 weeks versus monotherapy treated patients. Baseline glucose control was associated with early HbA1c target attainment and maintenance.

**Conclusion:** EMPA/LINA SPC was associated with a greater proportion of HbA1c attainment and maintenance from 12 to 52 weeks. Only baseline HbA1c and FPG predicted goal attainment and maintenance, among baseline characteristics assessed.
dysplasia compared to non-diabetic patients. Our goal was to assess endoscopic findings of GERD patients with diabetes especially a subset of patients with neuropathy as complications of T2DM.

**Methods:** In this retrospective cross-sectional study, all patients 18 years of age or older who underwent an outpatient endoscopy at Rutgers Robert Wood Johnson University Hospital from July 2011 until July 2015 were studied. Demographic information, clinical charts and upper endoscopic findings were reviewed.

**Results:** Of 567 patients who had an outpatient EGD, 376 (66.3%, mean age [SD]: 53 [13], female: 205 [56.2%]) had a clinical diagnosis of GERD (erosive reflux disease: 45 [12.3%]). There were sixty-five patients (17.3%) with T2DM and neuropathy was present in 17 patients. Diabetic patients were older (59 vs. 51, p <0.001), had higher mean BMI (32.6 vs. 30.0, p=0.006), and less erosive reflux disease (6.3 % vs. 13.6, p=0.14). Hiatal hernia was more common in non-diabetic patients (25.9% vs. 15.6%, p=0.08). Endoscopically suspicious Barrett’s esophagus (salmon-colored mucosa) was seen in 10.9% and 15.0% of GERD patients with and without T2DM, respectively. A subset of T2DM patients with neuropathy were noted to have higher rate of erosive reflux disease (10.5% vs. 5.6%, P: 0.50) and salmon-colored mucosa (21.1% vs. 5.6%, P: 0.08). A stepwise regression analysis in GERD patients with T2DM showed higher BMI (OR 1.28, 95% CI 1.01-1.62, P= 0.02), male gender (OR 15.5, 95% CI 1.01-238.70, P= 0.04) and diabetic neuropathy (OR 7.29, 95% CI 0.80-66.14, P= 0.07) as independent predictors for lower esophagus salmon-colored mucosa.

**Conclusion:** Our preliminary data show that although GERD patients with T2DM had less erosive reflux disease and salmon-colored mucosa compared to those without T2DM. However, a subset of patients with T2DM complicated by neuropathy may be at higher risk of erosive reflux disease as well as salmon-colored mucosa of the lower esophagus. This observation can potentially introduce a new category of patients who may benefit from intensified GERD treatment as well as BE screening. These result needs to be further investigated with a larger sample size controlled study.

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**Abstract #282**

**EFFECT OF 6-MONTH WEIGHT LOSS INTERVENTIONS ON GLYCEMIC CONTROL**

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**Objective:** Over the past four decades, obesity has become a growing health concern that has also come with a significant increase in the prevalence of prediabetes and type 2 diabetes mellitus. An estimated 86 million American adults have prediabetes with nine out of ten undiagnosed, and an additional 29.1 million Americans (8.1 million undiagnosed) have type 2 diabetes. With the widespread health, financial, and social effects of obesity and diabetes, healthcare providers and researchers have sought solutions for decreasing these deleterious effects. Marginal weight loss of 5% body weight has shown to yield significant improvements in blood pressure, triglycerides, HDL, and glycemia. Greater weight loss of 10-15% of body weight has also shown increased odds for significant health improvements. In a community endocrinology clinic, weight loss recommendations begin with lifestyle modification by way of improved dietary choices and increased physical activity. Pharmacotherapy is also an option in struggling patients or those with severe comorbidities. Healthcare providers may also recommend significant dietary intervention such as meal replacements programs like OPTIFAST, a medically supervised weight loss program.

**Methods:** A retrospective study was conducted to evaluate the effectiveness of phentermine therapy (PH) and the OPTIFAST diet program (OP) on 6-month weight and diabetes outcomes. A chart review was performed, yielding 15 patients who completed 6 months of phentermine treatment (10 female, 5 male) and 6 patients who completed 6 months of the OPTIFAST program (3 female, 3 male) with HbA1c greater than 6.0%.

**Results:** The RM ANOVA performed on HbA1c revealed a significant effect for condition by time interaction (p<.001) with a .06% increase for PH and 1.8% decrease in OP. Starting weight (229.6 lbs PH, 290.7 lbs OP) and SBP (124 mmHg PH, 144 mmHg OP) were significantly different at baseline and the ANCOVA revealed non-significant effects.

**Discussion:** Descriptively, OP participants decreased weight by 30.3 lbs (17.9%) and PH participants decreased weight by 13.6 lbs (6.0%). In addition to the weight loss, 30% of patients treated with phentermine had a reduction in diabetes medications, and all OPTIFAST participants
decreased diabetes medications by 50% or were able to discontinue their use. The attrition rate for participants in the OPTIFAST program was 34%.

**Conclusion:** The results of this retrospective study demonstrate that a significant improvement in glycemic control can be achieved during a 6-month, medically supervised meal replacement weight loss program. Despite reduced or discontinued diabetes medication, sustained weight loss promotes improvements in long-term blood glucose control.

Abstract #283

FUNCTIONAL MEASURES OF SMALL FIBER FUNCTION MAY HAVE GREATER IMPLICATIONS THAN NERVE STRUCTURE ALONE IN SUBJECTS WITH TYPE 2 DIABETES

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1. Eastern Virginia Medical School, 2. Weill Cornell Medical College

**Objective:** In vivo Corneal Confocal Microscopy (IVCCM) is a validated, non-invasive test for detecting early morphological alterations of small nerve fibers in the cornea and correlates with other measures of diabetic neuropathy (DPN) including intraepidermal nerve fiber density in the distal leg. However, the relationship between this, predominantly structural measure and other more functional measures of small fiber function has not been explored in detail. The aim of this study was to evaluate the association of structural and functional measures of small fiber function in subjects with T2DM.

**Methods:** Subjects with T2DM were evaluated with the following measures: neuropathy scores; bilateral eye IVCCM examination of the corneal nerve plexus using the Rostock cornea module of the Heidelberg Tomograph III; sudomotor function using SudoscanTM that measures electrochemical skin conductance (ESC) through reverse iontophoresis; time and frequency domain analysis of heart rate variability (HRV); skin blood flow response to heat using continuous laser Doppler on the lower limb (LL); and nerve conduction studies (NCS).

**Results:** We included 50 T2DM subjects (age 59.38±1.36, 56% female, 54% Caucasian, BMI 35.62±1.11, A1C 7.94±0.22, duration of DM 147.43±15.33 months). Corneal nerve fiber density (CNFD), branch density (CNBD), and fiber length (CNFL) were assessed by 2 independent observers. ICCs were calculated (CNFD=0.82, CNBD=0.79, CNFL=0.86). CNFD was significantly associated with feet ESC (r=0.36, p=0.02). CNBD & CNFL showed a weak, non statistically significant correlation with feet ESC (CNBD: r=0.28, p=0.08 & CNFL: r=0.27, p=0.09). CCM measures were significantly associated with skin blood flow response to heat (CNFD: r=0.37, p=0.03; CNBD: r=0.31, p=0.045; CNFL: r=0.41, p=0.01) and were not associated with neuropathy scores, HRV measures and NCS. On multivariate analysis, CCM measures were associated with DM duration whereas feet ESC was associated with DM duration, insulin levels and ethnicity, after adjusting for age and gender.

**Discussion:** This study shows a mild but significant correlation between structural and functional measures of small fiber function in subjects with T2DM. Nonetheless there was no correlation with more traditional measures of somatic and autonomic neuropathy. Whatever the case the study does illustrate the need for carrying out diverse measures of small fiber function if we hope to address the underlying pathogenic mechanisms of DPN.

**Conclusion:** The evaluations of the consequences of small fiber dysfunction needs to include both structural and functional quantification lest we fail to do justice to the attribution of cause and effect.

Abstract #284

REDUCING HOSPITAL READMISSION IN PATIENTS WITH TYPE II DIABETES

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University of Alabama in Huntsville

**Objective:** Diabetes mellitus (DM) affects over 387 million individuals worldwide and the number continues to rise due to an aging population, increase in obesity, and living longer. T2DM is the most common form of the disease. Individuals with this chronic illness may double costs for medical expenses due to the morbidity of the disease process. The objective was to use health coaching to improve glucose management and to decrease the 30-day hospital readmissions of patients with T2DM.

**Methods:** Bandura’s Self-efficacy Theory served as a framework for a 3-month project involving a convenience sample of patients with T2DM. Inclusion criteria were English-speaking, 20 years or older and voluntary participation with signed informed consent. Exclusion criteria were individuals that did not have a diagnosis of T2DM, unable to verbally communicate or non-English-speaking. The inpatients in an acute care hospital participated in a face-to-face semi-structured interview to
identify self-care priorities, set specific goals, and answer a diabetes knowledge quiz. Hennessy and Heryer’s concepts of collaboration, open-ended questions, proactive behaviors and encouragement (COPE) were used to promote self-management. Following their discharge, the investigator reinforced the desired lifestyle changes via telephone on days 3, 7, 14, and 28. Personal letters were mailed at the beginning and end of the project. The knowledge quiz was repeated on day 28 after hospital discharge.

**Results:** Demographic characteristics (n=20) revealed age range of 44-90 (BMI ranged from 21.7-49.3 kg/m2 49.3 (90%) had a BMI >24.9 kg/m2 and 50% had BMI +/- 30 kg/m2. The range of blood glucose (BG) upon admission was 72-343 mg/dL (25% had admission BG >/= 200 mg/dL. Participants had 1-9 comorbidities (Three females and one male were readmitted to the acute care facility within 30 days. Range for length of stay for readmissions was 7-28 days (Four participants reported improved glucose management although only 58% recorded daily readings. Sixteen participants (80%) were not readmitted within 30 days.

**Discussion:** The absence of a common goal or priority supports the individualization of education and health coaching. A recommendation for instituting an intervention program would be to embrace a multidisciplinary educational approach for all staff in being prepared to be engaged and to extend a warm handoff at discharge. While not all readmissions may be prevented, ongoing coaching may improve glucose management in the home.

**Conclusion:** This evidence-based practice project indicates that health coaching can lower readmissions, improve blood glucose levels, and achieve goals in patients with T2DM.

Abstract #285

**NOVEL APPROACH TO TREAT 25-HYDROXY-VITAMIN D-DEFICIENCY AND INSULIN RESISTANCE IN TYPE 2 DIABETES**

Sushil Jain

Louisiana State University Health Sciences Center

**Objective:** 25-hydroxy-vitamin D (25(OH)VD)-deficiency has become a world-wide epidemic. The deficiency of 25(OH)VD is associated with risk for insulin resistance (IR) and cardiovascular disease (CVD) in diabetes. This presentation describes a novel approach to increase the status of the VD regulatory genes rather than using high dose VD supplements to increase blood levels of 25(OH)VD and lower IR and inflammation biomarkers in diabetes.

**Methods:** VD-deficiency and diabetes was induced by feeding VD-deficient-High Fat diet (HFD) in mice. This approach is widely used to mimic development of insulin resistance and VD-deficiency as seen in diabetic patients.

**Results:** There was a significant decrease in blood 25(OH)VD and increase in IR and inflammation in VD-deficient HFD group; supplementation of L-cysteine (LC) along with VD (cholecalciferol) significantly increased blood levels of 25(OH)VD, and lowered IR (HOMA), HbA1C and TNF-α compared with VD alone-treated diabetic mice. Further, supplementation with VD+LC upregulated mRNA of VD regulatory genes (vitamin D binding protein, VD-25-hydroxylase, and VDR) in liver and skeletal muscle. Cell culture studies showed that LC can prevent the decline of VDBP/VDR and gluthathione (GSH) induced by hyperglycemia; additionally, GSH deficiency induced by an antisense approach led to a significant increase in ROS and decrease in VD regulatory genes in monocytes and hepatocytes.

**Discussion:** The potential mechanism for the increased blood levels of 25(OH)VD in VD+LC-supplemented mice could be the upregulation of GSH and of VD regulatory genes needed for the bioavailability and metabolic actions of 25(OH)VD and 1,25(OH)2VD.

**Conclusion:** This suggests that combined supplementation with low dose VD and LC and an improvement in VD regulatory genes status is a better and safer approach for increasing blood levels of 25(OH)VD and reducing IR and CVD in a population at risk for 25(OH)VD-deficiency/ inadequacy (supported by NCCIH RO1 AT007442).

Abstract #286

**WORSENING PANCREATOCGECIC DIABETES AFTER WHIPPLE PROCEDURE COMPLICATED BY HYPEROSMOLAR HYPERGLYCEMIC STATE**

Moses Ko¹, Timothy Quek²

1. Lee Kong Chian School of Medicine, Nanyang Technological University, 2. Tan Tock Seng Hospital

**Objective:** Many patients either develop diabetes mellitus (DM) or have worsening of pre-existing DM after undergoing pancreatic resection. We present a case of pancreaticogenic DM presenting with hyperosmolar hyperglycemic state (HHS) 2 months after a Whipple procedure.

**Case Presentation:** A 77 year old Chinese man with known hypertension and gout presented to our hospital in November 2014 with 2 weeks of abdominal pain, associated with worsening obstructive jaundice and anorexia. A 4 cm pancreatic head mass was found on abdominal imaging, and the patient underwent a Whipple procedure in December 2014. Histopathological examination confirmed the diagnosis of pancreatic adenocarcinoma. Though planned for adjuvant chemotherapy, he opted to delay his treatment for a trial of traditional medications.
Before chemotherapy could be initiated, the patient was admitted in February 2015 with confusion. Investigations on admission showed hypernatremia (Sodium 155 mmol/L), severe hyperglycemia (Glucose 54.4 mmol/L) and hyperosmolality (Osmolality 396 mosm/kg), as well as acute kidney injury (Creatinine 2.1 mg/dL). His HbA1c on admission was 11.0%.

The patient was diagnosed with HHS and treated emergently with fluid resuscitation and insulin. Precipitating causes identified included pneumonia, possible Strongyloides stercoralis superinfection and bilateral occipital lobe infarctions.

Retrospective review of his capillary blood glucose readings during his admissions in November and December 2014 revealed episodes of post prandial hyperglycemia of up to 16.7 mmol/L. His HbA1c in November 2014 was 6.9%. This showed that the patient had pre-existing DM, likely contributed to by his pancreatic malignancy. However, neither outpatient monitoring nor medications for DM were instituted.

The patient recovered after treatment, but declined further therapy for his pancreatic malignancy. He was discharged from the hospital on basal bolus insulin, but subsequently succumbed to metastatic pancreatic carcinoma 6 months later.

Discussion: Although there is often monitoring for pancreatic exocrine insufficiency after pancreatic surgery, pancreatogenic DM is a frequently forgotten complication. This patient’s admission for HHS may have been prevented if close outpatient monitoring and follow-up for DM had been instituted after surgery. Multidisciplinary collaboration among surgeons, endocrinologists, gastroenterologists and dietitians is important in managing the nutritional and metabolic problems in such patients.

Conclusion: A multidisciplinary approach and monitoring for pancreatogenic DM is essential after pancreatic surgery to avoid acute and chronic complications of hyperglycemia.

Abstract #287

AUTOIMMUNE LIVER DISEASES IN TYPE 1 DIABETES MELLITUS; PREVALENCE, ASSOCIATED CONDITIONS AND OUTCOME.

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1. Washington University Hospital, 2. University of Missouri at Kansas City

Objective: Autoimmune liver diseases (AILD) occur infrequently in patients with T1DM, but may have devastating outcomes. The purpose of this study is to define the prevalence, associated autoimmune diseases (AID) and outcomes of AILD in patients with T1DM.

Methods: 1055 T1DM patients from the Washington University Diabetes Center gave consent for a study of concomitant AID in T1DM. 8 patients with AILD are described here.

Case Presentation: Of the 8 AILD patients, 3 had primary biliary cirrhosis (PBC), 3 had primary sclerosing cholangitis (PSC), and 2 had autoimmune hepatitis (AIH). Mean age dx of T1DM was 26.6 yrs. Mean age dx of AILD was 34.1 yrs. Mean duration between the dx of T1DM and dx of AILD was 8.5 years. T1DM preceded AILD in 6 patients, was diagnosed at the time of AILD diagnosis in 1 and was diagnosed 18 years after AILD in 1. LFTs at dx of AILD were 115-635 IU/L for ALT, 26-339 IU/L for AST and 11-934 IU/L for alkaline phosphatase.

These patients had multiple other AID in addition to T1DM and AILD, mean of 2.4 additional AID (4.4 including T1DM and AILD). The other AID included: thyroid diseases 5, ulcerative colitis 4, Crohn’s 1, celiac 2, autoimmune ovarian failure 2, Addison’s disease 1, SLE 1, Sjogren’s syndrome 1, stiff person syndrome 1 and autoimmune hearing loss 1.

Liver outcomes include cirrhosis in 4, liver transplant in 2, cholangiocarcinoma in 1 and hepatocellular cancer in 1. Three patients are actively under treatment for AILD and only one patient with PBC is in remission. Death occurred in 2 patients; one due to cholangiocarcinoma and the other from mesenteric ischemia >15 years post liver transplant and protocolectomy. The patient with the HCC is s/p resection, no recurrence but has cirrhosis.

Discussion: AILD is a serious, potentially life-threatening autoimmune disease that occurs with increased frequency in patients with T1DM. In this small cohort, 3 men developed both ulcerative colitis and PSC at young ages, and had progression to liver failure; 2 were transplanted, the third developed cholangiocarcinoma and died. Two women developed autoimmune hepatitis at young ages; one of whom developed HCC 40 years later. The three
women with PBC have had a more indolent course, and are under treatment or in remission.

**Conclusion:** The prevalence of AILD in T1DM is 0.76%, compared to 0.12 – 0.13% in the population. Patients with T1DM and AILD have many additional AIDs, including IBD and celiac. AILD can be indolent or have devastating outcomes. Early recognition, treatment and long term follow-up are needed to prevent poor outcomes.

Abstract #288

**LOW INCIDENCE OF GASTROINTESTINAL ADVERSE EVENTS OVER TIME WITH A FIXED-RATIO COMBINATION OF INSULIN GLARGINE AND LIXISENATIDE VS LIXISENATIDE ALONE**

Jennifer Trujillo, PharmD, BCPS, CDE, BC-ADM, FCCP, Yan Yan, MS, Michelle Roberts, MD, Terry Dex, PharmD, John White, PA-C, PharmD, James LaSalle, DO, FAAFP


**Objective:** iGlarLixi, a titratable fixed-ratio combination of insulin glargine (iGlar) 100 U/mL and GLP-1 receptor agonist (RA) lixisenatide (lixi), was associated with low rates of nausea (N), vomiting (V) and diarrhea (D) (≤10% each) in the LixiLan phase 3 clinical program, leading to very low discontinuation rates (≤1%) each. This post hoc analysis assessed frequency and timing of gastrointestinal adverse events (GI AEs) in 2 trials evaluating iGlarLixi in patients with type 2 diabetes (T2D) uncontrolled with oral antidiabetes agents and/or basal insulin vs iGlar alone or lixi alone.

**Methods:** Pertinent data on N, V and D from the randomized, open-label LixiLan-O (NCT02058147) and -L (NCT02058160) trials were used in this analysis. The incidence of these GI AEs was calculated with descriptive statistics; results were summarized by treatment group.

**Results:** Within the first 60 days of treatment initiation, 11.7% and 9.6% of patients treated with iGlarLixi experienced N, V or D in the LixiLan-O and -L trials, respectively, compared with 27.5% of patients on lixi in LixiLan-O, and 4.7% and 1.4% of patients on iGlar in LixiLan-O and -L. The percentage of patients with onset of GI AEs from Day 60 to study end (~210 days) was 7.7% and 4.1% for iGlarLixi in LixiLan-O and -L, respectively, 6.9% for lixi in LixiLan-O, and 3.2% and 2.2% for iGlar in LixiLan-O and -L. After 80 days, incidences of new N, V, or D events were 3.4%, 1.1% and 3.0%, respectively, for iGlarLixi, compared with 2.6%, 1.3% and 2.6% for lixi in LixiLan-O. Most GI AEs reported for iGlarLixi were mild (53-78%) to moderate (22-45%) in severity, with only 1 reported severe N event in LixiLan-L and 0 severe GI AEs in LixiLan-O. The median durations of N, V, and D were 5.0, 1.0 and 3.5 days, respectively, with iGlarLixi vs 7.5, 3.0 and 3.0 days with lixi, and 2.0 days for each GI AE with iGlar in LixiLan-O. In LixiLan-L, the median durations were 6.0, 2.0 and 2.5 days with iGlarLixi vs 3.0, 1.0 and 2.0 days with iGlar.

**Discussion:** The occurrence of GI AEs is expected with the use of GLP-1 RAs. N, V, and D events associated with iGlarLixi treatment were predominantly transient, mainly occurring during the initial 8-week titration period in a small proportion of patients; by week 12 they were rare. As expected, the overall proportion of patients with GI AEs was higher with iGlarLixi than with iGlar, but lower than with lixi; this may be due to the slow increase in lixi dose in the fixed-ratio iGlarLixi combination.

**Conclusion:** Patients with T2D treated with iGlarLixi show a low rate of GI AEs compared to lixi, and these tend to occur early and to be transient and mild, rarely requiring discontinuation.

Abstract #289

**IN-HOSPITAL MORTALITY IN PATIENTS ADMITTED FOR ACUTE MYOCARDIAL INFARCTION: TYPE 1 DIABETES MELLITUS COMPARED TO TYPE 2 DIABETES MELLITUS**

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Mount Sinai West & Mount Sinai St Luke’s

**Objective:** Evaluate inpatient mortality rate and outcomes in patients admitted to hospitals in the United States with acute myocardial infarction with Type 1 diabetes mellitus (T1DM) compared to patients with Type 2 diabetes mellitus (T2DM).

**Methods:** This is a retrospective cohort study using the 2013 National Inpatient Sample (NIS). Patients were included if they were adults with a principal diagnosis of acute myocardial infarction (MI) and with secondary diagnosis of T1DM or T2DM. Our main outcome measurements were in-hospital mortality, length of stay and total hospitalization costs. Multivariate logistic regression was used to adjust for potential confounders including age, gender, race, median yearly income and comorbidities by the Charlson Comorbidity index for administrative data.

**Results:** This study included a total of 226,956 patients with Acute MI and DM of these 221,310 (97.5%) were type
2 diabetics and 5,655 (2.5%) were type 1 diabetics. The mean age of the population was 67.38 with SD 0.07 years although by group the mean age was lower in T1DM (57.8 SD 0.43 years) compared to T2DM (67.62 SD 0.79 years). The proportion of men in the total population was 59.17%. Patients with DM1 had an increased adjusted inpatient mortality rate (odds ratio [OR] 1.49; 95% confidence interval [CI], 1.12 – 1.99, P <0.01) when compared with patients with T2DM. There was an increase length of stay by 0.5 days (P = 0.02) in T1DM but there was no statistical significance in total hospital costs between both groups.

**Discussion:** There has been conflicting evidence when comparing cardiovascular mortality in patients with T1DM and T2DM. Despite this T1DM has been shown to cause earlier endothelial damage and autonomic dysinnervation causing impaired vasodilator response of coronary vessels when compared to patients with T2DM.

**Conclusion:** Patients with Acute MI and T1DM had a statistically significant increased rate of inpatient mortality compared with patients with T2DM. Nonetheless, the length of stay was only mildly increased in patients with T1DM and there was no difference in terms of hospital costs in both groups.

**Abstract #290**

REAL-WORLD PERSISTENCE AND HBA1C GOAL ATTAINMENT IN PATIENTS WITH TYPE II DIABETES MELLITUS INITIATED ON CANAGLIFLOZIN OR A GLUCAGON-LIKE PEPTIDE-1 RECEPTOR AGONIST

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**Objective:** Real-world evidence comparing sodium-glucose co-transporter 2 and glucagon-like peptide-1 (GLP-1) receptor agonists is scarce. This study compared persistence and HbA1c goal attainment in patients with type II diabetes mellitus (T2DM) initiated on oral canagliflozin 300 mg (CANA) versus injectable GLP-1 in the real-world setting.

**Methods:** Adults with T2DM newly initiated on CANA 300 mg or a GLP-1 (i.e., albiglutide, dulaglutide, exenatide, or liraglutide; the date of initiation being defined as the index date) were identified from the QuintilesIMS EMRs – US database (03/29/2012-04/30/2016). Inverse probability of treatment weighting was used to account for differences in baseline characteristics. Outcomes were compared using weighted Cox models (hazard ratios [HRs] and confidence intervals [CIs]) and Kaplan Meier curves and included time to: HbA1c <8%, discontinuation (gap >90 days), add/switch to a new antihyperglycemic agent (AHA), and the composite of failure to maintain HbA1c <8% or add/switch to a new AHA. Attaining an HbA1c goal of <8% was evaluated among patients with baseline HbA1c≥8%. Failure to maintain HbA1c<8% was evaluated among patients starting at or reaching HbA1c<8% (from the index date or first day with HbA1c below goal).

**Results:** A total of 11,435 CANA patients and 11,582 GLP-1 patients (62.6% initiated on liraglutide, 25.4% on exenatide, 8.2% on dulaglutide, and 3.8% on albiglutide) formed the weighted study cohorts which had well balanced baseline characteristics and HbA1c. Time to reach HbA1c <8% was comparable between the two cohorts (HR [95% CI]: 0.98 [0.91, 1.06]; p=0.642). However, CANA patients were 30% less likely to discontinue (HR [95% CI]: 0.70 [0.66, 0.74]; p<0.001), with a median time to discontinuation of 12.4 vs. 8.6 months versus GLP-1 patients. CANA patients were also 28% less likely to add/switch to a new AHA (HR: 0.72 [0.68, 0.77]; p<0.001; median 21.3 vs. 15.1 months). CANA and GLP-1 patients were not significantly different in terms of failure to maintain HbA1c <8% (HR: 1.00 [0.90, 1.11]; p=0.988) but CANA patients were 17% less likely to either fail to maintain HbA1c <8% or add/switch to a new AHA (HR [95% CI]: 0.83 [0.77, 0.90]; p<0.001; median 15.4 vs. 12.6 months).

**Discussion:** Using the combined endpoint of failure to maintain HbA1c goal and add/switch to a new AHA as a proxy for treatment failure, the current study showed that initiation of CANA resulted in fewer treatment failures.

**Conclusion:** Reaching and maintaining HbA1c below 8% was comparable between CANA and GLP-1 patients. However, this result was achieved with fewer CANA patients requiring the addition of or switch to a new AHA when compared to GLP-1 patients.
Abstract #291

IMPACT OF SKIN BUNDLE IMPLEMENTATION ON HOSPITAL AQUIRED PRESSURE FOOT ULCERS AND LENGTH OF STAY IN INPATIENTS WITH DIABETES

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Objective: To assess the impact of launching SKIN (Surface, Keep moving, Incontinence, Nutrition) bundle on development of pressure foot ulcers among in-patients with diabetes

Methods: The SKIN Bundle was launched at Dudley Group of Hospitals Foundation Trust in mid-February 2011. Data on pressure foot ulcers were collected among patients with and without diabetes admitted during February 2010-February 2011 and then from February 2011-March 2012, from pressure ulcer database.

Results: Between 14th February 2010 and 13th February 2011, the number of admissions to adults wards was 64,000. Of these, 5,452 were patients with diabetes. Out of the latter, 72 patients were having foot ulcers whilst being in the hospital, either admitted with them or acquired during their hospital stay. During the above year (Prior to implementation of SKIN bundle), 23 patients with diabetes had foot ulcers whilst being in the hospital, giving rise to 0.42% rate of development of hospital acquired foot ulcers among in-patients with diabetes. During the thirteen and a half month period following SKIN bundle launch (14th February 2011 – 31st March 2012), there were 13 patients who developed hospital acquired foot ulcers out of 6,232 in-patients with diabetes admitted during the same period, giving rise to a lower rate (0.21%) of development of foot ulcers in the hospital among patients with diabetes. The development of hospital acquired foot ulcers among patients with diabetes, therefore, dropped significantly by 51% (P value of 0.04) after the launching SKIN bundle.

The average length of hospital stay among patients with diabetes who had foot ulcers was significantly shorter by an average of 3.55 days, P value of 0.044 (P<0.05), after this SKIN bundle implementation.

Conclusion: SKIN bundle resulted in more than 50% reduction in pressure foot ulcers; an impact which was similar in those with and without diabetes. We suggest considering SKIN Bundle as a tool that can be used to reduce inpatient pressure Ulcers.

Abstract #292

GLYCEMIC CONTROL, WEIGHT LOSS, AND USE OF OTHER ANTIHYPERGLYCEMIC IN PATIENTS WITH TYPE II DIABETES INITIATED ON CANAGLIFLOZIN OR SITAGLIPTIN: A REAL-WORLD ANALYSIS OF ELECTRONIC MEDICAL RECORDS

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Objective: Real-world (RW) data showing benefits of canagliflozin (CANA) over sitagliptin (SITA) are emerging. This study assessed glycemic control, weight loss, durability of glycemic control, and use of other antihyperglycemic agents (AHA) in patients initiated on CANA versus SITA.

Methods: Adults with type 2 diabetes mellitus (T2DM) initiated on CANA or SITA (i.e., index date) were identified from the QuintilesIMS Real-World Data Electronic Medical Records – US database (03/29/2012-04/30/2016). Inverse probability of treatment weighting accounted for differences in baseline characteristics between cohorts. Outcomes included HbA1c over time and time to: reaching HbA1c goal (<7%, <8%, <9%), weight loss ≥5%, failure to maintain HbA1c goal, add/switch to a new AHA, and the composite of failure to maintain HbA1c goal or add/switch to a new AHA. HbA1c over time was assessed using moving averages at 3-month intervals pre and post-index. HbA1c goals were evaluated among patients with baseline HbA1c above goal. Failure to maintain HbA1c goal was evaluated among patients with baseline HbA1c above goal. Failure to maintain HbA1c goal was evaluated among patients with baseline HbA1c below goal or who reached goal following index treatment initiation. Time-to-event outcomes were compared using weighted Cox models and Kaplan Meier curves.

Results: A total of 14,165 CANA patients and 15,528 SITA patients formed the study population. Baseline characteristics and HbA1c were well balanced between weighted cohorts. Post-index, mean HbA1c declined in both cohorts and was significantly lower (p<0.01) in CANA versus SITA patients at each interval, up to 30 months (except 21 months, p=0.18). CANA patients were 12 to 15% more likely to maintain HbA1c goal (<7%, <8%, <9%) and 47% more likely to lose ≥5% of body weight (p<0.01), relative to SITA patients. CANA patients were 31% less likely to add/switch to a new AHA (median time to switch 20.3 vs. 13.1 months) and 10 to 15% less likely to fail to maintain their HbA1c
<7%, <8%, or <9% (all p<0.01). Combining these two endpoints as a proxy for treatment failure, CANA patients were 12 to 16% less likely to fail to maintain goal or add/switch to a new AHA (all p<0.01).

**Discussion:** CANA patients were more likely to reach and maintain HbA1c goals versus SITA patients. SITA patients were more likely to add/switch to a new AHA, suggesting inadequate glycemic control on the index therapy.

**Conclusion:** In a RW analysis, CANA patients were more likely to reach HbA1c goals, weight loss goals, and to maintain HbA1c below goal compared to SITA patients. They were also less likely to add new AHAs and to either fail to maintain or add/switch to a new AHA. These findings suggest a higher durability of glycemic control in patients initiated on CANA relative to SITA.

Abstract #293

**ASSOCIATION OF FRAILTY CHARACTERISTICS AND HEMOGLOBIN A1C IN ADULTS**

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**Objective:** The frailty syndrome is described as a condition of physiological vulnerability and multisystem dysfunction associated with an increased morbidity and mortality in the elderly population. There is some data to suggest that the presence of frailty syndrome is associated with glucose intolerance in older adults without diagnosed diabetes mellitus. The present study aims to report the relationship between frailty characteristics and glycosylated hemoglobin (HbA1c) in an ambulatory primary care population.

**Methods:** Prospective study that evaluated a convenience sample of adult patients presenting to a primary care clinic from 31st August 2016 to 15th November 2016. Frailty characteristics were evaluated using the FRAIL questionnaire. Patients were deemed pre-frail if they scored 1 or 2 points, and frail if they scored 3 points on the scale. Laboratory data including HbA1c and low density protein (LDL) were collected from medical records.

**Results:** A total of 91 individuals were included in the study. Mean age of patients was 52 ± 17 years, and 64 (70%) of these were female. Forty-eight (52%) individuals were either frail or pre-frail based on the FRAIL questionnaire. Median HbA1c was significantly higher in patients who had 1 or more characteristics of the frailty syndrome as compared to those without these characteristics (6.2 (IQR 5.8-7.8) vs 5.8 (IQR 5.5-6.2), p=0.0107). Patients with frail characteristics had a significantly higher prevalence of elevated HbA1c (greater than or equal to 6.5%) as compared to robust individuals (38% vs 16%, p=0.047). There were no significant differences in body mass index (BMI), age, gender or LDL between the two study groups.

**Conclusion:** The present study revealed a high prevalence and higher median levels of hemoglobin A1c in ambulatory adult patients with frailty characteristics. Further study is needed to determine if frailty characteristics in the adult population are associated with an additional risk of developing insulin resistance or are instead the result of a common pathophysiologic pathway.
HYPOGLYCEMIA

Abstract #300

FACTITIOUS HYPOGLYCEMIA WITH ELEVATED PROINSULIN LEVEL IN THE ABSENCE OF DIABETES

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Case Presentation: Factitious hypoglycemia is difficult to diagnose and treat, requiring a multidisciplinary team approach. Factitious hypoglycemia occurs with the surreptitious use of insulin or insulin secretagogues (sulfonylureas, meglitinides). This condition often puts the patient-clinician relationship in jeopardy. It is more common in women and health-care workers, seen in the third or fourth decades of life, and, among nondiabetic subjects. It can mimic an insulinoma leading to futile abdominal exploration and needless subtotal pancreatectomy. The appropriate application and interpretation of available tests is necessary for accurate diagnosis. Sulfonylureas stimulate release of insulin from the pancreatic β-cells via ATP-dependent potassium channels. Onset of hypoglycaemia coincides with peak plasma levels of sulfonylureas, which occurs 2–4 hours after ingestion. Duration of action may be increased significantly in overdoses and hypoglycaemia may last up to 72 hours.

We discuss a case of sulfonylurea induced hypoglycemia in a nondiabetic patient, mimicking insulinoma.

44 year old white male was admitted to multiple hospitals with recurrent episodes of hypoglycemia and Endocrinology was consulted. He had major depression, dependent personality, irritable bowel syndrome, hypertension, tobacco use, post-traumatic stress disorder, insomnia, a previous pulmonary embolism, GERD and was nondiabetic with A1C of 5%.

He was separated from wife, living with his mother, a diabetic embolism, GERD and was nondiabetic with A1C of 5%.

We case a discu of sulfonylurea induced hypoglycemia in a nondiabetic patient, mimicking insulinoma.

We present a case of sulfonylurea induced hypoglycemia in a nondiabetic patient, mimicking insulinoma. A 44-year-old white male was admitted to multiple hospitals with recurrent episodes of hypoglycemia and Endocrinology was consulted. He had major depression, dependent personality, irritable bowel syndrome, hypertension, tobacco use, post-traumatic stress disorder, insomnia, a previous pulmonary embolism, GERD and was nondiabetic with an A1C of 5%.

The patient was separated from his wife and was living with his mother, who was diabetic. He had a history of bilateral nephrectomy for renal cell cancer on hemodialysis, RYGB surgery, poor oral intake, chronic diarrhea, found to have a glucose of 41 with dizziness and falls and no distinct pattern to the episodes. His symptoms resolved with dextrose. Fasting protocol resulted in rapid symptomatic hypoglycemia. Labs revealed glucose of 57, insulin of 4.7 uIU/mL (<3), C-peptide elevation 2.29 nmol/L (<0.2), proinsulin 2.3 pmol/L (0-10), Beta-Hydroxybutyrate 0.06 mmol/L (0.02-0.27). Glucose increased from 35 to 115 after 12 minutes with glucagon.

Proinsulin/C-peptide ratio was normal. Thyroid function and morning cortisol were normal. Triple phase contrast computerized tomography and abdominal ultrasound were unrevealing. Endoscopic ultrasound with biopsy of the body of the pancreas showed benign lymph nodes. Throughout hospitalization, he required continuous intravenous infusion of dextrose 10% in water as well as intermittent doses of dextrose 50% due to hypoglycemia with attempted decrease in drip rate. Mixed meals did not alleviate episodes. He was not a candidate for diazoxide therapy due to significant cardiac disease and he could not tolerate acarbose due to history of severe diarrhea. We started octreotide injections every eight hours to decrease insulin secretion. Hypoglycemia frequency and severity improved. With switching to monthly sandostatin long-acting release, diarrhea and poor appetite resolved.

Discussion: RYGB causes increased risk of hypoglycemia that can be difficult to manage. Literature review has addressed treatment of this, however, our patient's presentation was complicated by bilateral nephrectomy which contributes to 20–40% of glucose intolerance. Proinsulin/C-peptide was normal which indicated that a disorder of beta cell insulin processing was not present. Octreotide inhibits glucagon-like peptide-1 release from intestinal L cells and inhibits insulin release from pancreatic beta cells. We demonstrate that in RYGB
complicated by absent renal gluconeogenesis, octreotide can successfully control chronic, severe hypoglycemia.

**Conclusion:** This case demonstrates the successful use of octreotide therapy to manage chronic, severe hypoglycemia in a patient with enhanced incretin response, chronic diarrhea, and absent renal gluconeogenesis following RYGB surgery and bilateral nephrectomy.

**Abstract #302**

PROLONGED SURVIVAL IN MALIGNANT INSULINOMA

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**Objective:** Insulinomas (INS) are rare neuroendocrine tumors with a prevalence of 4 cases/million/year, <10% of which are malignant. 10 year survival for benign INS is reported to be of 88% compared with 29% in malignant INS. We report a case of prolonged survival in a patient with malignant INS who later developed gastric adenocarcinoma (GA) and subsequent worsening hypoglycemia (HG).

**Case Presentation:** 76-year-old woman was seen by Endocrinology after being lost to follow up for recurrent HG. She had a complex medical history including papillary thyroid carcinoma in 1974 treated with surgical resection. She developed postsurgical hypoparathyroidism treated with calcitriol and calcium. INS was diagnosed in 1986 and treated with pancreatic enucleation. HG recurred in 1995 with increased insulin and C-peptide levels during prolonged fast. Imaging studies and calcium stimulation test (CST) could not localize tumor. In 1996, Octreotide scan was inconclusive and CST showed uncinate process as possible source. She had Whipple’s surgery with tissue confirmed diagnosis of INS. She was asymptomatic until 2001 and CST showed an increased insulin gradient at the SMA. She had revision of pancreaticojejunostomy with improvement in HG. HG recurred in 2002 and CST showed increased C-peptide and insulin at the superior mesenteric and portal veins. CT abdomen revealed subcentimeter hypervascular lesions concerning for development of hepatic metastatic disease. She declined further invasive testing and tried multiple regimens including octreotide, nifedipine, and dilantin without improvement. She had partial response to diazoxide and prednisone. She remained asymptomatic but controlled HG until 2016. In 2016, she was admitted for pulmonary embolism and underwent EGD for evaluation of anemia where a gastric mass was biopsied to detect GA. CT abdomen showed multiple low attenuation liver lesions, now measuring >1cm as well as multiple lymph nodes concerning for GA metastasis. Needle biopsy of hepatic lesions were consistent with GA, positive for CK7, CK19, CDX2 and negative for TTF -1, insulin, synaptophysin, and chromogranin. Meanwhile, severity of HG as well as hypocalcemia worsened. As an outpatient, she received radiation therapy (RT) followed by chemotherapy for GA. Interestingly, her HG resolved during RT, though recurred shortly after completion.

**Conclusion:** Malignant INS are rare neuroendocrine tumors with significant increased mortality. This case demonstrates prolonged survival despite malignant INS with only partial response to traditional therapy.

**Abstract #303**

PSEUDOHYPOGLYCEMIA: A DISCORDANCE IN PERIPHERAL AND CENTRAL GLUCOSE IN RAYNAUD’S

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**Case Presentation:** A 22-year-old African American man presented to the Emergency Department after a low capillary blood glucose (CBG) value of 32mg/dL was found incidentally during diabetes training as a medical assistant student. He was completely asymptomatic. He denied weight gain, surreptitious use of insulin or hypoglycemic agents. A continuous dextrose infusion was administered but he continued to have episodic hypoglycemia by CBG; although serial plasma glucose levels were never below 60mg/dL. Secondary causes for hypoglycemia were evaluated and excluded including: hypothyroidism, adrenal insufficiency, sulfonylurea and meglitinide screen. Hemoglobin electrophoresis was normal and HbA1c was 5.2%. CBG was measured with multiple Accuchek Inform II glucometers and different lots of glucose strips with minimal variation. Shortly after a 72hr fast was started, CBG level decreased to 18mg/dL. A simultaneous plasma glucose was sent to the lab for verification. Serum glucose level was 86mg/dL thus no insulin or C-peptide was obtained per protocol. Patient remained asymptomatic. Subsequent physical exam revealed cold hands and discolored fingertips. Upon further questioning, the patient recalled a previous diagnosis of Raynaud’s phenomenon while in the military. Active warming was done by placing the patient’s gloved hand in a basin of warm water for five minutes. Repeat CBG demonstrated an increase from 18mg/dL to 57mg/dL with a verified plasma glucose of 67mg/dL. A diagnosis of
pseudohypoglycemia was made. The patient was followed with plasma glucose monitoring without hypoglycemia and was discharged from the hospital.

**Discussion:** Pseudohypoglycemia was first defined in 1961 by Field who referred to the discordance in peripheral and central glucose as artifactual hypoglycemia. In non-diabetic patients, true hypoglycemic episodes are characterized by Whipple’s triad (WT) of low glucose, symptoms of hypoglycemia and resolution when glucose levels return to normal. Patients with pseudohypoglycemia display lower readings on CBG which is not reflective of their true serum blood glucose level. In the setting of Raynaud’s phenomenon, vasoconstriction causes prolonged blood transit time in the capillaries which increases glucose consumption. Other causes of pseudohypoglycemia documented in the literature that are associated with poor distal perfusion include: acrocyanosis, vasculitis and hemoglobinopathies.

**Conclusion:** Pseudohypoglycemia continues to be under recognized amongst health care professionals. Physicians should be aware of the limitations of glucose testing by CBG before proceeding to more extensive, cumbersome and costly investigations.

**Abstract #304**

**A CASE OF SEVERE PSEUDOHYPOGLYCEMIA**

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**Objective:** To describe a case with severe pseudohypoglycemia.

**Methods:** Pseudohypoglycemia is a condition when there is a low capillary glucose value but a normal venous plasma glucose level. We report a patient with severe asymptomatic pseudohypoglycemia with glucose of <20 mg/dL secondary to mixed connective tissue disease (MCTD). To our knowledge, there are only two reported cases of severely false low fingerstick glucose levels from 20 mg/dL due to MCTD worldwide.

**Case Presentation:** A 48-year-old African-American man with a past medical history of congestive heart failure (CHF), and popliteal deep venous thrombosis was noted to have multiple episodes of hypoglycemia during admission for acute exacerbation of congestive heart failure. Point-of-care fingerstick whole-blood glucose readings showed multiple blood sugar levels less than 45 mg/dL (fasting and postprandial) with the lowest less than 20 mg/dL over a span of five days during his admission. The patient remained asymptomatic during these hypoglycemic episodes. Physical exam was significant for bilateral dusky bluish fingertips with sclerodactyly and digital pitting ulcers suggestive of mixed connective tissue disease. Rheumatology ruled out Raynaud’s phenomenon due to constant change in fingertip color. His radial pulses were normal on palpation. Endocrinology was consulted for evaluation. The medical team was recommended to check fingerstick and plasma glucose at the same time. The point-of-care fingerstick showed glucose of 23 mg/dL, while plasma glucose taken at the same time came back as 79 mg/dL.

**Discussion:** In mixed connective tissue disease, there is destruction of capillary walls and fibrosis that leads to decreased blood flow in the digits. Pseudohypoglycemia occurs when there is reduced blood flow to the digits prolonging the availability of glucose in the capillaries, which allows for increased glucose uptake in tissues and causes falsely low fingerstick glucose measurements. Pseudohypoglycemia has also been reported in other medical conditions such as hypothermia, shock, and Raynaud’s phenomenon. Hypoglycemia in these patients needs to be confirmed by venous plasma sample. Alternate site testing at forearm can also be used to test glucose levels in these patients if they have diabetes and monitoring of blood sugars is required at home.

**Conclusion:** Mixed connective tissue disease can cause falsely low point-of-care fingerstick capillary blood glucose. It is important for healthcare providers to be aware of medical conditions leading to falsely low fingerstick glucose levels to prevent unnecessary testing, to use alternative glucose measurement sites, and to defray healthcare costs in persons with asymptomatic hypoglycemia.

**Abstract #305**

**ICED IN: A RARE CASE OF FOCAL NEUROLOGICAL DEFICITS IN THE SETTING OF HYPOGLYCEMIA**

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**Objective:** Hypoglycemia can present with an array of signs and symptoms, most common of which are diaphoresis, anxiety, palpitations, confusion and very rarely focal findings such as hemiplegia and aphasia. The most feared outcome, brain death, is caused by brain fuel deprivation leading to functional brain failure. Symptoms vary as the severity of hypoglycemia progresses. If not treated, hypoglycemia may lead to irreversible and life altering changes. This case demonstrated a less common presentation of severe hypoglycemia mimicking a cerebral stroke.

**Case Presentation:** The patient is a 64 year old African-American woman with a history of steroid induced hyperglycemia; she was taking prednisone for four years.
following a renal transplant owing to hypertensive kidney disease. At home she uses insulin and nebulizer treatments for her COPD. Due to her failing transplant, hemodialysis was re-initiated; she was often non-compliant with the dialysis schedule and was admitted multiple times with fluid overload. During her hospital stay, she was found to be acutely nonverbal and with a complete left sided hemiparesis. Moreover, she was able to follow commands but was aphasic. When asked to protrude her tongue, there was right sided deviation. Her finger stick glucose level was 43 mg/dL. She was then given glucose 25 grams IV; within five minutes an immediate transition was noted as her left upper extremity began to twitch. This twitching soon led to a return of coordinated movements with full strength and the aphasia resolved. Repeat finger stick glucose level was 173 mg/dL one hour later. Due to her rapid improvement no imaging was done. Throughout her hospital course she had no evidence of infection, nor was she on any insulin products which could have led to this hypoglycemia.

Conclusion: Hyperglycemia and hypoglycemia can both cause symptomatic neurological status changes. Therefore, changes in blood glucose concentrations should always be considered when evaluating patients with altered mental status or suspected strokes. Hypoglycemia can mimic middle cerebral artery strokes as we have seen in this case. It is important to note that the possibility of a transient ischemic attack in this case cannot be excluded. Failure to check blood glucose levels in the setting of an apparent stroke may lead to the unnecessary and potentially life threatening administration of tissue plasminogen activator. This case demonstrated a rare cause of severe hypoglycemia mimicking a cerebral stroke that resolved completely after the administration of glucose.

Abstract #306

THE EFFECT OF GLUCOMANANN SOLUBLE FIBER ON POSTPANDRIAL GLUCOSE AND INSULIN IN PATIENTS WITH ROUX-EN-Y GASTRIC BYPASS SURGERY

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Objective: Hyperinsulinemic hypoglycemia is one of the complications found in Roux-en-Y (RNY) gastric bypass patients. Currently, there is no standard treatment or prevention of this condition. Glucomannan is a dietary fiber that has viscosity property. We performed a pilot study using Glucomannan soluble fiber assessed its effect on postpandrial plasma glucose and insulin.

Methods: Adults who had undergone RNY gastric bypass and reported one or more episodes of hypoglycemia anytime post-surgery were included. At baseline stage, all patients received continuous glucose monitoring (CGM) device placement for five days. They were also given mixed meal tolerance test (MMTT), which comprising of standard meal dose of protein, carbohydrate, and fat. At treatment stage, all participants received 5 grams of Glucomannan soluble fiber treatment with regular meals and with MMTT. CGM data, and plasma glucose and insulin levels at 20, 30, 60, 90, 120 minutes post MMT were compared between two stages.

Results: Ten subjects completed the study and were included in the final analysis. From CGM data, there was no difference in the total number of daily excursions <70 mg/dL, nor did the total number of daily abnormal glucose excursions (hypoglycemic <70 mg/dL, plus hyperglycemic >180 mg/dL). From MMTT, there were significantly higher glucose readings at 60, 90, and 120 minutes post-meal with glucomannan as compared to baseline. There was also significantly lower insulin reading at 30 minutes post-meal with glucomannan.

Conclusion: Glucomannan soluble fiber seems to increase delay post-prandial glucose and decrease plasma insulin in post RNY gastric bypass patients. However, it does not prevent hypoglycemic episode. Large randomized-controlled trial will help answer the efficacy of glucomannan as one of potential treatment for postprandial hypoglycemia.

Abstract #307

FASTING-EVOKED EN-ROUTE HYPOGLYCEMIA IN DIABETES (FEEHD): AN OVERLOOKED IATROGENIC FORM OF HYPOGLYCEMIA IN CLINICAL PRACTICE

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Objective: Hypoglycemia is difficult to predict or prevent during the course of diabetes management. Preventable factors should always be sought and eliminated as a prevention measure. Missing breakfast while fasting for lab tests (e.g. lipid profiles) may invoke hypoglycemia if patients taking hypoglycemic medications are not properly informed. This form of hypoglycemia has been recently reported in few small studies, and was referred to as fasting-evoked en-route hypoglycemia in diabetes (FEEHD). A small pilot study by our group confirmed a
ABSTRACTS – Hypoglycemia

high prevalence of FEEHD, 27.1% in clinical practice. This study was designed to evaluate the prevalence of FEEHD in clinical practice.

Methods: We surveyed patients at 2 busy community diabetes clinics (Mid-Michigan Endocrine Consultants, in Flint and Lapeer, Michigan), utilizing a simple, 2-page questionnaire inquiring about any hypoglycemic episodes which occurred while fasting for labs in the preceding 12 months.

Results: A total of 429 patients with diabetes completed the survey. The mean age was 60.4(SD 13.3) years (18 to 90), 220 (51.3%) patients were females and 344 (80.2%) had type 2 diabetes. A total of 407 patients were on hypoglycemia-inducing medications (sulfonylureas and/or insulin with or without other anti-diabetic medications). Notably, 245 (57.1%) patients reported having experienced at least one hypoglycemic episode during the prior 12 months. Of the total patients at risk of hypoglycemia (n=407), 47 (11.5%) patients reported having one or more FEEHD events during the same period. This means that FEEHD contributed to 19% of all hypoglycemic events. Only 24 of FEEHD patients (51%) recalled having contacted their provider regarding the episode, and only 22 (46.8%) indicated having received some sort of FEEHD-prevention instructions.

Discussion: Our study shows a significant prevalence of FEEHD related events in the real world (clinical practice). Hypoglycemia is the rate-limiting factor in diabetes management, but FEEHD is especially dangerous as patients often have to drive to and from the laboratory facility. It also shows that we are not sufficiently educating our patients to change medication doses, when fasting tests are ordered. In parallel, recent studies have indicated that fasting for lipid panels may not be necessary. Recent position statements and guidelines from Europe and Canada have called for elimination of the fasting prerequisite for lipid profiles for most patients.

Conclusion: In view of the high prevalence of FEEHD in clinical practice, it may now be the time to change practice guidelines in the United States for the fasting requirement for laboratory orders (in particular lipid profiles) in patients with diabetes.

Abstract #308

PROINSULINOMA: A RARE CAUSE OF REACTIVE HYPOGLYCEMIA

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Objective: Pancreatic islet cell tumors are a rare cause of hypoglycemia. These tumors typically secrete insulin resulting in symptomatic sporadic hypoglycemia that occurs independent of meals, although rarely post prandial hypoglycemia has been observed. We present a case of a female with progressively severe reactive hypoglycemia due to a proinsulinoma.

Case Presentation: A 41 year old previously healthy woman was referred for evaluation of hypoglycemia. The patient presented with symptoms of disorientation, erratic behavior with flailing arms and bilateral leg weakness at work. Paramedics were called and a point of care blood glucose was 46 mg/dl. The patient was treated with parenteral glucagon and oral glucose gel with resolution of symptoms. A similar episode occurred six months prior and neurological evaluations including MRI brain scan and EEG were normal. The patient was provided with a glucometer for self monitoring and noted her blood glucose levels were lowest in late mornings about two hours after breakfast. She has never woken at night with symptoms of hypoglycemia and did not need to eat at night. However she started to eat frequent small meals to maintain her blood glucose level during the day. Initial investigations showed normal serum electrolytes, cortisol, thyroid, renal and liver functions. Two hours after a large oral carbohydrate load, blood glucose was 50mg/dl (70-99), beta-hydroxybutyrate 0.9mg/dl (0 – 3.0), insulin 10mU/l (2-22), C-peptide 2.4ng/ml (0.8 – 5.2) and proinsulin 137.8pmol/l (<8.0). After a fourteen hour fast, blood glucose was 53mg/dl, C-peptide 1.8ng/ml, insulin 7mU/l and proinsulin 127.5pmol/l. Data from a Continuous Glucose Monitor (Dexcom G4) showed stable overnight glucose levels in the range of 55-70mg/dl without symptomatic hypoglycemia whilst significant post prandial hypoglycemia was seen during daytime. Patient had to eat every one to two hours to prevent hypoglycemia symptoms. A repeat fourteen hour fast showed blood glucose 53mg/dl, C-peptide 1.8ng/ml, insulin 7mU/l and proinsulin 127.5pmol/l. Data from a Continuous Glucose Monitor (Dexcom G4) showed stable overnight glucose levels in the range of 55-70mg/dl without symptomatic hypoglycemia whilst significant post prandial hypoglycemia was seen during daytime. Patient had to eat every one to two hours to prevent hypoglycemia symptoms. A repeat fourteen hour fast showed blood glucose 53mg/dl, C-peptide 1.8ng/ml and proinsulin 137.8pmol/l. A CT scan of the pancreas showed a 1.6 cm well-defined hypervascular lesion in the distal pancreas. Patient underwent successful laparoscopic tumor enucleation. Pathology showed a grade 1 neuroendocrine tumor with less than 2% ki-67 proliferation index. Her hypoglycemia symptoms resolved post operatively.

Conclusion: Insulinoma generally produces both insulin
and proinsulin in excess, causing sporadic hypoglycemia. Our patient demonstrated that an islet cell tumor secreting proinsulin can cause predominantly reactive hypoglycemia.

Abstract #309

HYPOGLYCEMIC SYNDROME SECONDARY TO MULTIPLE PROINSULIN PRODUCING PANCREATIC TUMORS: ABOUT A CASE

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Results: Pancreatic neuroendocrine tumors are a rare group of tumors originated from pancreatic islet cells, which may be classified as functional or non-functional depending of the presence or absence of hormonal production. Among the functional, insulinomas are the most frequent pancreatic neoplasm (annual incidence of 1-4 for each 1,000,000 among general population). Most of them are solitary, sporadic, benign and 90% measure less than 2 cm.

We report a case of a 30 year-old male patient who presents the Whipple triad with adrenergic and severe neuroglycopenic symptoms, such as hunger, sweat, anxiety and tremor, that concluded in a tonic clonic seizure, with relaxed sphynters, eye rolling and drawling, lasting for more than 5 minutes. Serum glucose was 6 mg/dl, insulin: 65.7 mU/ml, C peptide: 8.0 ng/ml, and a Glasgow score of 10/15. The patient denied consuming alcohol or drugs prior to this episode, but referred having a similar episode 8 months ago. An abdominal CT scan was performed, finding two masses with pancreatic reinforcement, suspecting the presence of multiple insulinomas, being surgical resection the best treatment. Brain TC was normal, and the electroencephalogram noted the presence of chronic encephalopathy. Surgical resection was the best treatment. Brain TC was normal, and the electroencephalogram noted the presence of chronic encephalopathy. Surgical resection was performed, obtaining 3 nodules, the biggest one measuring 1.5 x 1.5 cm, 1 cm x 1 cm, and 0.5 cm x 0.6 cm. Pathological analysis described well differentiated cells with endocrine pattern, positive for proinsulin staining. After surgery, the hypoglycemic episodes ceased, and there was no evidence of tumor recurrence in the following evaluations.

Conclusion: Only 10% of insulinomas are multiple, and insulinomas that only secrete proinsulin are extremely rare (existing only 6-9 well reported cases in the revised literature); therefore we considere this an interesting and unique case.

Abstract #310

AN UNUSUAL CAUSE OF HYPOGLYCEMIA IN A CHILD WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Case Presentation: A 4 year old girl, on maintenance chemotherapy for acute lymphoblastic leukemia (ALL), was referred for evaluation of repeated hypoglycemic episodes for last 1 month. She was diagnosed to have ALL (B cell) one and half years back. She was in National Cancer Institute (NCI) high risk group for ALL with baseline WBC ≥50,000 per µL. She received chemotherapy as per Childhood Oncology Group (COG) AALL0232 (high risk study) protocol along with high dose methotrexate for 6 months. She underwent cranial irradiation for CNS involvement at the end of six months of chemotherapy. She has been on maintenance chemotherapy with 6-mercaptopurine (MP) and methotrexate for last 11 months. The maintenance therapy regimen also included oral prednisolone 12.5 mg twice daily for 5 days every 4 weeks. For last one month she developed symptoms of nausea, shivering and sweating in the morning that subsided after eating. Her fasting plasma glucose (FPG) was found to be 64 mg/dl. Subsequent blood glucose monitoring at home revealed daily occurrence of night time and early morning hypoglycemia (<70 mg/dL). The lowest documented glucometer reading was 42 mg/dL. Investigations revealed FPG of 59 mg/dL with a corresponding serum insulin level of 1.3 µU/mL, serum C-peptide level of 0.43 ng/ml and serum cortisol level of 17.1 µg/dL. Thyroid function tests and IGF-1 level were in normal range. These results ruled out insulin dependent hypoglycemia and hypocortisolism. The ultrasonography of abdomen and chest radiograph were normal. On the basis of above findings a diagnosis of MP induced hypoglycemia was made. The girl was put on complex carbohydrate and high protein diet and MP dose was shifted to morning. This resulted in partial improvement in hypoglycemia.

Discussion: Hypoglycemia due to MP, during maintenance phase of ALL, is an established but rare side effect. Medline search revealed only 3 case reports and 3 case series of purine analogue (MP or 6-thioguanine) induced hypoglycemia in ALL. Possible mechanisms of hypoglycemia due to MP are reduced hepatic glycogen stores and low levels of gluconeogenic amino acids, especially alanine. A correlation between hypoglycemia and 6 methyl-mercaptopurine, an inactive metabolite of MP, has been suggested. To prevent hypoglycemia, complex carbohydrate containing food should be given at bedtime.
Conclusion: Hypoglycemia due to MP is a rare complication observed during maintenance therapy of ALL. Dietary modification and morning dosing of MP can partially improve hypoglycemia.

Abstract #311

INSULIN AUTOIMMUNE SYNDROME AS A CAUSE OF RECURRENT HYPOGLYCEMIA: A CASE REPORT

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Objective: Autoimmune syndromes are a rare cause of hypoglycemia characterized by elevated levels of insulin in the presence of antibodies directed to endogenous insulin or to the insulin receptor. Most cases of Insulin Autoimmune Syndrome (IAS) have been reported in Japan and our case is one of the very few IAS cases reported from India. Though IAS is a rare entity, it should be considered as differential diagnosis of hyperinsulinemic hypoglycemia.

Case Presentation: We report a case of a 48 year old non diabetic Indian female who presented with recurrent episodes of spontaneous fasting and postprandial hypoglycemia with symptoms of palpitations, sweating, tremors and anxiety, relieved by carbohydrates ingestion. During the episodes, her blood gluoses were in the range of 40 to 60 mg/dL.

Past medical history was significant for hypertension treated with telmisartan and amlodipine. There was no history of use of any sulfhydryl containing drugs. The patient had a family history of diabetes mellitus in her mother. Physical exam was unremarkable with a BMI of 26.5 kg/m2.

Patient underwent a supervised fast which was terminated after 10 hours at patient’s request with a plasma glucose of 56 mg/dL and corresponding serum insulin level of >3000 μU/mL (2-25) & C-peptide of 10.53 ng/mL (0.81-3.85). Her renal function, liver function tests, thyroid profile, hemogram and serum protein electrophoresis were normal. Tests for anti-thyroid antibodies, rheumatoid factor and antinuclear antibodies were negative. Her HbA1C was 5.7 % & AM cortisol was 17μg/dL.

Her abdominal imaging including ultrasound, contrast enhanced CT scan and non contrast MRI did not reveal any mass lesion.

Serum Insulin Antibodies were measured by enzyme immunoassay (EIA) and were found to be 37.3 U/mL (<12) and diagnosis of IAS was made. She was put on a low carb diet with small frequent meals to reduce stimulus for insulin secretion but her hypoglycemic episodes continued at lower frequency, thus, she was started on acarbose and her symptoms gradually disappeared on two months follow up.

Discussion: Insulin Autoimmune Syndrome, also known as Hirata disease, is a rare cause of endogenous hyperinsulinemic hypoglycemia characterized by autoantibodies to endogenous insulin without previous exposure to exogenous insulin. IAS may be associated with other autoimmune diseases like Grave’s disease. In 80% of patients, IAS is a transient condition with spontaneous resolution within 3 to 6 months of diagnosis.

Conclusion: IAS should be considered as a differential diagnosis in all the patients with endogenous hyperinsulinemic hypoglycemia so that appropriate diagnosis can be made in a timely manner and unnecessary investigations and interventions can be avoided.

Abstract #312

A CASE OF SILENT PANCREATIC NEURO-ENDOCRINE TUMOUR OF CARCINOID VARIETY MASQUERADING AS AN INSULINOMA

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Objective: To highlight an unusual cause of hyperinsulinaemic hypoglycemia

Methods: Case Report

Case Presentation: A previously healthy and fit 52 year old gentleman of Asian descent presented with recurrent severe neuroglycopenic hyperinsulinemic hypoglycemic symptoms, suggestive of insulinoma. On several occasions he was confirmed to have severe hypoglycaemia with venous blood glucose values ranging between 1.5 to 2.7 mmol/l with inappropriate high level of insulin and C-peptide of 32 mc/unit/ml (N. 2-23) & 4.5 ng/ml (N. 0.78-5.19) respectively. Other hormonal assessment including pituitary hormones, chromogranin A, urinary 5-HIAA, and cortisol were all normal. CT imaging picked up a 4x4 cm well circumscribed lesion in the tail of the pancreas, with no lesion elsewhere. Endoscopic ultrasonography confirmed the mass to be avascular and within the pancreas. He underwent laparoscopic distal pancreatectomy uneventfully in February 2016. Histology of the tumour showed a well differentiated neuroendocrine tumour of a carcinoid variety, grade 2, with positive staining for chromogranin A, and Synaptophysin CK. Following surgery, the patient had no further
hypoglycemia and remained symptom free up to 9 months of follow up. Postoperative PET scan and CT scanning of chest, abdomen and pelvis showed no recurrence of the tumour, and no lesion elsewhere.

Discussion: Non-islet cell tumours induced hypoglycemia is generally caused by big IGF-II molecules secretion. Rarely carcinoid tumours were reported to secrete insulin but this is usually in the context of carcinoid syndrome and has been reported to arise from tumours in the lungs, appendix and the liver. For a silent pancreatic carcinoid tumour to cause hyperinsulinaemic hypoglycemia is rather unusual. Plausible mechanisms include processing and secretion of insulin from tumour cells. Alternatively secretion of insulin from adjacent islet cells may have been caused by paracrine effects. The exact mechanism in our case, however, only remains speculative.

Conclusion: Tumours of the pancreas causing hypoglycemia may not necessarily be insulinoma. Silent neuroendocrine tumour of the carcinoid (Argantafinoma) variety may be the culprit.

Abstract #314

HYPOGLYCEMIC AND HYPOKALEMIC SYNDROME ASSOCIATED TO A FIBROUS TUMOR OF THE PLEURA: ABOUT A CASE OF THE DOEGE POTTER SYNDROME

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Results: The Doege-Potter syndrome, characterized by the occurrence of hypoglycemic episodes associated to a fibrous solitary tumor of the pleura is very uncommon, even to a greater scale when finger clubbing is present, such as in the Pierre-Marie-Bamberg syndrome. Since 1981, less than 65 cases of Doege Potter Syndrome have been published in the English literature. Paraneoplastic hypoglycemia is present in only 5% of the solitary fibrous tumors of the pleura, and just 20% are found to be malignant. There has only been 1
reported case of Doege-Potter Syndrome with hypokalemia in the revised literature. We present the case of a 69-year-old female patient, with a tumor that occupies 80% of the left hemithorax, associated to hypoglycemic episodes with low concentrations of insulin and C peptide, as well as hypokalemia unresponsive to treatment. Biopsy of the tumor indicated the presence of a fibrous solitary tumor of the pleura. Complete surgical resection was performed, obtaining a 28x24x15cm tumor with macroscopic areas of necrotic appearance. Histological examination revealed spindle cells with moderate nuclear and cellular pleomorphism, alternating with a hemangiopericytoma-like vascular pattern, 5-6 mitotic figures per 40x fields, with necrotic areas. The cells stained positive for CD-34, vimentin and Bcl-2. These findings determined malignancy of the tumor. The patient, as well, was found to have finger clubbing during physical examination. The hypoglycemic episodes ceased during the postoperative, and the concentrations of IGF-II and potassium came back to normal. The chosen treatment to prevent recurrence of the symptoms and improve prognosis is complete surgical resection. Nineteen months after surgery, there have not been any hypoglycemic episodes and there is no evidence of tumor recurrence. Conclusion: Hypoglycemic episodes in these patients can be explained due to the secretion of a high molecular weight IGF-II by the tumor cells that activates insulin receptors, therefore stimulating the metabolic effects of this hormone. It is important to note that insulin and C peptide concentrations during the hypoglycemic episodes can be low or even suppressed. This IGF-II as well has the capability to induce the intracellular entrance of potassium, explaining the hypokalemia that can be present. Finger clubbing is the result of chronic hypoxia induced by these tumors, as well as the increased concentrations of cytokines like VEGF and PDGF. It is important to know that not only insulinomas cause paraneoplastic hypoglycemias, but a wide variety of non-islet cell tumors are capable of producing hypoglycemic episodes, such as fibrous solitary tumors of the pleura.

Abstract #315
SEVERE HYPOGLYCEMIA IN TYPE 2 DIABETICS REQUIRING HOSPITALISATION AND SHORT TERM MORTALITY
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Objective: We planned a prospective study to see short term mortality in diabetic patients with severe hypoglycaemia requiring hospitalisation in view of paucity of Indian data. Methods: A prospective study of diabetic patients with severe hypoglycaemia requiring hospitalisation and short term mortality outcomes in these patients as a primary end-point and study of the clinical profile, risk factors. Total 50 patients were enrolled in the study. We included diabetic patient presenting to the hospital with plasma glucose ≤ 70 mg/dl with altered consciousness and assessed by the physician that patient requires hospitalization for correction of hypoglycaemia and excluded those with malignancy/acute cerebrovascular event/symptomatic congestive heart failure/eGFR < 10.

Results: Most episodes of hypoglycaemia were observed in patients with type 2 diabetes (82%). Mean age of type 1 diabetes was 31.77±8.9 years and mean age of type 2 diabetes was 65.97±10.5 years. All patients presented to the emergency department with unconsciousness/altered behaviour and the mean plasma glucose was 36.62 ± 11.57 mg/dl. Fourteen patients had a previous admission with hypoglycaemia. Out of 50 patients, 26 were illiterate and 30 did not have knowledge about hypoglycaemia. Seventeen were on single drug (insulin or a sulfonylurea), 19 were on two drugs and 14 were on three or more drugs. Most often prescribed drug was sulfonylurea (32). Thirty two patients had a creatinine clearance <60 ml/min/1.73 m2. The mean creatinine clearance was 55.83 ± 26.5. The mean HbA1c was 8.58 ± 1.94%, glycemic variability may be the reason for relatively high HbA1c in our study. Followup up to 90-days all-cause mortality was 8% and all
were type 2 diabetic. This suggests that severe hypoglycemia is an important risk factor for short term increase in all-cause mortality particularly in type 2 diabetes.

**Conclusion:** Total in-hospital mortality was 4%, and 90-days all-cause mortality was 8%. As all patients who died were type 2 diabetics, all cause mortality was 9.7% in this group.

**Abstract #316**

**HYPOGLYCEMIA WITH PROLONGED APHASIA**

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**Objective:** Typical neurogenic symptoms of hypoglycemia include diaphoresis, increased hunger, and tachycardia, while neuroglycopenic symptoms consist of fatigue, blurry vision, and altered mentation. Hypoglycemia-induced neurological symptoms are relatively uncommon. The patient described in this case experienced aphasia associated with hypoglycemic state, a particularly rare focal neurological deficit.

**Case Presentation:** A 30 year old man with a four-year history of type 2 diabetes presented after an episode of hypoglycemia and persistent aphasia. The patient had a history of severe insulin resistance and had been taking insulin glargine 100 units bid, along with regular U500 insulin (U500), 250 units tid. On the day of hypoglycemia, fingerstick glucose was 59 mg/dl, but when rechecked on different glucometer, read “Hi”. A dose of 100 units of U500 was self-administered, and about one hour later a glucose reading of 49 mg/dl was recorded and new onset aphasia occurred. Evaluation in the emergency department, including CT, MRI/MRA of the brain was unremarkable. Six days after the event, the patient had persistent symptoms of severe dysarthria, where he was unable to make more than minimal grunting sounds, though cognition appeared to be intact. Patient was referred for speech therapy.

**Discussion:** There are several proposed mechanisms for hypoglycemia-induced focal neurological deficits, including cerebral vasospasm, regional differences in neuronal susceptibility to hypoglycemia due to variations in cellular metabolism and cerebral vasculature, and uneven cerebral blood flow in the setting of underlying cerebrovascular disease. This case highlights an unusual manifestation of hypoglycemia. The most prevalent hypoglycemia-induced neurological deficit is hemiplegia, which can be associated with aphasia. Hypoglycemia-induced neurological symptoms also typically promptly subside after the administration of glucose and resolution of hypoglycemia. Our patient experienced persistent aphasia, with ongoing symptoms six days after the hypoglycemic episode. Prolonged aphasia has been described in previous case studies in the setting of hypoglycemic coma, in contrast to our patient who had preserved mentation. There are no consistent findings on brain imaging in association with hypoglycemia-induced neurological deficits, as in our patient who did not have any abnormalities on brain CT or MRI.

**Conclusion:** Focal neurological deficits are an uncommon manifestation of hypoglycemia. Symptoms often abate with normalization of blood glucose level. The case highlights the possibility of prolonged aphasia despite re-establishment of normoglycemia.

**Abstract #317**

**COMPUTER BASED INSULIN INFUSION ALGORITHM IMPACT ON GLYCEMIC CONTROL IN CRITICALLY ILL PATIENTS**

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**Objective:** Computer-Based Insulin Infusion Algorithm (CBIIA) is an FDA approved computer software program that helps clinicians and nurses calculate the dose of insulin required to achieve normoglycemia.

**Methods:** This is a retrospective, single-center, before and after with a prospective cohort at Saint Luke’s health system ICUs in Kansas City. We reviewed patients records two Quarters before and two Quarters after use of the CBIIA in four of our system ICUs.

**Results:** A total of 21971 and 22175 glucose values and 3461 and 3525 days in which a patient had at least one reportable glucose value were recorded before and after the use of the CBIIA, respectively. There was no statistically significant difference in patients days with average daily glucose in range (110-180 mg/dL) before and after CBIIA (1675 vs. 1723 days, P = 0.69). We also found no statistically significant difference between the two groups in regards to days with average daily glucose more than 180 mg/dL (622 vs. 651 days, P = 0.59), or number of hypoglycemia episodes using both thresholds of 80 mg/dL (1097 vs. 1025, P 0.07) and 50 mg/dL (107 vs. 88, P 0.15) before and after using CBIIA, respectively.

**Discussion:** The CBIIA was used as the only insulin infusion method for our ICU patients with hyperglycemia. We reviewed the records of 1334 and 1406 patients before and after the use of CBIIA, respectively. Among these there were 72 and 85 patients whose diagnosis is either DKA or HNKC and all have used the CBIIA. The assumption was
that adoption of the CBIIA will increase insulin infusion use beyond these diagnoses and for other hyperglycemic patients, and so it will lead to better glycemic control. Our data shows that neither hyperglycemia nor hypoglycemia episodes were reduced using the CBIIA. This might relate to our optimal glucose management before the adoption of CBIIA. All four ICUs in the study are monitored by the eICU. A board certified eICU critical care physician rounds twice daily on glycemic readings and is fully empowered to manage hyperglycemia or hypoglycemia in our ICUs. Also our ICUs are equipped with protocols and order sets to standardize glucose management, which along with eICU coverage could have left no room for improvement after adoption of the CBIIA.

**Conclusion:** Adoption of CBIIA in our health system ICUs didn’t result in an increase in patients days with average daily glucose in range 110-180 mg/dL or a reduction in episodes of hypoglycemia < 50 mg/dL or 80 mg/dL. Such lack of benefit might be related to optimal glucose management before the intervention.

**Abstract #318**

**ANALYSIS OF HYPOGLYCAEMIC EPISODES IN DIABETICS IN AFRICANS USING ADEMOLUS CLASSIFICATION OF HYPOGLYCAEMIA**

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**Objective:** Hypoglycaemia as a management complication of diabetes mellitus (DM) is a world wide experience. In Africa, hypoglycaemia is an uncharted territory in literature. To add to the existing knowledge therefore, the following questions will be addressed using Ademolus Classification of Hypoglycaemia (ACH). Which is the commonest and the least common grade of hypoglycaemia in DM African patients? Which grade of hypoglycaemia is seen commonly in type 1 and in type 2 DM?

**Methods:** This is a retrospective study that analyses 203 (two hundred and three) documented hypoglycaemic episodes, symptomatic or asymptomatic in Africans with DM admitted between July 2007 and October 2016 (9 years and three months period) in the medicine departments of Lagos State University Teaching Hospital, Ikeja, Lagos Nigeria. A questionnaire was used as a tool to extract relevant information from each of the relevant 50 case files studied. Hypoglycaemia was defined as a blood sugar of 70mg/dl or less. Blood sugar check was with a glucometer. Results: The age range of the patients was 18 to 95 years. Now by using ACH to analyse the 203 hypoglycaemic episodes, 45.32% had grade 1 hypoglycaemia, 35.47% had grade 2 hypoglycaemia while 19.21% had grade 3 hypoglycaemia. In all type 2 DM studied, 48.50% had grade 1 hypoglycaemia, 35.93% had grade 2 hypoglycaemia while 15.57% had grade 3 hypoglycaemia. In type 2 DM patients on insulin therapy alone, 53.54% had grade 1 hypoglycaemia, 31.50% had grade 2 hypoglycaemia while 14.96% had grade 3 hypoglycaemia. In type 2 DM on both insulin and oral hypoglycaemic agents, 33.33% had grade 1 hypoglycaemia, 48.72% had grade 2 hypoglycaemia while 17.95% had grade 3 hypoglycaemia. In type 1 DM, 30.50% had grade 1, 33.33% had grade 2 while 36.11% had grade 3 hypoglycaemia. The lowest documented hypoglycaemia amongst type 2 DM was an asymptomatic fasting blood sugar of 20mg/dl (grade 3 hypoglycaemia)!

**Discussion:** By using ACH, there was no record of grade 4 hypoglycaemia in both type 1 and type 2 DM patients in this African study possibly because most individual with DM never suffer very severe hypoglycaemia. The commonest grade of hypoglycaemia is grade 1 (mild hypoglycaemia) in type 2 DM, this is not surprising since insulin resistance is pathophysiologically an issue whereas grade 3 (severe hypoglycaemia) is the commonest in type 1 DM where exogeneous insulin is used due to insulin deficiency. The least common grade of hypoglycaemia in type 2 DM is grade 3 while in type 1 DM, it is grade 1.

**Conclusion:** Asymtomatic hypoglycaemia can occur in grade 3 among African diabetics! A similar study is recommended in Americans, Europeans, Asians and all ethnic groups for possible racial differences or disparity in the findings of this research.

**Abstract #319**

**RECURRENT HYPOGLYCAEMIC EPISODES IN A TYPE 1 DIABETIC PATIENT**

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**Objective:** This case illustrates an uncommon but an important cause for recurrent hypoglycaemia in a type 1 diabetic patient.

**Methods:** Patient was appropriately investigated as an in-patient.

**Case Presentation:** A 58 year old male patient who has type 1 diabetes for 45 years referred to the diabetic clinic with recurrent hypoglycaemic episodes for 3 years. His background history was significant for previous bariatric surgery for morbid obesity 5 years ago. He was on basal bolus regime but very small doses (Novorapid 0-1 units with breakfast, 1 unit with lunch and 1 unit with the evening meal and Lantus 2 units noite).
He had very frequent hypoglycaemic episodes (6-8 per week) including few severe ones with impaired hypoglycaemic awareness. He has required paramedic help on few occasions prior to presentation. His diet was satisfactory and there was no evidence of injection site problems. He wasn’t on any other medication. He does not smoke or drink alcohol.

Given the severity of presentation, he was admitted for further investigation and his thyroid, adrenal axis were normal. There was no suggestion of insulin secreting tumours. Urinary c-peptide creatinine ratio was <0.2nmol/ mmol. His insulin requirements in the hospital (supervised by nursing staff) were 20-25 units per day (Novorapid 6 units 3 times daily and Lantus 6 units nocte) and he did not have any hypos whilst in the hospital. On direct questioning, patient thought this enhanced insulin requirements were due to lack of exercise whilst in the hospital. However, given the fact that he did not have any hypos even on higher doses of insulin raised the suspicion of insulin abuse. On enquiring with the primary care physician and the community pharmacist, it was confirmed that patient was actually collecting 10 Novorapid pens per month (3000 units). On further discussion and counselling about the help that can be offered, patient has later admitted that he was indeed abusing Insulin for many years. Possibility of underlying mental health issues were suspected and he has been referred to clinical psychology / psychiatry services and currently is well in himself.

**Discussion:** Recurrent hypoglycaemia in a type 1 diabetic patient is in fact a common problem faced by the diabetologists and Insulin abuse should be thought of as a cause once every thing else is ruled out and an in-patient admission may be required to prove this.

**Conclusion:** This case highlights the common and uncommon differential diagnoses of the hypoglycaemia in a type 1 diabetic patient. Insulin abuse due to mental health issues is a recognised cause and should be explored with the patient in a gentle, empathetic manner offering help to come out of this.
Pseudohyponatremia is associated with normal serum osmolality. However, the plasma water fraction may fall below 80% in patients with marked hyperlipidemia or hyperproteinemia, where the plasma water sodium concentration and plasma osmolality are unchanged, but the measured sodium in the total plasma will be reduced.

**Case Presentation:** A 26 year old male was admitted for increased fatigue, jaundice and pruritus for one month. He denied recent travel, intravenous drug use, new sexual partners or alcohol consumption. He has type I diabetes mellitus. The patient was only taking insulin. The physical exam showed scleral icterus with jaundiced skin. A laboratory workup revealed a cholestatic picture. Additionally, the serum sodium was 122 mmol/L with normal osmolality, total cholesterol of 2166 mg/dL, triglyceride of 272 mg/dL, low density lipoprotein (LDL) of 2104 mg/dL and high density lipoprotein (HDL) of 8 mg/dL. The apolipoprotein B was 169 mg/dL. Hepatitis A, B, and C antibodies, Epstein-Barr antibodies, infectious mononucleosis antibodies and Human immunodeficiency virus panels were all negative. Autoimmune hepatitis antibodies were negative. Hemochromatosis gene was negative. Abdominal ultrasound revealed homogenous liver. Magnetic resonance cholangiopancreatography (MRCP) was normal. Liver biopsy was consistent with acute pericholangitis. The patient was managed symptomatically.

**Conclusion:** Cholestasis causes reflux of lipoproteins back into circulation and leads to severe hypercholesterolemia. Those lipoproteins are called lipoprotein X, an abnormal lipoprotein containing mainly albumin in the core and apolipoprotein C on the surface. It accumulates in cholestatic conditions by reflux of unesterified cholesterol and phospholipids into the circulation. Lipoprotein X can form xanthomata but it does not contain apoprotein B and therefore, high levels are not atherogenic. There is a discrepancy between apoprotein B and total cholesterol in these patients. On the other hand, pseudohyponatremia is usually seen in hypertriglyceridemia.
and paraproteinemia. However, pseudohyponatremia in association with severe hypercholesterolemia caused by elevation of lipoprotein X is extremely rare. The hypercholesterolemia causes spuriously low serum sodium levels when measured by indirect potentiometry. The presence of low serum chloride and potassium may aid the diagnosis. Treatment is usually plasmapheresis. Published data revealed only 10 cases of hypercholesterolemia and pseudohyponatremia. All patients had cholestasis with causes ranging from graft versus host disease to primary biliary cirrhosis, hepatitis C, and pancreatic cancer.

Abstract #402

P(S470C) MUTATION: A RARE VARIANT OF FAMILIAL HYPERCHOLESTEROLEMIA

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Objective: Examining the pathogenicity of the rare p(S470C) mutation causing familial hypercholesterolemia.

Case Presentation: We present the case of a 34-year-old, obese Hispanic gentleman with past medical history of depression, chronic low back pain, and PTSD. He was found to have elevated blood cholesterol with LDL level more than 250mg/dL despite treatment with a statin. He had no history of cardiovascular disease. He denied family history of hereditary hypercholesterolemia, sudden death, cardiac disease, stroke, or other vascular disease. The physical examination did not reveal any signs of xanthomas, xanthelasmas, murmurs, carotid bruits, or abdominal bruits. He denied smoking and drug use but admitted to having 3 beers daily. On initial encounter, the lipid panel showed total cholesterol of 373 mg/dL, LDL of 303 mg/dL, HDL of 49 mg/dL, and triglycerides level of 204 mg/dL. The patient had similar levels on previous labs despite intensive statin treatment. Genetic testing for familial hypercholesterolemia was performed and the patient was found to have a p(S470C) mutation in the LDL receptor gene. Based on this finding, the patient was diagnosed with familial hypercholesterolemia. A trial of rosuvastatin and ezetimibe led to a significant drop in LDL level to 125 mg/dL. Genetic counseling for patient and his family is planned.

Discussion: Familial hypercholesterolemia (FH) is a common autosomal dominant disorder characterized by elevated LDL and premature atherosclerotic vascular disease. Impaired removal of LDL in FH results from mutations in the LDL receptor, apolipoprotein B, or PCSK9 genes. The p(S470C) mutation leads to substitution of the serine residue at position 470 of the LDL receptor gene with a cysteine residue. This mutation is of unknown significance and was reported only once in a Croatian woman. Although there are no functional studies to support the pathogenicity of this variant, a genetic study concluded that the proximity of the new cysteine residue to another unbound cysteine residue can lead to the formation of a disulfide bond, consequently causing structural alteration of the receptor. Such change would disrupt the clearance of LDL and lead to atherosclerotic vessel disease. Given the rarity of this mutation, reporting of this case is noteworthy to better understand the significance of this variant. This case will also shed light on the pathophysiology, diagnosis, and management of familial hypercholesterolemia.

Conclusion: The p(S470C) mutation of the LDL receptor gene is a rare variant of familial hypercholesterolemia with unknown significance. Genetic analysis can help predict the pathogenicity of such rare and novel mutation and guide clinical decisions.

Abstract #404

GESTATIONAL HYPERTENSION AND ASSOCIATED PREDICTOR RISK FACTORS AMONG ANTENATAL POPULATION

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Objective: The aim of this study is to determine the incidence of gestational hypertension and associated predictor risk factors among a population of pregnant women.

Methods: This is a cross sectional study with a multistage sampling technique to select 192 attendants of antenatal clinic. Anthropometric parameters, variations in blood pressure and heart rates were also measured in supine and sitting positions. Data was collected using structured interviewer administered questioners. All pregnant women in the reproductive age group were included in the study.

Results: A total of 192 pregnant subjects were studied. The mean age of the subjects was 32.59 years SD± 4.771. There is positive correlation between BMI and changes in mean arterial blood pressure at rest, at 30 seconds, at 60 seconds, at 90 seconds and 120 sec. The mean BMI of gestational hypertensive and normotensive subjects were 24.19±5.12 and 34.36±10.2 respectively. Out of the total of 192 pregnant subjects studied, a significant number of the gestational hypertensive women had abnormal body mass index of 86.3% (n=36 out of 42, p<0.001) that ranged from overweight to morbid obesity while the normotensive

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women had comprised 56% (n=84 out 150, p>0.001) of the subjects. BMI, Pulse Pressure, Systolic Blood Pressure, Diastolic Blood Pressure, Mean Arterial Blood Pressure, and Age were all significantly different across the groups, with the gestational hypertensive subjects having significant levels of each one of these variables.

**Discussion:** A total of 192 participants were included in the study with 21.9% of the women having gestational hypertension while 78.1% of the pregnant women were normotensive. The incidence rate of gestational hypertensive disorder is 21.9% which is quite high for the population when compared to other studies. The mean maternal age for all the subjects differed significantly with an increased maternal age associated with gestational hypertensive disorder. This study has revealed that women with gestational hypertension had increased body mass index when compared to their counterparts without gestational hypertension. This study found that obesity is a predictor risk factor for both gestational hypertension and preeclampsia. This study also revealed a positive correlation between gestational hypertension, mean arterial blood pressure and increased body mass index.

**Conclusion:** This study revealed that obesity is a predictive factor for hypertensive disorder in pregnancy apart from increasing maternal age. Therefore, pregnant women with obesity in pregnancy should be carefully followed up to prevent late diagnosis and maternal mortality.

**Abstract #405**

**A YOUNG BOY WITH XANTHOMA – A RARE CASE OF HYPERCHOLESTEROLEMIA**

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BSMMU

**Case Presentation:** A 4 year old boy was evaluated for widespread xanthomas and marked hypercholesterolaemia [total cholesterol 1042 mg/dl, high density lipoprotein (HDL) 36 mg/dl and low density lipoprotein (LDL) cholesterol 949 mg/dl]. Xanthoma tuberum and xanthoma planum were present on flexor surface of wrists, elbows, close to the heel and sacral region since he was one. Clinical examination revealed bilateral achilis tendon xanthoma and corneal arcs. His family history was remarkable as both of his parents and only brother (7 years old) had high cholesterol level. His maternal uncle had history of acute coronary syndrome at the age of 30. Laboratory work up excluded secondary causes and diagnosis of familial homozygous hypercholesterolemia (FHH) was made. Apolipoprotein-B (Apo- B) level was high with raised Apo-B: Apo-A1 ratio. Color doppler echocardiography revealed mild aortic regurgitation with thickened aortic valve but there was no coronary arterial osteal stenosis. Bilateral coronary arterial intima-medial thickness was normal. Patient was advised for low fat diet, simvastatin 10mg and ezetimibe 10mg daily and for regular follow up. On follow up after two months, his LDL level had reduced without any adverse effects.

**Discussion:** In children and adolescents, dyslipidemia is usually secondary but very high LDL is frequently associated with primary or genetic lipid disorders. FHH is one of the rare causes, with an occurrence rate of around 1 in 100,000 individuals. Children with FHH usually present within the first decade of life, commonly evaluated for presence of clinical findings such as cutaneous xanthomas, tendon xanthoma and corneal arcs as were observed in the present case. The lipid profile is strikingly abnormal in FHH subjects – the LDL cholesterol level often in the range of 500-1000 mg/dl, with reduced HDL cholesterol level between 20–40 mg/dl which conform well to that results observed in our subject. Children with FHH have severe and early cardiovascular diseases including coronary artery disease, aortic valve disease, and atherosclerotic aortic, carotid and peripheral vascular disease. A very important issue is that no patient takes it seriously until a severe myocardial infarction (often leading to sudden death) takes place. Better outcome occurs with lipid apheresis and liver transplantation. But these facilities are yet not available in a resource poor country like ours. Hence early diagnosis and prompt medical therapy is very important.

**Conclusion:** Early diagnosis and treatment with screening of first-degree relatives is essential to minimize the cardiovascular complications in these patients.
Abstract #406

THE EFFECT OF CONGESTIVE HEART FAILURE IN OUTCOMES OF HOSPITALIZED PATIENTS RECEIVING PARENTERAL NUTRITION.

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Objective: Patients with Congestive Heart Failure (CHF) are occasionally in need of nutritional support while admitted in the hospital. Enteral nutrition should represent the first choice when CHF patients need nutritional support. This preferential enteral approach partly explains the lack of robust trials of the effect of CHF in patients receiving parenteral nutrition (PN). We hypothesized that CHF has a negative effect on outcomes in patients receiving PN.

Methods: Retrospective cohort study using the 2013 National Inpatient Sample (NIS). Patients were included if they were more than 18 years old and had an ICD-9 procedural code for PN, and were further classified into presence or absence of CHF as a comorbid condition. The primary outcome was in-hospital mortality. Secondary outcomes were length of hospital stay, total hospitalization charges, intensive care unit (ICU) admission, shock and organ dysfunction. Multivariate logistic regression was used to adjust for potential confounders.

Results: There were 179,715 patients receiving PN included in the study and 22,755 (12%) patients had the diagnosis of CHF. The mean age of the population was 62.52 SD 0.19 years and 54% were female. Patients receiving PN with CHF had an increased in-hospital mortality rate compared to those without CHF, with an odds ratio (OR) of 1.59 (Confidence interval [CI] 1.44 – 1.75, P<0.01). There was also an increase in length of stay of 2.69 days (CI: 2.18-3.20, P<0.01) and increase in total hospital charges of 34,455 US dollars (CI: 27627-41283, P<0.01). Patients with the diagnosis of CHF also showed increase in the rate of ICU admission (OR 2.18 CI: 2.02-2.36, P<0.01), increased rate of shock (OR 1.89 CI: 1.73-2.07, P<0.01) and increased rate of organ dysfunction (OR 2.08 CI: 1.94-2.24, P<0.01).

Discussion: As we hypothesized, patients receiving PN who had CHF had increased in-hospital mortality compared to patients who received PN without CHF. There was also an increase in morbidity evidenced by higher rate of ICU admission, shock and organ dysfunction. These outcomes were also translated into increased resource utilization evidenced by longer length of stay and higher hospital charges. These worsening outcomes may be explained by the concern of fluid overload for these patients with reduced cardiac function while receiving IV nutrition. This study should prompt further discussion on the risks vs benefits of PN in patients with CHF.

Conclusion: Patients receiving PN had increased in-hospital mortality, morbidity, length of stay and hospitalization charges when they had CHF as a comorbid condition.
METABOLIC BONE DISEASE

Abstract #500

TRANSIENT SEVERE HYPERCALCEMIA DUE TO THE MILK-ALKALI SYNDROME

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Objective: To describe a case of severe hypercalcemia due to excessive calcium carbonate intake.

Case Presentation: An 80-year-old woman was brought to the hospital after having fallen at home. She had a one week history of weakness, fatigue, and poor appetite. She reported an intentional 40-pound weight loss over the past year, and admitted that she had refused any cancer screening tests as an adult. Home medications included hydrochlorothiazide, losartan, and metoprolol. She appeared lethargic and mucous membranes were dry; lab results showed elevated levels of calcium (20.3 mg/dL), carbon dioxide (34 mEq/L), blood urea nitrogen (38 mg/dL) and creatinine (1.69 mg/dL). PTH was low (8.4 pg/mL), and levels of phosphorus, magnesium, 25-hydroxyvitamin D, and TSH were normal. Treatment was initiated with normal saline, furosemide, and subcutaneous calcitonin. Over the next two days the calcium and PTH levels normalized and patient clinically improved. Additional lab results from admission returned with low calcitriol (12 pg/mL), normal SPEP, and normal PTH-rP. Upon further questioning, the patient admitted to regular use of calcium carbonate antacids, but would not quantify the daily intake. Her family reported that she might have been finishing a whole bottle of antacids every few days.

Discussion: Milk-alkali syndrome (MAS) is characterized by hypercalcemia, renal insufficiency and metabolic alkalosis, associated with large amounts of calcium and absorbable alkali intake. The increased availability and use of calcium carbonate preparations has caused a resurgence of this entity. Though the exact prevalence of MAS is unknown, in one series it was the second most common cause of severe hypercalcemia in hospitalized patients. In this elderly patient who presented with weight loss and PTH-independent severe hypercalcemia, malignancy was the initial presumed diagnosis. Ultimately the presence of metabolic alkalosis and renal insufficiency on presentation, along with the rapid correction of hypercalcemia with the discontinuation of calcium carbonate, confirmed the diagnosis of MAS. In this patient, risk factors for MAS included advanced age, treatment with a thiazide diuretic, and dehydration.

Conclusion: We present a case of unusually severe hypercalcemia that was presumed to be related to malignancy but proved to be due to MAS. In this era of increased use of calcium carbonate for bone health, as well as its ongoing use in the treatment of heartburn, patient education should be provided regarding safe dosing guidelines. A detailed history of supplement use is an important step in the evaluation of hypercalcemia.

Abstract #501

ATYPICAL FRACTURE OF FEMUR DESPITE BIS-PHOSPHONATE HOLIDAY

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Objective: Bisphosphonates are widely used in the treatment of osteoporosis. Two side effects associated with their use include osteonecrosis of the jaw and atypical femoral fractures (AFF). The incidence of AFF is fairly low. For bisphosphonate treated patients, the incidence is reportedly less than 2/100,000 person-years provided they have been on treatment for less than 2 years; however the risk does go up to as high as 113/100,000 person-years with treatment longer than 9 years. AFF are thought to occur with prolonged use of bisphosphonates and impaired bone remodeling as a result of suppression of bone resorption. This is considered to predispose patients to spontaneous non vertebral fractures and has led to the recommendations that a bisphosphonate holiday be considered in some patients.

Case Presentation: The patient is a 69 year old female who was first diagnosed with post menopausal osteoporosis in 2008 at the age of 61. She had never had fragility fractures and had not been on any hormonal therapy. She had an adequate amount of calcium and Vitamin D in her diet. She was started on Alendronate by her Primary care physician but developed gastric reflux, and had to discontinue it in a few months. She was then given intravenous zoledronic acid in November 2008, May 2010 and September 2011. She was first referred to the Endocrinology clinic in 2014 after a 3 year holiday. She had a bone densitometry which showed a T score of -3.6 in lumbar area and a T score of -2.3 in the femoral neck. Given the low bone density, she received another injection of zoledronic acid in 2014 and then again in October 2015.

In March of 2016, she developed pain in her left upper leg after swinging out of a car. She continued to have pain for a number of months which was treated with manipulation without help. She finally saw an orthopedist in September 2016 who diagnosed her to have a stress fracture of the right femur. This is being treated conservatively and she is clinically improving.

Conclusion: Most AFF are treated surgically, although some may be treated medically with anabolic agents such as teriparatide or with non-weight bearing in patients with an
incomplete fracture and minimal pain. It however seems the prevention might be more relevant. Most guidelines recommend that bisphosphonate therapy be reassessed in 3-5 years and patients be given a drug holiday based on their risk for fractures. That said, AFF have been reported even in patients who have been on drug holidays for 4 years. This patient clearly demonstrates both the need to consider AFF in a patient on bisphosphonates who presents with thigh pain and also our poor understanding on how to prevent them.

Abstract #502

FACTITIOUS HYPERCALCEMIA, CHEESE-THIAZIDE SYNDROME

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Methods: Background: Milk-alkali syndrome is an uncommon cause of hypercalcemia, but well reported in the literature. We are reporting an unusual cause of factitious hypercalcemia

Case Presentation: A 77 year old man was seen for hypercalcemia. He has chronic fatigue, constipation and severe osteoarthritis. The later makes him wheelchair dependent and on chronic opioid use. His wife reports 6 months of mild confusion. Recent intentional weight loss, 15 lb, by diet was reported also. Dietary history showed that he has been eating 2 pounds of cheese every 5 days for few years. He denied taking any anti-acid or excessive vitamin D. He was on Hydrochlorthiazide 12.5 mg a day for HTN since 1980s and Calcium 500mg BID. Few weeks before the Endocrine consult, Calcium was 12.4 mg/dL and was managed by IV hydration in the ER. No history of thyroid, parathyroid, Paget’s disease in the family. Colonoscopy was negative for malignancy in the last year. Albumin-corrected Calcium range was 10.6 to 12.4 mg/dl in the last 5 months. Calcium level had been normal before that. Given the excessive cheese intake, with its high calcium content, and Thiazide use, we decided to adjust the diet and hold Thiazide before doing extensive work up. The work up showed: PTH: 4 pg/ml with Calcium: 11.8 mg/dl, PO4: 3.4 mg/dl, 25-OH Vitamin D: 39.4, Vitamin D 1, 25 (OH)2 total: <8 pg/mL, TSH: 1.639 uU/ml, ACTH stimulation test showed normal adrenal response, Vitamin A: 136 mcg/dL, LDH: 122 U/L, PTH-RP: 21pg/mL, SPEP: normal and PSA: 0.8 Patient was advised to stop taking Hydrochlorthiazide, Calcium, and cut down on cheese. Repeated calcium just 5 days after stopping Thiazide and cheese was 9.9 mg/dl. 24 hour urine calcium: 99 mg/24HR. 5 months later, Calcium: 9 mg/dl and PTH intact: 64 pg/ml

Discussion: Our patient was taking 2.7 gm of calcium a day, 1000 mg from calcium and 1700 mg dietary from cheese. 2 pounds of cheese contain 8 gm of Calcium, which he was consuming over 5 days. Similar cases were reported in literature. Excessive cheese intake up to 2000 gm a day in anorexic patient caused severe hypercalcemia. Thiazide-associated hypercalcemia is often discovered after several years of treatment. Milk-alkali syndrome can occur with minimum of 5-7 g of Calcium carbonate daily, which contain 2-3 grams of elemental calcium daily, for few weeks

Conclusion: Similar to Milk-alkali syndrome, our patient displayed a factitious Cheese-Thiazide syndrome with total of 2.7 gram of calcium daily leading to symptomatic hypercalcemia that required intravenous hydration. Taking a nutrition history was the key in making the correct diagnosis in our case and still a key part of our evaluation as physicians

Abstract #503

SEVERE RECALCITRANT HYPOCALCEMIA POST PARATHYROIDECTOMY IN A PATIENT WITH PRIOR GASTRIC BYPASS

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Objective: To describe a case of severe calcitriol hypocalcemia after parathyroidectomy in a patient with prior Roux-en-Y gastric bypass

Case Presentation: 58 y/o female with history of Roux-en-Y bypass was referred to endocrinology clinic for normocalcemic hyperparathyroidism. Lab work showed PTH 107pg/ml (10-65pg/ml), serum calcium 9.5mg/dl (8.5-10.2mg/dl) and VitD 50ng/ml(20-50ng/ml). Parathyroid scan showed right lower parathyroid adenoma. DEXA scan showed osteopenia in the left hip. Serum bone markers were elevated. Due to osteopenia and increased risk for fractures, the patient was referred to ENT. She underwent subtotal parathyroidectomy and pathology was consistent with parathyroid adenoma. Patient developed hypocalcemia at calcium 7.6mg/dl on postoperative day # 2. After calcium replacement she was discharged on Oscal 1000 mg QID and calcitriol 0.25mcg bid. Patient was readmitted with symptomatic hypocalcemia. Lab work showed Ca-6.6mg/dl and PTH 41.9pg/ml. Was taking 7200 mg elemental calcium daily prior to surgery per review of home medications. After intravenous calcium replacement, she was discharged on oral Calcium carbonate 12000 mg daily,Calcitriol 1 mcg
daily, Magnesium 800mg daily. Despite taking a very high dose of calcium and calcitriol, her calcium level remains in low-normal range 8.8mg/dl with elevated phosphorus at 4.6mg/dl and inappropriately low PTH 38.8pg/ml

**Discussion:** Roux-en-Y gastric bypass can result in hypocalcemia and vitamin D deficiency due to many reasons. The duodenum and jejunum are preferential sites for calcium absorption by a vitamin D-dependent transcellular active transport and are bypassed in Roux-en-Y gastric bypass. Partial gastrectomy reduces gastric acidity resulting in an impaired absorption of calcium salts. Malabsorption of fat-soluble vitamins due to poor mixing of bile salts decreases the amount of vitamin D available and contributes further to the decreased calcium absorption. Parathyroid hormone plays a pivotal role in maintaining calcium level, hence subsequent parathyroidectomy results in severe hypocalcemia. Calcium citrate is preferred given achloridia. Teriparatide is not studied in this population. A few case reports have been published showing requirements of prolonged IV calcium, large doses of oral calcium and vitamin D after gastric bypass in patients following thyroid surgery complicated by hypoparathyroidism.

**Conclusion:** Prior Roux-en-Y gastric bypass patients who subsequently undergo parathyroidectomy are at very high risk for recalcitrant symptomatic hypocalcemia and should be monitored very closely with adequate prophylactic treatment for hypocalcemia.

**Abstract #504**

**A CASE OF HUNGRY-BONE SYNDROME IN AN 18-YEAR-OLD FEMALE AFTER REMOVAL OF A SINGLE ADENOMA FOR SEVERE HYPERPARATHYROIDISM**

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**Case Presentation:** Primary hyperparathyroidism is usually due to a single adenoma and mostly seen in elderly patients. Our patient was referred for resection of a single adenoma and endocrinology was asked to see her a few hours prior to the procedure. She initially presented with complaints of headaches and was found to have a calcium (Ca) level of 11.7 mg/dl with parathyroid hormone (PTH) levels over 1900 pg/ml and an alkaline phosphatase level of 1681 unit/L. X-rays showed significant osteopenia in multiple areas including chronic fracture of the proximal left humerus and areas in long bones characterized as “brown tumors” and evaluation with a sestamibi scan demonstrated a large right lower pole parathyroid adenoma. Postoperatively, levels of Ca, phosphorus (Ph) and magnesium (Mg) went as low as 5.6, 1.8 and 1.1mg/dl, respectively. To maintain Ca, Ph and Mg levels, she required electrolyte replacement both IV and Oral. Over a 7-day period, she received 140 grams of IV calcium gluconate and an additional 49.4 grams of oral calcium carbonate. This approximated about 30 grams of calcium with likely 3 grams of elemental calcium daily, available for absorption. In addition, Mg and Ph were replenished as needed. She was also found to be significantly deficient of Vitamin D (<13 ng/ml) which was replenished with Ergocalciferol daily and active Calcitriol increasing her Vitamin D level to 24 ng/ml by hospital discharge. The surgical pathology demonstrated a single parathyroid adenoma weighing 4.2 gm. Significant in this case is the elevated alkaline phosphatase together with the X-ray bone findings pointing to the long-standing and highly active bone turnover increasing the risk of postoperative hungry-bone syndrome. PTH levels declined after parathyroidectomy and were increasing by hospital discharge demonstrating active parathyroid tissue.

Discharge medication included oral calcium daily (2-3 grams) and Ergocalciferol 50,000 units weekly for 12 weeks with follow-up in Endocrinology clinic.

**Conclusion:** 1) Hungry-bone syndrome (HBS) is a rare complication following resection of a single parathyroid adenoma. It needs to be anticipated in severe cases like ours and requires aggressive and prolonged supplementation of Ca and other electrolytes. It is important to be hyper-vigilant about the electrolyte abnormalities that can occur in HBS which can be life-threatening if not treated. 2) While the pathology revealed a parathyroid adenoma, several facts about this case suggest that this may be a more severe variant than what is typically seen. These include young age, significantly elevated PTH, and degree of bone involvement. This may be suggestive of an underlying familial syndrome such as MEN1.
Abstract #505

SEVERE HYPERCALCEMIA IN CROHN’S PATIENT

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Case Presentation: Hypercalcemia is a relatively common condition seen in both the outpatient and inpatient setting. Granuloma formation causing hypercalcemia can be seen with Sarcoidosis and rarely with Tuberculous and systemic fungal infections. Inflammatory Bowel Disease also falls under this category as described in the patient case below. A 44 year old Caucasian female with relatively recent diagnosis of Crohn’s Disease presented to the Emergency Department with complaints of generalized fatigue, nausea and vomiting. She was found to have a serum calcium level of 16.8 mg/dL. Her creatinine was 1.74 mg/dL (previously normal), 25 Hydroxy Vitamin D of 56 ng/mL and PTH level of 6 pg/mL. The patient was treated with aggressive fluids, given a dose of Pamidronate and admitted for further hypercalcemic management. A PTH-related peptide level was undetectable; SPEP, TSH, liver enzymes and phosphorus were normal. A 1,25 Dihydroxy Vitamin D level was elevated at 105 ng/mL (ref range 29-79). Additional information given by patient was that she had been taking Hydrochlorothiazide 25 mg for around 3 months (normal calcium two months after starting medication). The patient was also taking combined Vitamin D 200IU/Calcium carbonate 500mg tablet daily as well. At a one week follow up, the patient’s calcium had remarkably improved to 10.6 mg/dL and creatinine of 0.96 mg/dL, with resolution of symptoms.

Conclusion: One of the hallmarks of Crohn’s disease is non-caseating granulomas found in the gut. Given the patient’s previous history of Crohn’s disease and significant elevation in 1,25 Dihydroxy Vitamin D level, with other labs being normal, it was proposed that granuloma formation greatly contributed to her severe hypercalcemia. The proposed mechanism is increased 1-alpha hydroxylase activity from the macrophages, which causes increased conversion of 25 hydroxy Vitamin D to 1,25 dihydroxy Vitamin D leading to increased gut absorption, decreased renal excretion of calcium and release of calcium from the bone. As been shown in the few case reports involving hypercalcemia with Crohn’s Disease treatment of her underlying condition as well as steroids could lead to stabilization of her calcium levels.

Abstract #506

FUNCTIONAL PARATHYROID CYST- A RARE CAUSE OF HYPERPARATHYROIDISM

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Objective: Parathyroid cysts are usually nonfunctional and a rare cause of hypercalcemia. Diagnosing these with a minimally invasive test could decrease surgical exploration for the treatment of this unusual cause of hyperparathyroidism. Our objective is to describe a case report highlighting the importance of neck ultrasound imaging in the management of primary hyperparathyroidism.

Case Presentation: We present a 61 year old female referred for asymptomatic persistent mild hypercalcemia. Serum calcium ranged from 10.5 to 11.5 mg/dl (8.6-10.2 mg/dl) with intact Parathyroid hormone level of 91 pg/ml (15.00-65.00 pg/ml). Twenty four hour urine calcium and serum creatinine were normal. Bone mineral density was in the osteoporotic range. Parathyroid scan with single-photon emission computed tomography revealed focal increased uptake in the inferior pole of the left thyroid lobe. Thyroid ultrasound revealed a cystic mass, posterior to the left lobe of thyroid gland measuring 2.61 x 0.76 cm in size. Ultrasound guided fine needle aspiration of the cyst revealed bloody fluid. The cyst appeared larger and irregular on ultrasound imaging after the fine needle aspiration procedure. Intact parathyroid hormone level in the cyst fluid was 774 pg/ml. The serum parathyroid hormone and calcium levels were 99.94 pg/ml and 11.1 mg/dl respectively. Cytopathology revealed few parathyroid cells but no nuclear atypia was seen. The patient was subsequently referred for parathyroidectomy.

Discussion: This case illustrates the importance of performing a pre-operative thyroid ultrasound during workup of primary hyperparathyroidism. Sestamibi parathyroid scan may not localize the hyper secreting parathyroid gland and cannot distinguish between an adenoma and functional cyst. Functional parathyroid cyst although a rare cause of hyperparathyroidism, can be localized and confirmed pre-operatively with ultrasound and fine needle aspiration of the cyst. Thus neck ultrasound may be a necessary adjunct to nuclear imaging studies for localization of the hyper-secreting parathyroid gland.

Conclusion: We suggest that further studies need to be done to evaluate the cost-effectiveness, efficacy, and diagnostic specificity of parathyroid imaging techniques used alone or in combination. Thus, neck ultrasound may be a necessary adjunct to nuclear imaging of suspected parathyroid adenomas to better characterize the lesion.
Abstract #507

TUMOR-INDUCED OSTEOMALACIA, A RARE CASE

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Objective: Tumor-induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by tumor production of fibroblast growth factor-23 (FGF-23), leading to high renal phosphate wasting and consequently severe hypophosphatemia and osteomalacia. Majority of TIO cases have been described as mesenchymal origin, with significantly fewer cases related to malignant tumors. We described a rare case of TIO associated with metastatic prostate cancer presenting with hypophosphatemia.

Case Presentation: 61 year-old Caucasian male with a background history significant for advanced chronic lymphocytic leukemia (CLL) and metastatic prostate cancer with diffuse skeletal involvement, treated with chemoradiation and denosumab, who presented with symptoms of extreme fatigue, generalized muscle weakness and bone pain. He was admitted for management of severe hypophosphatemia 0.6 mg/dl (ref 2.7-4.5). Additional lab evaluation was significant for secondary hyperparathyroidism (intact PTH 364 pg/ml, ref 15-65) due to hypocalcemia (7.9 mg/dl, ref 8.4-10.2) and vitamin D insufficiency (total vitamin D 25-OH 20 ng/ml). Alkaline phosphatase was also elevated at 435 U/L (ref 35-129) with normal renal function. Diagnosis of TIO was confirmed by elevated urinary phosphate excretion at 3.8 g/24 hr (ref 0.4-1.3 g/24hr) and elevated FGF-23 at 401 RU/ml (ref <180). In this case, osteomalacia was likely masked by osteoblastic bone metastasis from prostate cancer. Recommendation against further use of denosumab was advised, and patient’s symptoms were alleviated after providing calcium, phosphate and active vitamin D supplementation.

Discussion: Our patient likely had a combination of factors contributing to his electrolyte abnormalities, including denosumab, secondary hyperparathyroidism and FGF-23 mediated phosphuria. While denosumab has proven benefit in decreasing skeletal events in castration-refractory prostate cancer, caution must be used in these patients due risk of lowering calcium and subsequent secondary hyperparathyroidism, further inducing urinary phosphorus excretion. The utility of FGF-23 in assessing prostate cancer aggressiveness has been described, however more observation must be determined if levels correlate with the extent of underlying cancer, response to treatment and degree of phosphate wasting.

Conclusion: This rare case demonstrates the importance of keeping TIO in the differential diagnosis for hypophosphatemia, bone pain and weakness. The recognition of this disease is critical as tumor identification and resection is curative. When tumors cannot be identified or are not amenable to cure, medical treatment can be successful though periodic surveillance is necessary.

Abstract #508

DENOSUMAB-INDUCED PROLONGED HYPOCALCEMIA: NEED FOR HIGH-DOSE CALCIUM AND CALCITRIOL SUPPLEMENTATION

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Objective: Denosumab, a fully human monoclonal antibody to receptor activator of nuclear factor-kB ligand (RANKL), decreases osteoclastogenesis, reduces bone resorption and increases bone density, and is prescribed at 60 mg every 6 months for the treatment of osteoporosis. A higher dose (120 mg) every 4 weeks is used for prevention of skeletal-related events (SREs) in patients with bone metastases from solid tumors. Severe hypocalcemia is reported in 15% of patients treated with denosumab. We report a case of prolonged hypocalcemia from denosumab in a patient with prostate cancer metastatic to the bone. Intravenous calcium infusion, high doses of calcium and calcitriol were required for resolution of symptoms and improvement in serum calcium levels.

Case Presentation: An 83 year old man with castration-resistant prostate cancer metastatic to bone, presented to the emergency department with generalized weakness and altered mental status. He received denosumab 120 mg subcutaneous injection 8 days prior to presentation. On exam he did not have Chvostek’s sign or Trousseau’s sign. He had a corrected calcium of 5.4 mg/dL (8.7-10.1 mg/dL), creatinine of 1.6 mg/dL, GFR of 45 ml/min/1.73m2 (> 60 ml/min/1.73m2), PTH of 419 pg/mL (15-65 mg/ml), alkaline phosphatase of 237 IU/L (0-140 IU/L), magnesium of 1.7 mg/dL (1.8-2.3 mg/dL), phosphorus of 2.5 mg/dL (2.5-4.5 mg/dL), 25-hydroxy vitamin D of 41 ng/mL (> 20 ng/mL) and PSA of 163.5 ng/mL (< 4.0 ng/mL). Electrocardiogram showed QTc prolongation. Despite multiple intravenous boluses of calcium gluconate he had to minimal improvement of serum calcium levels. Patient was admitted to the intensive care unit for continuous calcium gluconate infusion for 36 hours. Serum calcium increased to 7.2 mg/dL (8.6-10.4 mg/dL) and ionized calcium to 1.0 mmol/L (1.0-1.35 mmol/L). Despite oral calcium carbonate supplementation with at least 3 gms per day and calcitriol 4 mcg per day, he returned to the hospital twice over a 5 week period.
for asymptomatic hypocalcemia. Continuous calcium infusion was administered with improvement in calcium levels. At 7 weeks after denosumab, he required 4 gms of oral calcium carbonate, 10 mcg of oral calcitriol and 2000 IU of vitamin D3 daily. 

**Conclusion:** Risk factors for denosumab-induced hypocalcemia include osteoblastic metastases, high PSA levels, high alkaline phosphatase levels, renal dysfunction and vitamin D deficiency. It is important to check and correct calcium and vitamin D levels prior to administration of denosumab. Calcium and vitamin D supplementation should continue during and after denosumab administration. Prolonged calcium infusion and high dose calcitriol may be required to correct severe hypocalcemia.

**Abstract #509**

**RECURRENT UROTHELIAL CARCINOMA PRESENTING WITH HYPERCALCEMIA**

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Rowan University

**Objective:** Rare case of Humoral Hypercalcemia of malignancy

**Case Presentation:** A 75-year-old male with PMH of CHF, DM, HLD, HTN, CKD II, urothelial carcinoma with a one-month history of generalized weakness. He was diagnosed with high-grade invasive urothelial carcinoma in 2010 and had multiple procedures, chemotherapy and radiation. The patient never had elevated calcium levels. When he presented to hospital, his serum calcium was elevated to 12.2mg/dL with a serum albumin of 2.6g/dL. The patient was admitted and treated with intravenous fluids. A repeat calcium was 12.1mg/dL. The patient was noted to be very lethargic on physical exam and cachectic-appearing. His family reported that he had not been eating well and become bed-bound. He was treated with Pamidronate 60mg IV x 1 dose over 8 hours. An evaluation for hypercalcemia was performed. Serum PTH level was 6.1pg/mL, serum TSH 6.081, serum ACE level 28U/L, serum Vitamin D 25 20.5ng/mL, Vitamin D 1,25 <8pg/mL and PTHrP was 147pg/mL. A skeletal radiographic survey was negative. A chest x-ray showed potential small nodularity in right lung base. The patient had numerous CT abdomen studies prior that were unchanged. He did have an AKI after infusion of pamidronate with creatinine increasing up to 3.92 mg/dL. His kidney function did recover throughout his hospitalization. Following treatment with Pamidronate, the serum calcium decreased to 8.5mg/dL within one week. The patient’s overall status showed little improvement and he was discharged home on hospice.

Histopathologic examination of the bladder tumor seen from the transurethral resection demonstrated a high-grade papillary urothelial carcinoma with invasion into muscularis propria. This tumor showed positive staining with P63 and high molecular weight cytokeratin immunohistochemical stains. Neuroendocrine markers were positive.

**Conclusion:** This is a unique case of recurrent urothelial carcinoma with hypercalcemia due to PTHrP secretion. Humoral hypercalcemia of malignancy is caused by the ectopic production of PTHrP by tumor cells. 7 The PTHrP binds to parathyroid hormone receptors, inhibiting the action of osteoblasts and stimulating osteoclasts. PTHrP also promotes renal tubular calcium reabsorption.1 Urothelial carcinoma is a reported but rare cause of humoral hypercalcemia of malignancy.2 Our patient’s urothelial carcinoma manifested years ago but he did not have any clinically elevated calcium. There is only one other published case report showing recurrent urothelial carcinoma manifesting with hypercalcemia due to PTHrP secretion.3 Other case reports have shown co-secretion with G-CSF although our patient did not have any chronic elevations in his WBC, this was not directly measured.4, 5

**Abstract #510**

**TRANSIENT OSTEOPOROSIS OF THE RIGHT HIP IN A PATIENT WITH OSTEOGENESIS IMPERFECTA**

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University of Alabama at Birmingham

**Objective:** We present a case of transient osteoporosis of the right hip in a patient with osteogenesis imperfecta.

**Case Presentation:** A 32-year-old Caucasian male with osteogenesis imperfecta (OI) was referred to endocrinology clinic two months after an episode of sudden-onset right hip pain following intense exercise. He reported a diagnosis of OI with an arm fracture in childhood. His father and daughter also had OI. Shortly after this episode, right hip x-ray showed no abnormality. He returned 2 weeks later without relief. Given concern for stress fracture, he underwent cannulated screw fixation of the right hip. X-ray 2 weeks post-operatively showed almost complete resorption of the femoral head and neck with no significant areas of visible bone in the region. At the time of endocrinology referral, basic metabolic profile,
serum phosphorus, albumin, alkaline phosphatase, CBC with differential, FSH, LH, prolactin, intact PTH, 25-OH vitamin D, free testosterone, total testosterone, and sex hormone binding globulin were all within normal limits. Repeat x-ray of the right hip showed significant osteolysis involving the hip joint without identifiable fracture. Teriparatide was prescribed. Repeat evaluation is pending. Discussion: Transient osteoporosis of the hip is a rare disorder, often described in women during the third trimester of pregnancy and, less commonly, in middle-aged men. Typical presentation is acute onset of pain with x-rays showing demineralization and MRI showing marrow edema of the femoral head and neck. The condition has been infrequently described in patients with osteogenesis imperfecta. The pathophysiologic relationship between these two conditions is uncertain, though prior findings suggest that microfractures may play a role. In reported cases of patients with both conditions, symptoms and radiologic findings often resolved with conservative therapy over a period of months. Therapies, including teriparatide and prostacyclin PGI2 analogs, have been used in isolated cases with reported success. Conclusion: The relationship between osteogenesis imperfecta and transient osteoporosis is not well defined, but the development of microfractures is thought to play a role. No clear treatment is known, but purported benefit has been seen with vasodilators and anabolic bone agents.

Abstract #511

HYPERCALCEMIA IN A PATIENT FOLLOWING TOTAL THYROIDECTOMY

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Objective: Hypoparathyroidism is a potential complication in patients following total thyroidectomy. Protocols exist for repletion of serum calcium during hospitalization, however, there are few guidelines describing post-hospitalization management. We present a case of calcitriol toxicity during treatment of postoperative hypoparathyroidism, and discuss methods for preventing this potentially life-threatening adverse event.

Case Presentation: A 66-year-old man with hypertrophic cardiomyopathy, hypertension and recently diagnosed papillary thyroid cancer presented three weeks after total thyroidectomy with three days of lethargy, anorexia and nausea with non-bilious vomiting. He had undergone bilateral central and lateral neck dissections, and had developed hypoparathyroidism requiring multiple doses of intravenous calcium supplementation. His regimen at discharge included 1 gram of calcium carbonate three times daily, 667 mg of calcium acetate three times daily, 1 mcg of calcitriol twice daily, and ergocalciferol 50000 units weekly. He was followed weekly with measurement of serum calcium, with an ionized calcium of 4.5 mg/dL (normal 4.4-5.4 mg/dL) five days prior to presentation. He was hypertensive and in mild distress, but alert and oriented. Exam was notable for healing surgical incisions and dry mucus membranes. Cardiovascular exam and ECG were unremarkable. Laboratory assessment demonstrated an ionized calcium of 9.4 mg/dL and PTH of 3 pg/mL. Serum creatinine was elevated at 1.9 mg/dL. He was placed on telemetry and treated with intravenous normal saline and supportive measures. At discharge his ionized calcium was 3.9 mg/dL; he was provided 0.25 mcg of calcitriol daily and one gram of calcium carbonate twice daily.

Conclusion: Transient hypoparathyroidism, typically lasting from 1 to 3 months, occurs in up to 30% of patients after total thyroidectomy. Permanent hypoparathyroidism, as defined by a duration greater than 1 year, has been described in up to 3% of patients. Replacement therapy in the form of calcium salts is common, however, some instances require activated vitamin D analogs to maintain appropriate serum calcium levels. An uncommon but potentially life-threatening complication of these therapies is hypercalcemia, particularly when calcitriol is used. Our patient required high doses of calcium and calcitriol. His calcium had stabilized over three weeks, and he was feeling well until days prior to his presentation. In addition to frequent monitoring of serum calcium, preemptive reductions in calcitriol and calcium doses should be made to avoid hypercalcemia, especially in patients discharged on high doses of these supplements.

Abstract #512

A CASE OF SEVERE VITAMIN D DEFICIENCY MASQUERADING AS POSSIBLE PARATHYROID CANCER.

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Objective: Constellation of atypical test results sometimes triggers consideration of rare diagnosis. We present such a case.

Case Presentation: A 46 year old woman is referred for genetic testing for CDC73 mutation to rule out parathyroid cancer after surgical resection of a parathyroid adenoma. She was found incidentally with hypercalcemia. She was asymptomatic. Pre-operative workup showed elevated PTH of 1153 pg/ml, calcium of 12.6 (reference range
8.7-10.2 mg/dl), 24 hour urine calcium of 325 mg per grams/24 hrs (ref range is 0-216 mg per gram), severe vitamin D deficiency, osteoporosis (T score of -2.5 in the hip, femoral neck). She underwent resection of a left inferior parathyroid adenoma (size: 3.1 x 2.3 x 1.2 cm on pathology). Cytopathology showed “focal mild cytological atypia.” Post-operatively, she was lost to follow up and did not start calcitriol.

On her first visit to our facility three months later, she complained of hypocalcemia symptoms. She has visited the emergency room twice since her surgery for these symptoms. Significant past medical history includes primary hyperparathyroidism, pre-diabetes, mitral valve prolapse. She has no family history of pituitary, jaw or neuroendocrine tumors; nephrolithiasis or osteoporosis. Examination reveals poor dentition, various missing teeth, negative Chvostek’s sign. She had no face or neck tumors. Laboratory and imaging results reveal: Ionized Calcium = 1.12 (Ref range 1.12 – 1.32 mmol/L); Phosphorus = 2.9 (Ref range 2.5 – 4.5 mg/dL); Parathyroid Hormone (PTH) = 213 (Ref range 15 – 65 pg/ml); 25-hydroxy Vitamin D = 5 (<10 ng/dl = severe vitamin D deficiency); Alkaline Phosphatase = 101 U/L (Ref range 35 – 105 U/L); normal renal ultrasound. She was diagnosed with secondary hyperparathyroidism due to vitamin D deficiency and started on calcitriol 0.5 mcg twice daily and calcium carbonate. Laboratory test one week later showed PTH = 74.7 pg/mL; Ionized Calcium = 1.24 mmol/L; Phosphorus = 2.5 mg/dL; Alkaline Phosphatase = 102 U/L. She started cholecalciferol 50,000 international units daily for 2 weeks. 25-hydroxy vitamin D after treatment was 39 ng/mL. Testing for celiac disease and CDC73 mutation were negative.

Discussion: Patient’s degree of hypercalcemia relative to that of PTH suggests additional etiology, as clued in by the finding of severe vitamin D deficiency. The decrease in the PTH level well into the normal range in response to calcitriol strongly suggested a secondary cause of hyperparathyroidism and makes parathyroid cancer unlikely.

Conclusion: Uncommon findings sometimes raise the possibility of rare conditions. Severe presentation of primary hyperparathyroidism in the setting of severe vitamin D deficiency has been described in the literature.

Abstract #513

HYPOPHOSPHATEMIA: A CASE OF TUMOR-INDUCED OSTEOMALACIA

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UT Health San Antonio

Case Presentation: A 72-year-old Hispanic man presented to clinic reporting widespread bone pain and a history of multiple fractures. At age 60 he sustained his first hip fracture and over the next 3 years developed a second hip fracture along with multiple rib fractures. Initial dual-energy x-ray absorptiometry (DXA) at age 66 demonstrated low bone mineral density (BMD) which progressed to osteoporosis with a lowest T-score of -4.4 on repeat scan 6 years later. Laboratory data showed persistent hypophosphatemia since age 62 (as low as < 1.0 mg/dl), elevated serum alkaline phosphatase (>200 IU/L) and low vitamin D3 1,25 (17 pg/ml) levels. In 2016, alendronate and phosphate supplementation were ordered. Patient was referred to Endocrinology for osteoporosis but given his lab abnormalities there was a concern for tumor-induced osteomalacia (TIO). Alendronate was discontinued, calcitriol was added and phosphate supplementation was continued pending serum fibroblast growth factor-23 (FGF23) level; FGF23 level returned elevated at 979 RU/mL (normal < 180). Follow-up octreotide scan revealed focal activity at the head of the pancreas.

Discussion: Osteoporosis is diagnosed either by the presence of a fragility fracture and/or T-score by BMD < -2.5. Osteomalacia can present as osteoporosis but the mechanism is very different. Osteoporosis is due to bone loss from increased osteoclastic bone resorption whereas osteomalacia is due to a mineralization defect. While bisphosphonates are an excellent choice for treating osteoporosis, it is contraindicated and can do harm if used in the treatment of osteomalacia. TIO is a rare but potentially curable paraneoplastic syndrome causing renal wasting of phosphate and bone demineralization leading to muscle weakness, fractures and low T-scores. Tumors are typically benign, mesenchymal tumors located in the extremities which secrete FGF-23. FGF23 causes both an increased urinary loss of phosphate resulting in persistent hypophosphatemia leading to elevated alkaline phosphatase (bone-specific isoenzyme) and a low or inappropriately normal vitamin D3 1,25 level.

Conclusion: Distinguishing osteoporosis and osteomalacia presents a challenge to clinicians as they are undifferentiated by DXA or fragility fractures. Attention to serum phosphate may provide earlier detection for TIO and prevent progressive bone loss and fractures leading to improved overall bone health and quality of life. Patients
with TIO require long-term monitoring and aggressive repletion of phosphate and calcitriol until the causative tumor is found. Though tumor removal is curative, they are often difficult to find resulting in an average delay of 5 years from time of diagnosis to tumor localization.

Abstract #514

HYPOVITAMINOSIS D IS ASSOCIATED WITH PSORIASIS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Hypovitaminosis D is associated with a variety of autoimmune diseases such as rheumatoid arthritis, Vitiligo, Sjogren’s syndrome and etc. We conducted a meta-analysis of relevant studies to establish whether there was a relationship between hypovitaminosis D and psoriasis.

Methods: Research design
Systematic review and meta-analysis. We conducted a comprehensive search in the MEDLINE and EMBASE databases through September 2016 to identify relevant cohort studies and to assess 25-hydroxyvitamin D (25(OH)D) levels in adults with psoriasis. The primary outcome was the mean difference in serum (OH)D level between psoriatic patients and controls.

Results: Our initial search identified 107 articles. Fifteen studies met the criteria for full paper review. Meta-analysis was conducted from ten prospective cohort studies involving 6217 controls and 693 cases. The pooled mean difference in serum 25-hydroxyvitamin D level between psoriatic patients and controls was −6.13 ng/ml (95% confidence interval, −10.93 to −1.32, P-value = 0.01). The between-study heterogeneity (I²) was 98%, P-value < 0.00001.

Conclusion: Our meta-analysis demonstrated a significant relationship between low 25-hydroxyvitamin D levels and psoriasis but does not establish a causal relationship. Our findings focus on the importance of measuring 25-hydroxyvitamin D levels in patients with psoriasis. Further studies will be required to establish whether vitamin D supplementation benefits patients with psoriasis.

Abstract #515

DENOSUMAB INDUCED SEVERE HYPOCALCEMIA IN THE TREATMENT OF HYPERCALCEMIA OF MALIGNANCY

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Objective: Hypercalcemia occurs commonly among cancer patients, with an estimate of 20-30%. Hypercalcemia of Malignancy is the most common cause of hypercalcemia in the inpatient setting. It occurs in patients with both solid tumors and hematologic malignancies. Denosumab is a human monoclonal antibody, commonly used for the treatment of osteoporosis as well as hypercalcemia from malignancy and bone metastases. It specifically targets nuclear factor-kappa ligand (RANKL) by inhibiting its binding to RANK receptor thereby preventing osteoclast formation and resulting in decreased bone resorption and increased bone mass.

Case Presentation: A 60-year-old female presented to an outside hospital with hip pain and elevated calcium of 15.5 in the setting of a locally aggressive right hip mass. The mass was biopsied and confirmed Diffuse Large B Cell Lymphoma with no evidence of distant metastases. The patient was then given a dose of denosumab 60mg and was transferred to our hospital. She subsequently developed hypocalcemia about 2 weeks after denosumab was administered. Her corrected calcium was 6 and ionized calcium was 0.7. PTH was appropriately elevated at 570 with phosphorous of 1.2. She did not exhibit overt symptoms of hypocalcemia and EKG didn’t show QT prolongation. She was given multiple boluses of calcium chloride and gluconate and was started on oral calcium carbonate, which was later switched to calcium citrate titrated up to 1900mg four times daily, along with calcitriol 0.5mcg three times daily. Her 25(OH) vitamin D was 24 and she was started on vitamin D 2000 IU daily.

After several days of aggressive calcium replacement, up to 5 grams daily, the patient was eventually discharged on a stable calcium regimen with calcium citrate, calcitriol and vitamin D. She was scheduled a follow up with Oncology as an outpatient for further management of her lymphoma.

Discussion: Our case highlights hypocalcemia as an important adverse event from denosumab. The prevalence of hypocalcemia related to denosumab is approximately 1.7% and is usually mild and transient. Denosumab is not cleared by the kidneys and can be used in patients with chronic kidney disease but with greater risks of hypocalcemia.

Conclusion: It is crucial to recognize hypocalcemia which could be fatal following the use of denosumab. It may be prudent to lower the dose and correct for hypovitaminosis D among at risk patients.
Abstract #516

OVERCOMING OSTEOPOROSIS: THE STORY OF A GERMAN CONCENTRATION CAMP SURVIVOR

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Objective: During World War II, conditions in German concentration camps and ghettos lead to famine, malnutrition and severe starvation. Although studies are limited, reports on this population have addressed the effects of extremely diminished food intake subsequently leading to low bone mass and increased fracture risk. This case reflects the impact of early life severe malnutrition on overall bone health and quality.

Case Presentation: The patient was an 82-year-old woman who was detained as a child at age 10 years, and placed in a German work concentration camp for 1 year. Prior to that her family was in hiding and food availability was limited. She reached menarche at age 10 years; however, experienced amenorrhea for several years due to malnourishment and weight loss. After liberation, she was admitted to a Red Cross hospital for treatment of severe malnutrition. Menses ultimately resumed and she had 2 pregnancies and natural menopause at age 51. She was diagnosed with osteoporosis 20 years ago after a fall during which she sustained a wrist and a L1 fracture. She initially was treated with 8 years of oral bisphosphonates (BP). She sustained a right hip fracture treated surgically after another fall from standing height in 2004, and was treated with teriparatide for one year, followed by oral BP. During this time on BP, she went on to have another fracture (pelvic ramus). In 2012, she was started on denosumab and did well for several years with BMD improvement. However, in 2014 she once again fell and had a right proximal humeral fracture, and then another left proximal humeral fracture in November 2015. Neither of these required surgical repair, and she recovered good function. After recent humeral fractures, teriparatide was added to denosumab (3/2016). Recent laboratory evaluation was normal, with bone-specific alkaline phosphatase 13.3 mcg/L, Urine NTX 54 nmol BCE/mmol Cr, 25 OH Vit D 33ng/dl.

Discussion: In a case series examining Holocaust and ghetto survivors, the effect of chronic, severe starvation during childhood and adolescence on bone health were not completely reversible with relative return of normal nutrition. The survivors were reported to have higher risk of early onset osteoporosis with increased risk of fractures.

Conclusion: Early life severe malnutrition and starvation has been shown to cause biochemical and physiological consequences leading to risk of severe adult osteoporosis and fractures. Given the importance of bone health during every stage of life, the impact of adequate nutrition in childhood and adolescence for attainment of peak bone mass and maintenance of regular menses, such as were likely factors in our case, deserves critical attention.

Abstract #517

IMPROVING VITAMIN D TESTING IN PATIENTS WITH OSTEOPOROSIS

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Objective: Vitamin D deficiency is associated with an increased risk of hip and non-vertebral fractures. The American Association of Clinical Endocrinology recommends maintaining a 25(OH)D level between 30-60 ng/ml for bone health. The Endocrine Society guidelines for the management of osteoporosis recommends a target 25(OH)D level of 30 ng/ml for men at high risk of fracture. Maintaining optimal vitamin D level is also essential for the effectiveness of osteoporosis treatment. Carmel et al. found that a 25(OH)D level >33 ng/ml was associated with a 4.5 fold increase in the likelihood of a favorable response to bisphosphonates. To assess whether an order set is needed to link vitamin D lab testing with an osteoporosis medication order, we initiated a quality improvement study at the Dayton VAMC.

Methods: We reviewed vitamin D status in all patients prescribed various osteoporosis medications (alendronate, risedronate, ibandronate, calcitonin, or raloxifene) from January 2015- January 2016 at the Dayton VAMC and its outpatient clinics. Demographic and clinical data including indication for therapy and type of osteoporosis medication were obtained. We determined whether vitamin D levels were checked within the twelve months prior to or at the time of initiation of osteoporosis treatment.

Results: For 253 veterans, mean age at initiation of therapy was 65 years (range 42-95). Of these, 77.1% were men and 22.9% were women. Indications for therapy included osteoporosis prevention (6.3%), osteopenia (24.5%), and osteoporosis (68.8%). The majority of veterans were initially prescribed alendronate (94.5%). Other medications included risedronate (3.2%), calcitonin (1.6%), raloxifene (0.4%), and ibandronate (0.4%). Only 24.1% of patients had serum vitamin D levels checked in the twelve months preceding or at the time of treatment initiation. Among veterans with vitamin D levels, 42.6%...
had a vitamin D level >30 ng/ml and only 29.5% had a vitamin D level >33 ng/ml.

Discussion: We found that only 24.1% percent of veterans had their vitamin D level checked before or at the time of osteoporosis treatment. Optimum vitamin D is essential in maintaining favorable bisphosphonate response. Low 25(OH)D level is a modifiable risk factor that can be corrected using inexpensive and safe vitamin D supplementation.

Conclusion: Vitamin D assessment and treatment for veterans receiving osteoporosis medication should be improved at the Dayton VAMC. We plan to incorporate a pop-up reminder about vitamin D levels when osteoporosis medications are ordered, along with an educational component regarding its significance. After implementation, we will review the impact of the improvement.

Abstract #518

RECURRENT METATARSAL FRACTURES IN A POSTMENOPAUSAL WOMAN WITH LOW SERUM ALKALINE PHOSPHATASE (ALP): A RARE DIAGNOSIS NOT TO MISS

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Objective: Hypophosphatasia (HPP) is a rare inborn error of metabolism due to a loss-of-function mutation in the gene for tissue non-specific isoenzyme of alkaline phosphatase (TNSALP) that results in low levels of ALP. The clinical presentation of HPP is variable and in adults can easily be misdiagnosed as other forms of osteomalacia.

Case Presentation: A 53-year-old Caucasian female presented recurrent metatarsal fractures. She reports her first metatarsal fracture at age 21, and since then had at least 8 more metatarsal fractures over her lifetime. She reported history of gait disturbance as a child and dental issues (spacing and loosening). Labs showed normal serum calcium, phosphorus and PTH, but low serum ALP <20 IU/L and high N-telopeptide. Foot X-ray showed several healed and non-healed metatarsal fractures and bone densitometry revealed osteopenia. She was treated with calcium and vitamin D. A year later she had a new metatarsal fracture and a non-traumatic pelvic fracture. Teriparatide therapy was attempted but not tolerated. Due to suspicion of HPP vitamin B6 levels were checked and found to be elevated at 263 mcg/L. Given her clinical presentation and low ALP levels with elevated vitamin B6, the diagnosis of HPP was made.

Discussion: Over 300 mutations have been reported in the TNSALP gene, which is mostly expressed in the liver, skeleton and developing teeth. TNSALP is expressed ubiquitously, and its physiological role is evident in bone mineralization, a deficiency in which can manifest in many ways, including rickets or osteomalacia. HPP is classified into seven forms according to age of onset and severity: perinatal, prenatal benign, infantile, childhood, adult, odonto-HPP and pseudohypophosphatasia. Early presentation and lower ALP levels are associated with worse prognosis. Diagnosis relies on clinical presentation and low alkaline phosphatase level. Elevated serum vitamin B6, phosphoethanolamine and inorganic pyrophosphate support the diagnosis. Bisphosphonates are not helpful in treatment, and use of teriparatide is controversial. No established treatment for HPP was available until the recent FDA approval of enzyme replacement therapy (ERT). This bone-targeted recombinant tissue-nonspecific alkaline phosphatase (asfotase alfa) is approved for perinatal, infantile and juvenile HPP. It is expected that therapy with asfotase alfa will markedly improve the prognosis of HPP.

Conclusion: Clinicians should be attentive to a history of recurrent low trauma fractures, premature loss of deciduous teeth and persistently low serum ALP to suspect this diagnosis. Early case detection with the availability of ERT may avoid years of undiagnosed morbidity.

Abstract #519

STANDING IMPROVES BONE MINERAL DENSITY IN CHRONIC SPINAL CORD INJURY (SCI) – A CASE REPORT

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Objective: Osteoporosis complicates SCI and is multifactorial in etiology. Bone loss occurs immediately after SCI and affects distal femur / proximal tibia disproportionately. By ten years after SCI, net bone loss of 10-21% may occur. Weight-bearing exercises with standing frames and bikes, using forms of functional electrical stimulation (FES), have been shown to be effective when started within 6 weeks of injury but are ineffective in preventing osteoporosis or restoring bone mineral density (BMD) in the population with chronic SCI. We report a case of a male with chronic SCI in whom weight bearing exercises significantly improved BMD.

Case Presentation: A 41 year old male presented for evaluation of osteoporosis diagnosed on DEXA scan. Patient suffered an incomplete C5 C7 quadriplegia from a sports injury at age 26 and has been wheelchair bound. His medical history included well controlled type 1 diabetes on insulin pump and spasticity controlled by Baclofen via
intrathecal infusion. He has no history of nephrolithiasis or or fracture. DEXA showed lowest Z score -3.5 at left femoral neck (BMD 0.499g/cm²), with Z scores range of -3.1 to -2.5 in other femoral site measurements. L1 – L3 Vertebral Z score was -0.7. Laboratory investigations: Serum calcium 8.9mg/dl (8.5 – 10.7), phosphorus 2.7mg/dl (2.7-4.5), alkaline phosphatase 47U/l (<125), 25 OH vitamin D 57 ng/ml (30-100), 24 hour urine calcium 263mg (50-250), parathyroid hormone 25pg/ml (15-65), N-Telopeptide (NTx): 40 nmol BCE/mmol creat (9-60).

Patient received intravenous Zolendronic acid 5mg one time to prevent further bone loss. Patient then embarked on an exercise regimen at a gym specialized in treating SCI. For 3 hours sessions three days per week, patient used a standing frame and progressively increased his duration of standing time until he reached 30 minutes each session. After three years of regular exercises, patient was able to “walk” 50 feet aided only by a walking frame strapped to his forearms. Repeat DEXA showed lowered Z score improved to -3.1, with increase BMD of 19.3% in Spine and 4.7% to 12.7% in femoral measurements. Patient gained 6cm in thigh circumference due to increased muscle mass. Repeat N-Telopeptide (NTx) was 16nmol BCE/mmol creat. The BMD improvement is more than expected from one dose of bisphosphonate treatment alone.

**Conclusion:** This case illustrates weight bearing exercises may be of value in improving BMD in chronic SCI patients.

**Abstract #520**

**PRIMARY HYPERPARATHYROIDISM PRESENTING WITH HYPOKALEMIC PARALYSIS**

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**Objective:** To present a case of primary hyperparathyroidism (PHPT) presented with hypokalemia paralysis.

**Case Presentation:** A 45-year-old female presented with a sudden weakness in her lower limbs for 3 days before admitted to a private hospital. During hospitalization, her weakness worsened and she had similar weakness in her hands. Her laboratory findings revealed hypokalemia of 1.5 mmol/L. Upon suspicion of polyradiculopathy, she was then referred to our hospital. No history of gastrointestinal (GI) loss but she recalled frequent passing urine and often felt thirsty. History of abdominal pain and passing urinary stone were denied. No history of fracture but she felt pain on her feet that occasionally bothered her when walking. No significant past medical history. Her physical examination demonstrated a transient high blood pressure, pallor conjunctiva and lower limb weakness. Laboratory result showed anemia (hemoglobin 9 g/dL), serum potassium of 1.98 mmol/L, 24-hour urine sample collection obtained 5,900 mL (urinary potassium of 32 mEq), and transtubular potassium gradient of 11.9. Thyroid function and anterior pituitary laboratory panel were normal. Further evaluation revealed serum calcium level of 11.9 mmol/L, albumin of 3.8 mg/dL, PTH level of 568 µgram/mL and 24-hour urinary calcium of 814.2 mg. Neck ultrasound identified a nodule in thyroid left lobe and a hypoechoic lesion located inferior to the left thyroid lobe suggesting an adenoma. Further abdominal ultrasound found no kidney stone and normal kidney parenchyma. Sestamibi scan confirmed a functioning adenoma in this patient. Magnetic Resonance Imaging of the abdomen and brain revealed no structural abnormality of other endocrine glands. The presence of medullary thyroid carcinoma as part of possible multiple endocrine neoplasia (MEN) has not been ruled out.

**Discussion:** PHPT is often asymptomatic. Polyuria and polydipsia in this patient did not prompt the suspicion since her limb weakness was consistent with severe hypokalemia due to renal loss. Polyuria occurred in around 30% PHPT patient as a result of antagonizing hypercalcemia effect to arginine vasopressin on renal distal tubules and collecting ducts. Common hypokalemia precipitants were not identified in this patient. High blood pressure possibly attributable to aldosterone excess was unlikely due to its transient nature and possibly was part of clinical manifestation of PHPT. Hence, increased distal urinary flow may contribute to potassium loss in this case.

**Conclusion:** Hypokalemic paralysis as a presenting symptom in this patient hindered the prompt suspicion of hypercalcemia in the presence of polyuria, polydipsia and bone pain.

**Abstract #521**

**A CASE OF A HUNGRY BONE**

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**Objective:** To present an undiagnosed Primary Hyperparathyroid patient who underwent Parathyroidectomy due to bilateral Parathyroid Adenomas who developed Hungry Bone Syndrome post operatively. To discuss the pathophysiology of a rare case of severe hypocalcemia post parathyroidectomy secondary to Hungry Bone Syndrome, and present its diagnosis and management.

**Methods:** Case Report

**Case Presentation:** A 57-year old man had a history of multiple repeated fractures in the past without any apparent diagnosis, was admitted due to sudden onset of body...
malaise associated with loss of appetite which progressed to significant deterioration in mental function. Evaluation revealed a significantly elevated serum calcium of 14 mg/dl (8.5-10.2 mg/dl) with an intact PTH of 641.2 pg/ml (10-55 pg/ml) consistent with a diagnosis Primary Hyperparathyroidism (PHPT). Several imaging studies were done to localize the lesion including a Sestamibi scan and Neck ultrasound which showed negative results. A Multislice spiral CT scan of the neck was then ordered which revealed 1.5x1.6cm, 2.7x1.8cm and 5.2 cm right parathyroid mass consistent with a parathyroid adenoma. Aside from the history of multiple fractures, patient likewise had nephrolithiasis and severe osteoporosis. Due to significant symptomatic hypercalcemia with mental deterioration, a hemodialysis procedure was done and eventual parathyroidectomy which confirmed histologically the presence of a parathyroid adenoma. Due to the prolonged duration of the disease and significant hypercalcemia, he developed significant symptomatic hypocalcemia due to Hungry Bone Syndrome postoperatively.

Discussion: Primary Hyperparathyroidism is a generalized disorder of calcium, phosphate, and bone metabolism due to an increased secretion of Parathyroid hormones (PTH). However there are no specific symptoms associated and therefore a routine serum calcium evaluation that is elevated should raise the suspicion of this diagnosis. Since calcium evaluation during annual examination is now routinely done, a delay in the diagnosis of Primary HPT is a rare entity and therefore the development of severe hypocalcemia resulting in Hungry Bone Syndrome is seldom observed.

Conclusion: We report and describe a case of a patient developing severe hypercalcemia due to a delay in the diagnosis of Primary Hyperparathyroidism resulting in severe symptomatic hypocalcemia due to Hungry Bone Syndrome postoperatively.

Abstract #522

EXTREMES IN HYPERPARATHYROIDISM: MANAGEMENT OF PARATHYROID CARCINOMA

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Objective: Parathyroid carcinoma (PC) is a rare cause of primary hyperparathyroidism (PHPT), accounting for less than 1%, with an equal gender distribution and an average age of diagnosis in the fifth decade of life. The diagnosis of PHPT is based on the laboratory finding of high levels of immunoreactive PTH in the presence of severe hypercalcemia.

The only potentially curative treatment for PC is surgery. Early surgery is the most important factor for optimal outcome. This case series is based on a multidisciplinary review of four patients with parathyroid cancer, describing their therapeutic management and follow-up.

Methods: Imagistic evaluation was performed by ultrasound (US), computed tomography scan (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and Technetium-99m sestamibi scintigraphy, for detecting the primary tumor, its local extent and remote metastases.

Case Presentation: Between 2008 and 2014 four patients were diagnosed with PC in our clinical department, three men and a woman, with a mean age of 50 years ± SD 13.22 (range 38-68). had family history of hyperparathyroidism or hormonal disorders suggesting multiple endocrine neoplasia. All had severe hypercalcemia (15.3-19.4 mg/dl) and elevated PTH levels ranging from 15 to 45 times above normal value. Tumor size ranged from 3.2 to 7 cm; two of them had thyroid gland invasion and one thymic invasion. Three patients underwent parathyroidectomy with hemithyroidectomy and one underwent parathyroidectomy with thymectomy and cervical dissection. Schulte stage at diagnosis was between II and IV, while all were classified as high risk. Conformational radiotherapy of the tumor bed was used in 2 cases. Cinacalcet treatment was tried in one case and chemotherapy regimen in another, without significant improvement. Three patients had local recurrence and the time from the initial surgery to recurrence ranged from 1 month to 1 year.

Discussion: Parathyroid cancer are diagnosed in the context of severe hyperparathyroidism, metastases and very high PTH levels. Diagnosed is certified by pathology of metastases.

Conclusion: Parathyroid carcinomas are rare endocrine cancers, with high relapse rate and poor prognosis. Multidisciplinary approach requires detailed imaging, skilled surgeons, endocrinologist and oncologist.
Abstract #523

VITAMIN D STATUS IN ROMANIA

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Objective: Romania is located in the Northern hemisphere, with a latitude between 44 and 48 degrees. The vitamin D status is unknown, particularly in subjects without a diagnosis of low bone mineral density. Our aim was to evaluate the vitamin D status (serum 25-hydroxyvitamin D [25OHD]) in an adult Romanian population.

Methods: We retrieved from our endocrinology center electronic database all 25OHD measurements between May 2012 and November 2016. We also evaluated age, sex, diagnosis and date of blood sampling. 25OHD was measured by chemiluminescence (Liaison XL) or electrochemiluminescence (Cobas E601 C).

Results: There were 2772 subjects of which 1520 did not have a diagnosis of low bone mass (osteopenia or osteoporosis). In the 1520 subjects mean serum 25OHD was 18.8±9.3 ng/mL. 0.98%, 18.09%, 59.86% and 88.15% of subjects had a serum 25OHD level below 4, 10, 20 and 30 ng/mL respectively. Serum 25OHD showed a marked seasonal variation, with highest levels in September (24.65±9.6 ng/mL) and lowest levels in March (14.05±7.40 ng/mL; p<0.001). Men (n=256) had serum 25OHD levels with 2.3 ng/mL (CI 95% 1.05-3.55) higher than females (n=1264). There was a clear trend for decreasing serum 25OHD with age: 20.42±9.57, 18.78±9.21 and 17.64±9.14 ng/mL in the 18-39 (n=306), 40-64 (n=892) and +65 (n=322) years of age groups (ANOVA p=0.001).

Discussion: To our knowledge this is the largest study on vitamin D status in Romania. Although this is not a sample from general population it excludes patients with a diagnosis of low bone mass in whom treatment with vitamin D is most probable. Also, the vast majority of subjects were community living and in good general health. The vitamin D status in our Romanian population mirrored the seasonal and age variation of other European population. However, the prevalence of vitamin D deficiency and insufficiency was higher.

Conclusion: Vitamin D deficiency and insufficiency is highly prevalent in Romania.

Abstract #524

BROWN TUMOR PRESENTING AS PARAPARESIS

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Objective: Background: Primary hyperparathyroidism presenting as brown tumours is becoming a rare entity due to early recognition of hypercalcemia and easy accessibility to investigations.

Case Presentation: A 62 year old male presented to the neurology department with paraparesis with bowel and bladder involvement for 6 months. He also had multiple painless swellings of varying sizes at various sites in upper limb and lower limb (shoulders, forearm, both legs) and midline in back (lumbar region), which developed over 2 years. Biochemistry revealed low Hb (6.4g/dL), elevated creatinine (3.5mg/dL), hypercalcemia (11.3mg/dL), phosphorus (5mg/dL), ALP (169U/L). Skeletal survey showed multiple expansile lytic bony lesions in left humerus, ulna, proximal phalanx of middle finger, rib, femur, right fibula and a punched out lesion in right tibia. Bone scan revealed multiple hot spots at sites corresponding to x-ray findings. A presumptive diagnosis of metastatic bone disease was made, and then endocrine opinion was sought for hypercalcemia. There was no history suggestive of headache, abdominal pain, polyuria, bone pains, and no noticeable changes in vision, behaviour, level of consciousness or weight. Suspecting hyperparathyroidism with multiple brown tumors, serum PTH (intact) levels were done and were elevated (2048 pg/ml). Tc-99 sestamibi scan showed left inferior parathyroid adenoma (3 cm x 2 cm). Left Inferior parathyroidectomy was done. Post-operative period was uneventful, except for hypocalcemia on day 2 which was managed. Histopathology was consistent with parathyroid adenoma.

Conclusion: Incidence of brown tumors in PHPT is < 2%. They do not have the malignant or neoplastic potential of real giant cell lesions; there are no pathognomic histological changes. The tumors resolve once the abnormal metabolic condition is controlled. In severe cases, bone fragility may require surgical stabilization. A diagnosis of hyperparathyroidism must be kept in mind while evaluating any patient with osteolytic lesions.
**Abstract #525**

**THE BENEFIT OF HIGH DOSE VITAMIN D SUPPLEMENTATION IN PRIMARY HYPOPARATHYROIDISM**

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**Objective:** To report a case of hypoparathyroidism which exacerbated by Vit D deficiency.

**Case Presentation:** A 17-YO girl with primary hypoparathyroidism presented to ER with severe symptoms of hypocalcemia. She had positive Chvostek and Trouseau signs. Total Ca was 4.12 mg/dl, ionized Ca 0.55 mEq/L, PO4 2.52 mmol/L, PTH 5.02 pg/ml, mag 1.4 mg/dl, 25 OHD 15.38 ng/ml. On admission, she received IV Ca, magnesium, 200000 IU of vitamin D 3 IM. She was discharged on 1600 mg Ca carbonate, calcidol 1 mcg bid, Vitamin D3 50000 IU weekly, HCTZ 12.5 mg QD. However, two weeks later, she was readmitted for the same symptoms and treated with IV Ca and magnesium. Her vitamin D rose to 25 ng/ml. We discharged her after marked improvement on 1600 mg of elemental calcium, HCTZ 12.5 bid, and calcidol 1 mcg TID, Vitamin D 3 50000 IU weekly. Six months later, the patient remained stable; her 25 OHD level went up to 51 ng/ml. We were able to lower her calcium to 400 mg of elemental calcium QD, calcidol 1 mcg QD, vitamin D 5000 IU weekly, HCTZ 12.5 mg QD. Now, the patient has been stable for the past 16 months.

**Discussion:** Current therapy for primary hypoparathyroidism includes Ca, and active vit D: calcidiol or calcitriol. Vitamin D is not routinely given due to lack of PTH necessary to activate CYP 27B1 to produce 1,25(OH)2 D the active form. 25OHD is biologically inert unless present in intoxicating concentrations in the blood. In spite of PTH absence in patient with primary hypoparathyroidism, it is still possible to generate 25(OH)D from 25OHD due to the ubiquitous distribution of cytochrome P450 27B1 in the body. Animal experiments involving vitamin D3 intoxication have shown that 25(OH)D3 can reach concentrations up to 2.5 mol/L, at which it is accompanied by hypercalcemia, and accompanied by elevations of its precursor, vitamin D3, as well as by rises in many of its dihydroxy- metabolites but not 1,25(OH)2D3. So, possibly at pharmacologic concentration of 25(OH)D3 can overcome vitamin D receptor affinity disadvantages to directly stimulate transcription, or that total vitamin D metabolite concentrations displace 1,25(OH)2D from vitamin D binding, increasing its free concentration and thus increasing gene transcription. In another animal study, Vitamin D intoxication was produced with oral doses either vitamin D3 or 25-hydroxyvitamin D3 in CYP27B1 −/− (1α-hydroxylase knockout) indicating Vit D may work in patient with primary hypoparathyroidism.

**Conclusion:** We believe Vit D deficiency exacerbates the patient’s symptoms and restoring her Vit D level by high dose Vit D helped to decrease her requirements of calcium and calcidiol. Routine 25 OHD check and VitD supplementation in primary hypoparathyroidism is recommended.

**Abstract #526**

**CLINICAL VERTEBRAL FRACTURE AND MORTALITY DURING HIGH-DOSE GLUCOCORTICOID TREATMENT IN JAPANESE FEMALE PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES.**

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**Objective:** We investigated whether clinical vertebral fracture is a risk factor of 10-year mortality in female patients with autoimmune rheumatic diseases receiving high-dose GC treatment.

**Methods:** Design and Setting: This was a single-center observational cohort study conducted at Shimoshizu National Hospital (Chiba-Shimoshizu Rheumatic Cohort). Patients : Among female patients aged ≥18 years who were newly treated with high-dose GC (initial doses ≥20 mg prednisolone equivalent per day) for at least 6 months between 1986 to 2006, 42 patients who died within 10 years from treatment initiation, and 223 alive patients who were followed for 10 years were studied.

**Outcome Measure:** Rate of clinical vertebral fracture.

**Results:** The diseased group had significantly older age (61.2 ± 13.2 vs 39.1 ± 13.5, p<0.001), lower daily dose (38.3 ± 12.5 vs 45.6 ± 15.8 g/day, p<0.001), lower BMI (20.0 ± 2.9 vs 21.2 ± 3.1, p<0.05), higher rate of smoking (31.0 vs 15.7%, p<0.05) and higher prevalence of clinical vertebral fracture (64.3 vs 17.9%, p<0.001) compared to the alive group. Cox regression model demonstrated that the independent risks for mortality were age (>50 years) [HR (95% confidence interval): 4.79 (1.98-11.60), P=0.001], smoking [2.30 (1.17-4.53), p=0.016], and clinical fractures [3.07 (1.52-6.23), p=0.002].

**Discussion:** The precise causal relationship between clinical vertebral fractures and mortality during GC treatment was not clear in the present study. The relation between excess mortality and vertebral fractures in primary osteoporosis is also not clear, and it was reported that the number of deaths attributable to the fracture
itself was very limited, suggesting that vertebral fractures have an intrinsic role for mortality, and adversely affect comorbidities that contribute to mortality. The further study must be necessary.

**Conclusion:** Clinical vertebral fracture was independently associated with mortality in female patients receiving high-dose GC treatment for autoimmune rheumatic diseases.

**Abstract #527**

**GENDER DIFFERENCE IN CLINICAL PRESENTATION OF PRIMARY HYPERPARATHYROIDISM (PHPT)**

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**Objective:** PHPT is a common endocrine disorder, asymptomatic in most patients nowadays, with a female-to-male ratio of 3:1. Data about gender impact on clinical presentation of PHPT are still lacking.

**Methods:** We evaluated gender difference in biochemistry and clinical presentation in a single center series of 417 patients with PHPT (93 males aged 58.6±14.5 yrs, 324 females aged 61.7±12.8 yrs).

**Results:** Male PHPT patients resulted significantly younger (p=0.046) and more frequently symptomatic than women (62.3% vs. 47%, p=0.016).

Renal stones occurred more frequently in males than in females (50.5% vs. 33%, p=0.003).

Osteoporosis, defined as T score <-2.5 at any site, was significantly more frequent in women than in men (56.5% vs. 39.3%, p=0.015), while no difference was found in osteitis fibrosa cystica occurrence (21.5% vs. 20.7%).

However, no gender difference was found in biochemical parameters (serum PTH, calcium, phosphorus, creatinine, vitamin D, and urinary calcium).

Finally, the proportion of patients who should be referred for surgery (symptomatic patients and asymptomatic patients meeting surgical criteria recommended by current guidelines) was similar between males and females (84.6% vs. 84.9%).

**Discussion:** Even though biochemical activity of PHPT does not seem to be influenced by gender, clinical presentation is different, with males usually younger than females and more frequently affected by a symptomatic form of the disease. Moreover, renal stones are significantly more frequent in men, and osteoporosis in women. In spite of this gender difference, surgical indication is reached equally in males and females.

**Conclusion:** PHPT occurrence is lower in males, but more frequently symptomatic than in females. Clinical presentation is influenced by gender, despite no difference in biochemical profile.

**Abstract #528**

**THE INCREASING PROBLEM OF SUBCLINICAL AND OVERT HYPERVITAMINOSIS-D IN INDIA**

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**Objective:** In spite of high prevalence of vitamin-D deficiency (70-90%), there have been recent reports of vitamin-D toxicity from India. This study aimed to determine the changes in serum 25-hydroxy-vitamin-D (25OHD) distribution at our institute over last 6 years and compare with global trends.

**Methods:** Audit of 25OHD, calcium and parathyroid hormone (iPTH) reporting was done from January 2011 to February 2016. For patients having multiple assessments, only initial tests were considered. References for review were identified through searches of PubMed, Medline, and Embase for articles published till August 2016.

**Results:** 6963 reports of 25OHD from 5614 different patients (male: female=2251:3276) were evaluated; of which initial reporting from 5527 patients were analyzed [excluded: hypoparathyroidism (n=58) and primary hyperparathyroidism (n=29)]. Calcium and iPTH were available for 5501 (99.5%) and 1787 (32.3%) patients respectively. Vitamin-D deficiency and insufficiency was observed in 59.4% and 77.3%. Hypervitaminosis-D (HVD) (25OHD>250nmol/L) was noted in 225 (4.1%) patients, of whom 151 (2.7%) had vitamin-D intoxication (VDI) (25OHD>375nmol/L). Patients <20 years age had higher HVD (6.8%; 84/1233), compared to those in 20-40 (2.3%; 41/1817), 40-60 (4.1%; 76/1837) and >60 (3.8%; 24/640) years age groups (P<0.001). Overt HVD (elevated calcium and/or suppressed iPTH) was noted in 46.22% (104/225) patients with 25OHD>250nmol/L [10/74 patients (13.51%) in 25OHD 250-375nmol/L group and 94/151 patients (62.25%) in 25OHD>375nmol/L group]. Orthopedics, pediatrics and surgery had highest rates of HVD (7.9%, 7.2% and 7.0% respectively; P<0.001). An increasing trend for HVD was observed (1.48%, 3.62%, 3.90%, 4.78%, 6.21% and 7.82% in 2011, 2012, 2013, 2014, 2015 and 2016 respectively).

**Discussion:** A similar steady upward trend in 25OHD testing has been reported from Ireland, England, Canada and Australia. However HVD reports are scant, and has not increased in the developed world. Food fortification with vitamin-D is non-existent in India. Hence this increase can be attributed to increased pharmacologic
supplementation. Contrast to global trends, 25OHD testing at our institute has been constant over years. Hence, empiric unmonitored vitamin-D supplementation has increased over years High costs of 25OHD testing in India (USD 15-30/test) with regards to supplements may explain this [single intramuscular cholecalciferol injection (600000U) or sachet (60000 U) is USD 0.5].

Conclusion: There is a disturbing trend of increased HVD at our institute. Empiric, unmonitored, prolonged vitamin-D supplementation, especially intramuscular should be discouraged.

Abstract #529

MCCUNE-ALBRIGHT SYNDROME AND PRIMARY HYPERPARATHYROIDISM: AN UNSUSUAL CASE PRESENTING WITH COEXISTING BROWN TUMORS AND FIBROUS DYSPLASIA

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Objective: To present an uncommon case of McCune-Albright Syndrome (MAS) and primary hyperparathyroidism (PHPT) with coexisting brown tumors and fibrous dysplasia (FD).

Case Presentation: A 26-year old female with a history of MAS and kidney stones presented for evaluation of progressive hand deformities. She was diagnosed as a child with MAS with features of precocious puberty, café-au-lait spots, short stature and bowing. Examination showed soft tissue myxomas of her hands and breast and FD deformity of her right arm. Initial lab testing showed PTH 86-105 pg/ml and calcium 10.6-11.1 mg/dL consistent with PHPT. Lab testing also revealed vitamin D deficiency with a 25 OH vitamin D of 14 ng/mL. With replacement the level rose to 33 ng/mL with persistently elevated calcium and iPTH. A SPECT/CT sestamibi parathyroid scan revealed a 1.7 cm x 1.7 cm abnormal parathyroid gland extending into the superior mediastinum. Also noted were expansile lytic bone masses of the right and left scapula and right 2nd and 3rd anteromedial ribs which were typical of brown tumors. She subsequently underwent successful parathyroidectomy with normalization of her serum calcium and iPTH.

Discussion: MAS is a rare disorder characterized by bone, skin and endocrine abnormalities. While our patient had multiple features that were characteristic of MAS including FD, PHPT is uncommon in MAS. An unusual finding in our case was the radiographic findings consistent with brown tumors. Brown tumors are an uncommon complication of hyperparathyroidism. These benign tumors are typically seen in individuals older than 50 years while FD lesions tend to occur in younger patients. Brown tumors are characterized by locally destructive cystic lesions of cortical bone while FD typically results in more intense fibrosis. Despite some of these differences, however, both can present as expansile lytic lesions and can involve any skeletal region. Indeed, distinguishing between FD and brown tumors is difficult even with histopathology, and the diagnosis is often made in context with the clinical presentation. This similarity is likely related to the common downstream activation of PTH G protein coupled receptor (Gsα). In FD, this is due to an activating mutation encoding Gsα where in PHPT it is due to stimulation by excess PTH, both of which result in increased osteoclast activity and resorption.

Conclusion: MAS and coexisting brown tumors resulting from PHPT is not well documented. These bone manifestations are difficult to differentiate from one another and may represent disease overlap due to a shared pathogenesis. More research into the association between FD in MAS and brown tumors would assist in better understanding these rare bone disorders.

Abstract #530

HYPOCALCEMIA COMPLICATING PROSTATE CANCER TREATMENT

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Case Presentation: Case of a 77 y/o man with metastatic prostate adenocarcinoma, chronic kidney disease stage IV, obstructive uropathy, diabetes mellitus type 2 and hypertension who received a single dose of enzalutamide 160mg and denosumab 120mg for his prostate cancer in a routine hematology/oncology follow up visit. Six days later, he was diagnosed with hypocalcemia by routine labs. At the Emergency Room, the albumin corrected calcium was 6.8 mg/dL. He was given calcium gluconate intravenously and was discharged home in oral calcium carbonate. Four days later, the patient returned to ER and corrected calcium was found at 6.9 mg/dL. His physical examination showed a chronically ill, bedridden nonverbal man without acute findings. He was admitted to ward and the Endocrinology service started him on a continuous intravenous calcium drip to provide 30mg of elemental calcium per hour, oral calcitriol 0.25 mcg two times a day, and the oral calcium carbonate was switched to calcium citrate. The patient’s calcium normalized and the calcium drip was weaned off over the following 48 hours.

Discussion: Denosumab is a human monoclonal antibody with affinity for osteoblast receptor activator of nuclear
factor-kappa-B ligand (RANKL). The osteoblasts release RANKL that binds to RANKL receptors on the osteoclasts to increase bone resorption. Denosumab binds to the RANKL and thus avoids the osteoclast activation. In consequence, this leads to decreased bone resorption, our main mechanism to obtain calcium from the bone. Our patient had evidence of extensive diffuse metastatic lesions in a bone scan done 5 months earlier, progressive increase in his alkaline phosphatase and advanced CKD. His pre Denosumab albumin corrected calcium was 9.2mg/dL and when admitted his 25 Hydroxy Vitamin D level was 35 ng/mL and intact parathyroid hormone was 288 pg/mL. Therefore, the patient was dependent on the osteoclastic bone resorption to maintain adequate calcium levels in the presence of diffuse osteoblastic metastasis and increased bone turnover related to his CKD. Upon blocking his compensatory osteoclastic activity with Denosumab, the patient developed significant hypocalcemia.

Conclusion: Lack of recognition of the pathophysiological mechanism and knowledge of the half life of denosumab prevented recognition of a Grade 3 adverse event and optimal therapy, eGFR under 50 ml/min, increased alkaline phosphatase and poor performance score has been associated with Denosumab induced hypocalcemia. The primary endpoint of this case is to identify risks and increase awareness of secondary effects of Denosumab when used in the management of frequent conditions in order to optimize patient’s monitoring and treatment.

Abstract #531

A RARE CASE PRESENTATION OF A BROWN TUMOR OF THE LEFT FEMUR ASSOCIATED WITH PRIMARY HYPERPARATHYROIDISM

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Objective: We demonstrate a case of a patient with a Brown Tumor of the left femur who presented with hypercalcemia associated with Primary Hyperparathyroidism.

Case Presentation: A 52-year-old female with a pelvic mass and hypercalcemia presented with nausea, vomiting and early satiety. She was admitted to the gynecology service where she was evaluated with CT scan of the abdomen and pelvis. CT scan findings revealed a large uterine fibroid, pancreatic mass, lytic lesion of the ribs, pelvis, and proximal femur. Follow up head and chest CT scans revealed salt and pepper skull appearance and an anterior mediastinal mass. Endocrinology was then consulted. Initial biochemical assessment revealed: Calcium 13.6 mmol/L (ref range 8.7-10.5), PTH >2500 pg/mL (ref range 9.0-77), Ph 2.8 mg/dL (ref range 2.7-4.5), ionized Ca 2.06 mmol/L (ref range 1.06-1.42), Alk Ph 558 U/L (ref range 55-135), and Vitamin D 22 ng/mL (ref range 30-96) . In the setting of hyperparathyroidism and a pancreatic lesion, MEN-1 Syndrome was assessed with a Prolactin level 10.1 ng/mL (ref range 5.2-26.5) and an MRI of the brain, which did not reveal a pituitary mass. Subsequently, she underwent a sestamibi scan which revealed a mediastinal mass and uptake in the right side of the neck. She then underwent three and a half a gland parathyroidectomy. Pathology of the parathyroid gland revealed hypercellular parathyroid tissue weighing 40 grams. She then underwent prophylactic nailing of the left femur with biopsy of the lytic lesion. Pathology of the lytic lesion revealed giant cells with hemosiderin consistent with Brown tumor. On post-operative day one, lab values included Corrected Calcium 8.06 mmol/L, Ph 4.8 mg/dL, PTH 6.0 pg/mL, ionized Ca 0.92 mmol/L, and Alk Ph 362 U/L. At the time of discharge, patient was transitioned to oral calcium and ergocalciferol supplementation; PTH was in the normal range 73 pg/mL, and ionized calcium was slightly below range 0.99 mmol/L.

Conclusion: This case presented a patient with a Brown tumor associated with primary hyperparathyroidism. This condition is only represented in less than two percent of all cases of primary hyperparathyroidism. The markedly elevated parathyroid level in addition to the hypercalcemia and confirmatory biopsy of the tumor supports the diagnosis of a Brown tumor. Following parathyroidectomy, the patient’s PTH level appropriately declined along with her calcium level. Expectantly, she also had improvements of her symptoms. While this condition maybe rare, it is prudent to be vigilant as there is a risk of pathological fracture and failure to heal even after parathyroidectomy is performed.

Abstract #532

1,25-DIHYDROXYVITAMIN D-MEDIATED HYPERCALCEMIA DUE TO DISSEMINATED MYCOBACTERIUM AVIUM COMPLEX

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Objective: High serum calcium levels in hospitalized patients are commonly due to underlying solid organ or hematogenous malignancy. In the absence of an obvious malignancy, an elevated 1,25-dihydroxyvitamin D level with a suppressed PTH expands the differential diagnosis to include granulomatous disease, most commonly tuberculosis and sarcoidosis. We describe a case of non-PTH mediated hypercalcemia in a hospitalized patient with
**Abstract #533**

**EFFECTS OF TENOFOVIR ON BONE ULTRASOUND PARAMETERS AND BONE METABOLISM IN HIV-POSITIVE PATIENTS**

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**Objective:** Tenofovir (TDF) is one of the most prescribed anti-retroviral drug in the world. It is highly effective in controlling HIV replication, but it may induce osteoporosis and bone fractures. In the general population, bone ultrasonography (QUS) can predict osteoporotic fractures like dual X-ray absorptiometry (DXA). However, DXA is not easily available, whereas QUS can be used by every doctor without any problem of dosimetry. The aim of our study was to evaluate whether TDF exposure may alter QUS parameters. As a secondary endpoint we investigated bone metabolism parameters.

**Methods:** Data were collected on 234 HIV-positive patients (147 males, 87 females). The patients on TDF treatment were 167 (72%), with no significant difference in treatment regimens among men and women, both menopausal and fertile. Patients’ mean age was 47 ± 12 years. All the subjects underwent QUS and the following parameters were measured: Speed of sound (SoS), Broadband Ultrasound Attenuation (BUA), Stiffness index (SI) and T-score. Blood parameters of bone metabolism were also measured.

**Results:** TDF-treated patients compared with those on other anti-retroviral drugs, showed lower SoS (1554 ± 40 m/sec vs. 1569 ± 51 m/sec; p=0.018), lower BUA (107.1 ± 12.8 vs. 112.0 ± 13.9; p=0.010), lower SI (86.6 ± 16.9 vs. 93.9 ± 21.5; p=0.007) and lower T-score (-1.01 ± 1.32 vs. -0.46 ± 1.32; p=0.008). TDF-treated patients had also higher PTH (58.5 ± 31.3 pg/ml vs. 48.6 ± 24.9 pg/ml; p=0.024) and bone alkaline phosphatase (22.5 ± 11.9 vs 18.8 ± 12.7 IU/l; p=0.045). No difference between groups was found for age, BMI, duration of both HIV-infection and anti-retroviral therapy.

**Conclusion:** Many data are available on TDF negative effect on bone mineral density (BMD) measured by DXA. Some papers have demonstrated QUS ability in detecting HIV-induced osteoporosis. QUS represents an ultrasonography technique that does not require a radiologist for its use. QUS is also inexpensive and mobile.
and training for its use is very easy. Our data clearly show that QUS is able to detect TDF-induced bone loss. In fact, patients on TDF showed lower QUS parameters than subjects treated with other drugs. The secondary endpoint of our study also demonstrated higher PTH and bone alkaline phosphatase in TDF-treated patient. Since both parameters are elevated in osteomalacia we can hypothesize that TDF-induced bone loss is mainly due to low bone mineralization rather than to osteoporosis. In contrast to this hypothesis, however, we did not find any difference in blood phosphate between the two groups. Further studies are necessary in order to validate QUS in HIV-positive patients.

Abstract #534
THE EFFECT OF 25(OH)VITAMIN D LEVELS ON CHARACTERISTICS IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM
Anjana Divakaran, MD, Beatrice Wong, MD, Kenneth Sluis, MD, Hyon Kim, MD, Xiangbing Wang, MD, PhD

Rutgers Robert Wood Johnson Medical School

Objective: To examine the relationship between 25(OH)Vitamin D levels and the clinical characteristics in patients with primary hyperparathyroidism (PHPT).

Methods: 337 patients were included in this retrospective chart review of PHPT patients presenting at Robert Wood Johnson University Hospital from January 2000 to December 2013. Patients were classified based on their 25(OH)Vitamin D status in accordance with the Endocrine Society definitions: deficient (<20ng/ml), insufficient (20ng/ml-30ng/ml), and sufficient (>30ng/ml). The following characteristics were compared between the 3 groups: age, sex, body mass index (BMI), serum calcium levels, iPTH, 24-hour urine calcium, and creatinine. Data analysis was conducted with student T-tests.

Results: Of the 337 patients, 100 patients were 25(OH)Vitamin D deficient, 120 patients were 25(OH)Vitamin D insufficient, and 117 patients were 25(OH)Vitamin D sufficient. PHPT patients with sufficient vitamin D levels when compared to those that are deficient were: older (62.60 vs. 55 years, p<0.05), had a lower BMI (28.03 vs. 33.23, p<0.05), lower iPTH (135.28 pg/ml vs. 191.03 pg/ml, p<0.05), lower serum calcium (10.81 mg/dl vs. 11.06 mg/dl, p<0.05) and urine calcium (319.66 mg/24hr vs. 418.62 mg/24hr, p<0.05).

Discussion: Several studies have investigated the relationship between Vitamin D levels and PHPT. It has been reported that there is an inverse correlation between 25(OH)Vitamin D levels and the severity of the biochemical and clinical phenotype of PHPT. Both free and total 25(OH) vitamin D have also been reported low in PHPT. Our study confirmed prior findings that vitamin D sufficient PHPT patients presented with a less severe disease profile (lower iPTH, serum and urine calcium levels). However, our results also demonstrate differences in the demographic data with vitamin D sufficient patients being older with lower BMIs than vitamin D deficient PHPT patients.

Conclusion: In our study we saw Vitamin D deficient PHPT patients tend to be younger, have a higher BMI, higher calcium levels, and iPTH levels in comparison with vitamin D sufficient patients. Our study adds to the growing body of literature exploring the complex relationship between Vitamin D levels and PHPT. Though this relationship has been explored in several studies, the underlying physiological mechanism as well as other associated clinical characteristics is still not well understood. Further evaluation with a larger population size is needed to elucidate the details and significance between vitamin D and PHPT.

Abstract #535
CLINICAL CHARACTERISTICS OF PRIMARY HYPERPARATHYROIDISM AMONG DIFFERENT AGE GROUPS
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Objective: To compare the clinical presentations of patients with primary hyperparathyroidism (PHPT) with respect to age.

Methods: A retrospective chart review of PHPT patients who were evaluated at Robert Wood Johnson University Hospital from January 2000 to December 2013 was conducted. Patients were stratified according to their ages into the following categories: younger than 50 years old, 50-59 years old, 60-69 years old, 70-79 years old, and 80 years old and older. The age groups were then compared based on: gender, body mass index (BMI), serum calcium, iPTH, 24-hour urine calcium, and creatinine. Data analysis was conducted with student T-tests.

Results: A total of 555 PHPT patients were included in the study. The distribution of patients among the age groups were as follows: 113 patients younger than 50 years old (20.36%), 167 patients aged 50-59 years old (30.09%), 152 patients aged 60-69 years old (27.39%), 79 patients aged 70-79 years old (14.23%), and 44 patients aged 80 years old and older (7.93%). A greater percentage of
the aged 80 and above cohort was female (88.63% vs. 76.11%-86.08%). This elderly population compared to the age group of 50 and younger presented with higher 25-OH vitamin D levels (33.52 ng/mL vs. 24.09 ng/mL, \( p<0.05 \)) and lower 24 hour urine calcium levels (264.81 mg/24hr vs. 445.80 mg/24hr, \( p<0.05 \)). PHPT patients 80 years old and above also had a lower rate of renal stones compared to other age groups (11.36% vs. 17.96%-22.12%).

**Discussion:** Prior studies have associated the severity of PHPT with higher iPTH levels, higher serum Ca levels, lower 25-OH vitamin D levels and nephrolithiasis. Our study found that PHPT patients aged 80 and above were more likely to be female, present with lower 24-hour urine calcium levels, higher vitamin D levels, and a lower prevalence of nephrolithiasis. These findings suggest a less severe presentation of PHPT in the elderly. This has important implications for the treatment of PHPT in the elderly since there remains no consensus regarding the optimal treatment of PHPT in this age group. However, the less severe presentation of PHPT in the elderly suggests that a conservative treatment approach may be appropriate.

**Conclusion:** PHPT patients aged 80 and older in our study present with less severe disease characteristics. Therefore, medical management may be suitable for these patients. These results highlight the importance of further investigation into PHPT presentation among different age groups with a larger cohort of patients. We expect that these analyses will have further implications in determining the optimal treatment of PHPT in the elderly.

Abstract #536

**COEXISTING PARATHYROID ADENOMA AND PAPILLARY THYROID CARCINOMA**

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PGIMS Rohtak

**Objective:** The coexistence of parathyroid adenoma and papillary thyroid carcinoma is rare.

**Case Presentation:** 42 year female presented with complaints of bodyaches, proximal muscle weakness and neck swelling. Examination showed swelling left side of neck. Left sided cervical lymphnodes were palpable. Blood pressure was 128/77 mm Hg. Chest / CVS / CNS / Abdomen examination was normal. Biochemical investigations showed Parathormone (PTH) dependent hypercalcemia. Serum calcium was 14.0 mg/dl (normal 8.5- 10.5mg/dl), serum phosphate level was 2.0 mg/dl (normal 2.5-4.5 mg/dl), serum albumin 3.9 g/dl (3.5-5 g/dl), PTH level was 1900 pg/ml(normal 14- 72 pg/ml), serum alkaline phosphatase level was increased 2112 U/L (normal 50-136 UL), S.thyroglobulin level was 89.5/
OBESITY

Abstract #600

BARIATRIC SURGERY IN THE ELDERLY: NEVER TOO LATE

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Objective: Bariatric surgery is one of the fastest growing surgical procedures performed worldwide, with an estimated 200,000 operation/year in the United States. Although morbid obesity rates in patients >65 years of age are increasing, few centers have reported bariatric surgery outcomes in elderly patients. We describe a case of Roux-en-Y gastric bypass surgery in a 69 year old patient with an excellent outcome.

Methods: Case Presentation

Case Presentation: A 69 year old female with type 2 diabetes mellitus, hypertension, dyslipidemia and morbid obesity who underwent Roux-en-Y gastric bypass surgery in 5/2015 at age of 69. Her weight prior to surgery was 265.4 lbs. (120.57 kg) with a body mass index (BMI) of 47.16. Her A1C was 7.7% and the patient was on Levetiracetam (total daily dose 45 units), Novolog (total daily dose 15 units), Metformin extended release (750 mg twice daily) and Bydureon.

On her last follow up visit 15 months post operatively, she lost around 72 lbs. and Her A1C now is 6.0%. She was able to stop 3 of her diabetic medications. She is currently on Metformin extended release (750 mg twice daily) and Bydureon. Her lipid profile improved and she is off Simvastatin now. Her blood pressure improved now and 2 of her antihypertensive medications were discontinued.

Discussion: Obesity is a well known risk factor for type 2 diabetes mellitus, hypertension and dyslipidemia. Bariatric surgery has been approved as an effective treatment for type 2 diabetes mellitus in obese patients. Remission or improvement of diabetes, hypertension and dyslipidemia is well documented after bariatric surgery, however, there is a paucity of literature on perioperative mortality and morbidity of this procedure in elderly patients. In this abstract, we report the case of a 69 year old female with morbid obesity, type 2 diabetes mellitus, dyslipidemia and hypertension who underwent Roux-en-Y procedure and had favorable outcome. She had significant improvement in her diabetes, hypertension and dyslipidemia and was able to stop most of her medications for these conditions. She achieved a desirable weight loss and enjoyed a better quality of life.

Conclusion: Despite the paucity of literature about bariatric procedures in elderly patients, few studies report effectiveness of this procedures in elderly with a favorable outcome. Age alone should not be an exclusion for bariatric surgery in elderly.

Abstract #601

ASSESSMENT OF PATIENT AWARENESS OF RISKS ASSOCIATED WITH OBESITY AND THEIR PREFERRED INTERVENTION; A CROSS-SECTIONAL STUDY

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Objective: Obesity is a complex multifactorial disorder where excess body fat accumulation leads to a multitude of health related risks. In order to plan an effective organized effort we need to understand patient’s perspective of the problem and their preferred intervention.

Methods: 120 patients from our community clinics participated in a cross-sectional study based on surveys with multiple choice questionnaires. Inclusion criteria were age between 25-40 yrs and BMI between 27-40. The survey was designed to equate the risks associated with increased body fat and a question regarding patient’s preferred intervention.

Results: We found that 26% of the patient were unaware of their obesity based on their BMI measurements. Patient awareness regarding the correlation of heart disease and hypertension with obesity was the highest, while it was low for risks of cancer and renal diseases.

Discussion: Obesity is a complex multifactorial disorder where excess body fat accumulation leads to a multitude of health related risks. In order to plan an effective organized effort we need to understand patient’s perspective of the problem and their preferred intervention.

Conclusion: Patient showed an adequate awareness of BMI and weight circumference measures. In order to optimize the control of obesity epidemic, their is a need of a team based approach with effective communication utilizing available resources to reinforce healthier life styles. With the help of our onsite dietitian, an educational document was created. The document includes a meal plan, a 10 point instruction for dietary control along with informational apps and websites. This document will be included with the clinical visit summary of the patients. We plan to devise a program with our nutritionist to improve the counseling skills of the primary providers through small group discussions.
Conclusion: A healthier life style is well recognized as an effective management of obesity and its related co-morbidities. Understanding the patient perspective of obesity as a disease and its management is very important. We are proposing that, if patients are driving the change in their life style, it will be easier to adapt to those changes. Increasing communication, group therapy with the nutritionist, training primary providers as well as enhancing the available educational resources are a few of the proposals for bringing an effective change to control this epidemic.

Abstract #602

NECK CIRCUMFERENCE IS POSITIVELY CORRELATED WITH INSULIN RESISTANCE AND METABOLIC SYNDROME COMPONENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Neck circumference is an index for upper-body subcutaneous adipose tissue distribution. However, it remains unknown whether neck circumference affects insulin resistance. We performed this meta-analysis to investigate the relationship between neck circumference, insulin resistance and metabolic syndrome.

Methods: We comprehensively searched the databases of MEDLINE, EMBASE, and Cochrane databases from inception to July 2016. The inclusion criterion was published cross-sectional or cohort studies assessing neck circumference. The outcomes were body weight, body mass index, HOMA-IR, blood pressure, glucose, triglyceride, HDL-C, and LDL-C. We calculated pooled correlation (r) with 95% confidence intervals (CI) using random-effects model between neck circumference and these outcomes.

Results: Eight observational studies were included in the meta-analysis. There was significant positive correlation between neck circumference and body weight (r= 0.73, 95% CI: 0.67 to 0.78), body mass index (r= 0.66, 95% CI: 0.61 to 0.70), HOMA-IR (r= 0.35, 95% CI: 0.30 to 0.40), systolic blood pressure (r= 0.31, 95% CI: 0.24 to 0.37), diastolic blood pressure (r=0.27, 95% CI: 0.21 to 0.33), glucose (r=0.17, 95% CI: 0.12 to 0.21), LDL-C (r=0.25, 95% CI: 0.15 to 0.34), and negative correlation for HDL-C (r=-0.14, 95% CI: -0.25 to -0.01).

Conclusion: In the present meta-analysis, neck circumference is positively correlated with BMI, insulin resistance, and components of metabolic syndrome.

Abstract #603

EXERCISE REDUCES HEALTHCARE COSTS IN OLDER ADULTS WITH OBESITY BY REDUCING ANTI-HYPERTENSIVE AND ANTI-HYPERGLYCEMIC MEDICATIONS

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Objective: Exercise is a crucial intervention for healthy aging. However, it is not covered by the Veterans Health Benefits Package (HBP). The Gerofit exercise program is a clinical demonstration project that offers access to exercise interventions for older Veterans, who endure a greater prevalence of chronic diseases such as hypertension and Type 2 Diabetes. We aim to assess their impact on healthcare costs due to the medication reduction, providing evidence to support sustainability of these interventions for aging Veterans.

Methods: We evaluated data of 57 veterans engaged in Gerofit, an exercise program that empowers older Veterans to take charge of their health and improve their function. We collected demographics, anthropometrics, metabolic and clinical parameters, at baseline and after 16 months of follow up. In addition, we evaluated and compared anti-hyperglycemic and anti-hypertensive medication use.

Results: Average age was 64.1 ± 7.6 years, BMI was 31.1 ± 5.9, 95% were male, 91% with HTN and 46% with T2D. The average SBP was 125 ± 14 mmHg on 1.7 anti-hypertensive prescriptions/patient and average HbA1c was 6.5 ± 1.5 on 1.8 anti-hyperglycemic prescriptions/patient. After 16 months of intervention, 44% of participants had a reduction in weight, 44% had mild reduction in HbA1C, and 35% decreased their SBP. Regarding medication use, anti-hypertensive prescriptions were not increased, but actually reduced (1 less prescription in total, and 11 subjects decreased their medication dosages). Regarding T2D, anti-hyperglycemic medications did not increase either, as expected with T2D as a chronic progressive disease. Rather, prescriptions were reduced (2 less prescriptions in total, and 11 subjects decreased their medication dosages). Of the 11 people who decreased their dose of anti-hypertensive medications, 2 had reductions in weight and 6 had lower SBP. Of the 7 people who decreased their dose of anti-hyperglycemic medications, 5 had reductions in weight and 5 had lower SBP. For those who had a reduction in medication dosage, the average weight loss was 11.2 pounds.
Abstract #604

VITAMIN D AND HISTOLOGIC SEVERITY OF NONALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease worldwide. NAFLD and vitamin D deficiency often coexist and epidemiologic evidence has shown that both of these conditions share several cardiometabolic risk factors. Recent studies investigating the relationship between vitamin D levels and severity of NAFLD showed conflicting results. Thus we conducted a systematic review and meta-analysis to evaluate association between vitamin D and NAFLD histologic severity.

Methods: A comprehensive search of the databases of the MEDLINE and EMBASE was performed from inception through November 2016. Observational studies compared serum vitamin D levels among NAFLD patients with high and low histologic severity, which was determined by NAFLD activity score (NAS) and fibrosis score. We calculated pooled mean difference (MD) of 25-hydroxyvitamin D levels with 95% confidence intervals (CI) using random-effects model. The between-study heterogeneity of effect-size was quantified using the Q statistic and I2.

Results: Data were extracted from 6 studies involving 974 NAFLD patients. We found no significant difference in 25-hydroxyvitamin D levels among NAFLD patients with high NAS (score of ≥ 5) compared with those with low NAS with the pooled MD of -0.93 (95%CI -2.45 to 0.58), I2 = 0%, Pheterogeneity = 0.64. We also found no difference in patients with high fibrosis score (score of ≥2) compared with those with low fibrosis score with the pooled MD of 0.88 (95%CI -2.65 to 4.42), I2 = 64%, Pheterogeneity = 0.62.

Discussion: This is the first meta-analysis on the relationship between serum vitamin D and NAFLD histologic severity. Our study found no association between serum 25-hydroxyvitamin D levels and disease severity as determined by NAS and fibrosis score among patients with NAFLD.

Conclusion: Despite evidence implicating vitamin D in NAFLD pathogenesis, serum 25-hydroxyvitamin D is not associated with NAFLD histologic severity.

Abstract #605

WEIGHT LOSS RESULTS IN REDUCED LIVER ENZYME LEVELS IN OBESE PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objective: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide and is the third most common indication for liver transplant in North America. Epidemiological data show a strong correlation between NAFLD and the increased prevalence of obesity, diabetes, and the metabolic syndrome. This study investigated the effect of a medically supervised weight loss program on liver enzymes in patients with a clinical diagnosis of NAFLD by comparing data at baseline, 4 weeks, 12 weeks, and after 1 year of weight loss therapy.

Methods: This research consisted of a retrospective analysis of adult patients voluntarily enrolled in a physician-directed, community-based, weight management program from 2009 to 2014. Patients in the program consumed at least 800 kilocalories per day, attended weekly behavioral education classes, and expended approximately 300 kilocalories per day in physical activity. The primary outcome of reductions in liver enzyme levels was assessed by comparing weight loss with AST and ALT levels. Data analysis was conducted to control for potential confounders including age, BMI, ethnicity, gender, and statin use.

Results: A total of 97 patients with an average weight of 287 pounds, BMI of 45, with baseline elevations in AST and ALT were included in the study. Following 12 weeks of therapy, patients lost approximately 13% of their body weight and had a 10% reduction in waist circumference. Analysis revealed a positive correlation of 0.45 between weight loss and ALT levels (p=0.03) and 0.53 between weight loss and AST levels (p=0.01) at 1 year. A 44% reduction in ALT and a 41% reduction in AST were observed after 12 weeks of therapy, with ALT levels reduced by an additional 6% at 1 year. No differences were observed between genders, and adjustments for confounding risk factors showed no difference when comparing weight loss and liver enzymes.
Discussion: Weight loss programs that utilize a multidisciplinary approach are an effective treatment for patients with NAFLD. This study shows a 40-50% reduction in ALT and AST levels in obese patients following intensive weight loss therapy, with a positive correlation between weight loss and reduced liver enzyme levels at 1 year.

Conclusion: Weight loss is currently the most effective treatment for patients with NAFLD. This study showed a statistically significant reduction in liver enzymes in obese patients with a clinical diagnosis of NAFLD who underwent intensive weight loss utilizing a multidisciplinary approach. Organized weight loss programs play a pivotal role in treating patients with NAFLD and may decrease progression to end stage liver disease.

Abstract #606

COMPARISON OF WAIST-TO-HIP RATIO AND BODY MASS INDEX IN FIRST TRIMESTER AS SURROGATE MARKERS FOR DEVELOPMENT OF PREECLAMPSIA

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Objective: The objective of this study was to identify the relationships of body mass index (BMI) and waist-hip-ratio (WHR) as surrogate markers for preeclampsia.

Methods: This was a prospective randomized study of 380 pregnant women with singleton gestations in their first trimester. Anthropometric parameters including WHR and BMI were measured at the first antenatal visit during the first trimester of pregnancy (≤12 weeks of gestational age). The subjects were monitored and assessed after 20 weeks of gestation for development of preeclampsia. The sociodemographic data and obstetric outcomes were assessed for each subject. All of the statistical tests were performed using SPSS software, version 20.

Results: The maternal WHR and BMI at the beginning of pregnancy were significantly associated with the occurrence of preeclampsia (P=0.005 and P=0.001, respectively). The incidence rate of preeclampsia in this study is 5% of the subjects. The mean WHR is 1.04±0.12SD while the mean BMI is 34.36±10.22SD. However, this study revealed that waist-hip-ratio measured in the first trimester is significantly associated with increased risk of development of preeclampsia when compared to BMI. This study revealed that waist-hip-ratio and body mass index had relative risks of 3.317 (CI: 1.5–6.75) and 2.418 (CI: 1.25–5.15) respectively for preeclampsia.

Discussion: Preeclampsia is defined as gestational hypertension and significant proteinuria occurring in the second half of pregnancy. It is associated with increased maternal and neonatal morbidity and mortality. Among the studied subjects, WHR increased with increasing maternal age and parity. The findings revealed that women with gestational hypertensive disorders have higher BMI and WHR when compared with normal pregnant women. The risk of developing gestational hypertension was significantly associated with increase in WHR when compared to BMI. These findings about WHR support those of other researcher’s findings. This study found that WHR will detect more women at risk if used as an important risk factor for preeclampsia especially during the first trimester.

Conclusion: This study revealed that first trimester measurement of waist-to-hip ratio can detect more women that are at risk of preeclampsia compared to body mass index which is used routinely at the population studied. This will help in early detection of mothers at risk.

Abstract #607

GASTRIC BYPASS SURGERY IS ASSOCIATED WITH A REDUCTION IN VASOCONSTRICTIVE MEDIATORS

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Objective: Obesity is known to be associated with hypertension. Since gastric bypass surgery is associated with a reduction in blood pressure, we hypothesized that weight loss following surgery in morbidly obese patients is associated with a decrease in plasma concentrations of vasoconstrictors and an increase in the concentrations of vasodilators.

Methods: Fourteen patients with morbid obesity and diabetes were investigated at baseline and 6 months after Roux-en-Y gastric bypass (RYGB) surgery. Fasting blood samples were collected and plasma and serum s separated for the measurement of vasoconstrictors, angiotensinogen, renin and angiotensin II; and vasodilators, ANP, BNP, cGMP, and cAMP. The expression of angiotensin converting enzyme (ACE) in circulating MNC was also measured.

Results: Six months following RYGB, BMI fell from 51.3±12.0 to 41.6±10.4 kg/m2 and there were significant improvements in the HbA1C. Systolic but not diastolic blood pressure fell significantly at 6 months (from 135±13 to 124±11 mmHg; p=0.05). Plasma concentrations of angiotensinogen, angiotensin II and renin fell significantly at 6 months by 22±10% 22±8% and 35±13%, 9p=0.05 for
all) respectively, at 6 month following surgery.

**Discussion:** Plasma concentrations of angiotensinogen, angiotensin II and renin fell while ANP concentrations increased significantly by 24±13% at 6 months. There was no significant change in BNP, cAMP or cGMP concentrations and ACE mRNA expression.

**Conclusion:** It is thus likely that the hypertension of obesity is associated with an activation of RAS which diminishes with weight loss. Simultaneous with an increase in ANP suggests that this vasodilator may contribute to the fall in blood pressure following RYGB.

**Abstract #608**

**IMPROVING GLYCEMIC CONTROL WITH MIFEPRISTONE IN CUSHING’S SYNDROME PATIENTS MAY LEAD TO SIGNIFICANT WEIGHT-LOSS.**

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**Objective:** Obesity is a prominent feature of Cushing’s syndrome (CS), with 70-80% of patients overweight or obese, and most patients seek advice due to rapid weight gain. Prolonged exposure to hypercortisolemia leads to insulin resistance, hyperglycemia, weight gain and cardiovascular complications. Medical therapy is usually aimed at reducing the degree of hypercortisolemia. However, durable normocortisolemia is difficult to achieve with steroidogenesis inhibitors and somatostatin analogs, and doesn’t always translate into meaningful improvements in glycemic control or weight-loss. Glucocorticoid receptor antagonism with mifepristone (MIFE, Korlym®, Corcept Therapeutics) offers an alternative mechanism of action. In the pivotal SEISMIC trial (n=46), average weight-loss was 5.7%, mean FPG decreased from 149 to 104mg/dL and HbA1c from 7.43 to 6.29% despite increases in cortisol levels. We present four CS cases with weight loss ≥8% on MIFE therapy.

**Case Presentation:** Case 1: 37yo woman (adrenal CS) lost 30lbs (352 to 322lbs; 8.5%) after 3 mo on MIFE 600mg/d. There was a significant decrease in HbA1c (7.3 to 6.4%) and FBG (206 to 112mg/mL) without changes in antidiabetic medications (sitagliptin 100mg/d). Case 2: 46yo woman (pituitary CS) lost 40lbs (258 to 218lbs; 15.5%) after 11 mo on MIFE 600 mg/d. Both HbA1c (9.0 to 6.5%) and FBG (247 to 136mg/mL) decreased, while Levemir (54IU /d), Humalog (24IU TID) and metformin (1000mg/d) were stopped and linagliptin (5mg/d) was continued. Case 3: A 55yo woman (pituitary CS) lost 45lbs (220 to 175lbs; 20%) after 9 mo on MIFE 600mg/d. Both HbA1c (7.5 to 6.6%) and FBG (153 to 129mg/mL) decreased without changes in antidiabetic medications (sitagliptin 100mg/d)

**Case 4:** A 45yo woman (pituitary CS) lost 50lbs (178 to 128lbs; 28%) after 23 mo on MIFE 1200mg/d. Patient has had T1DM since 25yo and is on an insulin pump (lispro). Both HbA1c (9.9 to 7.3%) and FBG (300 to110mg/dL) decreased, along with the insulin daily requirement.

**Conclusion:** These cases illustrate a significant weight-loss in parallel with a significant improvement in glycemic control by treatment with a glucocorticoid receptor antagonist (MIFE) in patients with DM. In all cases, there was no intensification of antidiabetic regimen, and the weight loss was greater than previously reported in SEISMIC. Further research is needed to understand the metabolic benefits of long-term treatment with MIFE in patients with Cushing’s syndrome.

**Abstract #609**

**CHILDHOOD PREDICTORS OF CARDIOVASCULAR DISEASE IN ADULTHOOD. A SYSTEMIC REVIEW AND META-ANALYSIS**

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**Objective:** Childhood obesity predicts the risk of adult adiposity, which is associated with the earlier onset of cardiovascular disease and dysglycemia. It is not known whether childhood obesity directly contributes to the presence of adult atherosclerotic cardiovascular disease-ACVD: hypertension, carotid intima media thickness (CIMT) stroke or ischemic heart disease (IHD).

**Methods:** Data sources were: Web of Science, MEDLINE, PubMed, CINAHL, Cochrane, SCOPUS, ProQuest, and reference lists. Studies measuring Body Mass Index, skinfold thickness, or waist circumference were selected.

**Results:** Childhood BMI predicted CIMT: OR, 3.39 (95% CI, 2.02 to 5.67, P <0.001) and risk of impaired glucose tolerance in adulthood, but its ability to predict ACVD events (stroke, IHD; OR, 1.04; 95% CI, 1.02 to 1.07; P<0.001) and hypertension (OR, 1.17, 95% CI 1.06 to 1.27, P = 0.003), was weak-moderate. BMI was not predictive of systolic blood pressure (r -0.57, P =0.08) and weakly predicted diastolic blood pressure (r 0.21, P =0.002). SF in childhood weakly predicted CIMT in female adults only.
(spearman rank correlation 0.09, P < 0.05).

**Conclusion:** Childhood BMI predicts the risk of dysglycemia and abnormal CIMT in adulthood but its ability to predict hypertension and ACVD events was weak and moderate respectively. SF was a weak predictor of CIMT in female adults.

**Abstract #610**

**PHYSICAL ACTIVITY ASSESSMENT AMONG MALE ADOLESCENTS AND ITS RELATION TO BODY MASS INDEX**

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**Objective:** During the last 3 decades, the prevalence of obesity has tripled among persons aged 6-19 years. Schools have a responsibility to help prevent obesity and promote physical activity. Active commuting to school may reduce the risk of obesity, but not necessarily overweight

The primary outcome of the study is to assess the activity level among the participants and to assess its relationship to BMI, lifestyle and dietary habits.

**Methods:** A cross-sectional study that includes students from Intermediate and High schools located in Taif city, Saudi Arabia between April 2014 and June 2015. Student’s height and weight were measured and body mass index (BMI) was calculated. Baseline characteristics, lifestyle and eating habits data were self-reported. Those with chronic medical condition and learning or physical disabilities were excluded.

Physical activity index (PAI) was assessed using previously validated questionnaire (Mota and Esculcas 2002). The questionnaire has 5 questions with 4 choices each, maximum points are 20. Student’s total score (0–5) considered sedentary, (6–10) low active, (11–15) moderately active, and (16–20) vigorously active.

**Results:** A total of 400 male students were participated, mean age 15.2 years old (SD 1.6), mean BMI of 22.5 kg/m2 (SD 7.7), mean waist circumference (WC) 78.3 cm (SD 13.7), and 22.8% attending private school. The mean PAI score was 10.7±3.6, with 5.7% were considered sedentary, 45.7% low active, 38.2% moderately active, and 10.4% vigorously active.

Overall 83.4% live with both parents, 70.6% watch TV < 3hrs /day, 21.9% eat fruits daily, 33.6% drink soda daily, 21.6% don’t eat fast food, 34.1% usually walk to and from school,35.7% play video game daily, and 6% were active smokers.

Compared to those who were moderately/vigorously active, those who were sedentary/low active group has mean age of 15.2 vs 15.1 yrs (p 0.45), mean BMI 22.5 vs 22.5 (p 0.99), mean WC 78.9 vs 77.4 cm (p 0.29), 82.6 vs 83.6% live with both parents (p 0.22), 72.9 vs 67.8% watch TV < 3hrs /day (p 0.56), 16 vs 29.4% eat fruits daily (p 0.004), 37.5 vs 29.4% drink soda daily (p 0.123), 22.4 vs 19.8% don’t eat fast food (p 0.76), 27.8 vs 41% usually walk to and from school (p 0.16), and 34.6 vs 39% play video game daily (p 0.63).

**Conclusion:** Majorities considered being in the low active group and minorities are considered to be sedentary. Although there was no statistical difference in the BMI or WC according to activity level, but those who were in the moderate/vigorous active group were significantly more likely to eat fruits daily and to routinely walk to and from school.

**Abstract #611**

**CHANGE IN BODY MASS INDEX (BMI) AFTER HIGHLY ACTIVE ANTIRETROVIRAL THERAPY AMONG HIV PATIENTS IN KANO, NORTHWESTERN NIGERIA**

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**Objective:** Highly Active Antiretroviral Therapy (HAART) has improved the health and wellbeing of people living with HIV, but at the same time, it causes excessive weight gain through abnormal fat distribution (lipodystrophy). Overweight and obesity have implications on the cardiovascular status of these patients.

We aimed to determine the change in BMI after the commencement of HAART and the factors associated with this change.

**Methods:** It was a longitudinal prospective study. One hundred and eighty HIV patients that met HAART criteria were recruited before the commencement of therapy. Their weight, height, waist and hip circumferences, blood pressure and laboratory investigations were done. Six months into HAART the anthropometric and laboratory parameters were repeated. Only data of 150 participants were available at the end of the study.

**Results:** The mean age of the participants was 35.7±10.0 years, and 64% of them were females. Mean BMI pre-HAART was 19.4±5.9 kg/m2 while post-HAART mean BMI was 24.0±6.0kg/m2 (p < 0.000). Before commencement of HAART, 46.0% of the participants were underweight, 40.0% of normal weight, 10.0%
overweight and 4.0% obese. After initiation of HAART, 12.7% were underweight, 55.3% of normal weight, 16.7% overweight and 15.3% obese. The factors associated with increased BMI were impaired fasting glucose, Diabetes, Insulin resistance, raised triglyceride, low HDL, increased waist circumference and waist-hip ratio and metabolic syndrome (p < 0.05). There was a statistically significant association between development of obesity and increased CD4 cell count (p=0.007).

Discussion: Exposure to HAART causes stabilization of weight in the majority of the participants and in others they became overweight and obese. This finding is similar what was found in other short-term studies that looked at weight changes following HAART initiation in other parts of the world. Duration of HAART and type of regimen has no effect on this weight change. Weight gain causes metabolic derangement which can cause cardiovascular problems in these patients.

Conclusion: Exposure to HAART causes weight gain and its attendant complications in HIV patients. There is the need for adequate metabolic follow-up for these patients.

Abstract #612

EATING DISORDERS PREVALENCE AND ITS RELATION TO BODY MASS INDEX AND LIFESTYLE HABITS

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Objective: Eating disorders are characterized by a persistent disturbance of eating that impairs health or psychosocial functioning. More than 55% and 30% of high school girls and boys report disordered eating symptoms and engaged in ≥1 maladaptive behaviors (vomiting, laxatives, binge-eating) to induce weight loss.

The primary outcome of the study is to assess the prevalence of eating disorders among the participants and to assess its relationship to lifestyle and dietary habits.

Methods: A cross-sectional study that includes students from 15 different Intermediate and High schools located in Taif city, Saudi Arabia between April 2014 and June 2015. Student’s height and weight were measured and body mass index (BMI) was calculated. Baseline characteristics, lifestyle and eating habits data were self-reported. Those with chronic medical condition, psychological illness and learning disabilities were excluded.

We used SCOOF questioner to screen for eating disorders. An answer of ‘yes’ to ≥2 questions out of the total 5 questions were considered to be positive.

Results: A total of 543 students were participated, 75.3% were boys, mean age 15.6 years old (SD 1.6), mean BMI of 21.6 kg/m² (SD 6.1), mean waist circumference (WC) 78.8 cm (SD 14.1), 11.2% attending private school. The mean SCOOF score was 1.64+1.3 and 47.7% screened positive for eating disorders.

Overall 6.8% were smokers, 57.6% of the mothers have high school or less, 44.5% reports sleeping for 6-8 hrs/night, 35.5% reports daily soft drink consumption, 29.9% reports eating fast food at least once weekly, 17.9% eating fruits daily, and 40.3% reports sedentary lifestyle.

Compared to those who screened negative for eating disorders, those screened positive has mean age 15.6 vs 15.7 yrs (p 0.41), 76.8 vs 73.9% were boys (0.44), BMI of 23.1 vs 20.1 (p <0.001), WC 82.3 vs 75.6 cm (p <0.001), 12 vs 10.9% attending private school, has mean SCOOF score 2.81 vs 0.57 (p <0.001), 61.6 vs 54% of the mothers have high school or less (p 0.04), 40.5 vs 47.9% reports sleeping for 6-8 hrs/night (p 0.18), 16.9 vs 19.3% eating fruits daily (p 0.55), 39.3 vs 31.4% reports daily soft drinking (0.07), 31.4 vs 28.7% reports eating fast food at least once weekly (p 0.26), and 39.6 vs 42.4% reports sedentary lifestyle (p 0.88).

Conclusion: 47.7% screened positive for eating disorders and those were significantly more likely to have higher BMI, larger WC and have less educated mothers. Except for sedentary lifestyle, those screened negative for eating disorders were more likely to report better dietary and sleeping habits but none were statically significant. No difference observed in regards to gender or age between the groups.

Abstract #613

PREVALENCE OF HYPERTENSION AND PRE-HYPERTENSION AND ITS RELATION TO BODY MASS INDEX AND LIFESTYLE HABITS

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Objective: Among the several risk factors for hypertension, the commonest is obesity. A cross-sectional study assessed 6790 adolescent in Houston school showed that 9.5% were pre-hypertensive and 9.4% were hypertensive and it increased with increasing body mass index (BMI).

The primary outcome of the study is to assess the prevalence of HTN and preHTN among the participants and to assess its relationship to BMI and lifestyle and eating habits.

Methods: A cross-sectional descriptive study that includes students from the Intermediate and High schools located in Taif city, Saudi Arabia was conducted between April 2014 and June 2015. Student’s height and weight were
measured and body mass index (BMI) was calculated. Baseline characteristics, lifestyle habits data were self-reported. Those with chronic medical condition and learning disabilities were excluded.

Age and gender blood pressure (BP) calculator was used with percentile <90 been normal, 90-94.9 prehypertension (preHTN), and >95 hypertension (HTN).

**Results:** A total of 424 students were participated, 74.8% were boys, mean age 15.44 years old (SD 1.5), mean BMI of 22.3 kg/m2 (SD 5.8), and mean waist circumference (WC) 82.1 cm (SD 14.8). 14.2% have preHTN and 26.4% have HTN.

Overall 6.5% were smokers, 31.5% reports daily soft drink consumption, 23.5% reports daily milk drinking, 13.7% reports daily potato chips eating, 77.9% reports eating fast food at least once weekly, 17.2% eating fruits daily, 38.6% at least walk once a week to and from school, and 34.8% reports sedentary lifestyle.

Compared to those with normal BP, those either HTN or preHTN has mean age 15.6 vs 15.2 yrs (p 0.002), 67.4 vs 79.8% were boys (p 0.001), BMI of 24.7 vs 20.6 (p <0.001), WC 87.6 vs 78.3 cm (p <0.001), 7.6 vs 6.7% were active smokers (p 0.91), 24.9 vs 36% reports daily soft drink consumption (p 0.08), 25.7 vs 22% reports daily milk drinking (p 0.43), 12.9 vs 14.2 reports daily potato chips eating (p 0.58), 78.4 vs 77.6% reports eating fast food at least once weekly (p 0.54), 13.5 vs 19.8% eating fruits daily (p 0.50), 40.6 vs 37.2% at least walk once a week to and from school (p 0.32), and 35.7 vs 34.3% reports sedentary lifestyle (p 0.95).

**Conclusion:** 40.6% have either HTN or preHTN and those were significantly more likely to be older, girls, have higher BMI, and have larger WC. No significant difference observed in regards to lifestyle or eating habits between the groups.

**Abstract #614**

**WERNICKE’S ENCEPHALOPATHY AFTER TREATMENT OF DIABETIC KETOACIDOSIS IN A PATIENT WITH TYPE 1 DIABETES AND PREVIOUS BARIATIC SURGERY**

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**Objective:** Wernicke’s encephalopathy (WE) is caused by thiamine deficiency, an essential coenzyme in carbohydrate metabolism. Classic findings include a triad of confusion, ataxia and ocular symptoms. In the absence of alcoholism, other states of nutritional deprivation must be considered including malabsorption from weight loss surgeries.

**Case Presentation:** Clinical Case

49 year old female with type 1 diabetes was admitted for diabetic ketoacidosis (DKA) after two weeks of anorexia and diarrhea. Glycemic control was poor with A1C of 11.8% and BMI of 26.5.

Past history included morbid obesity (BMI 44.4) requiring laparoscopic roux-en-Y gastric bypass 4 years prior to admission. Post-operative complications included gastric necrosis with marginal ulcers, severe malnutrition with feeding intolerance requiring gastrostomy and recurrent DKA with intra-abdominal sepsis.

Anion gap metabolic acidosis with serum ketones was identified. Blood glucose was 8.6 mmol/L at ER after a 20 unit patient-administered insulin bolus at home. Fluid resuscitation with both saline and 5% dextrose along with insulin infusion was initiated. Acidosis resolved within 24 hours. However, confusion was noted along with right medial rectus ophthalmoplegia, prominent upper limb dysdiadochokinesia and severe truncal ataxia.

Collateral history revealed a 2-year history of unsteady gait with cognitive and behavioral changes, resulting in a leave of absence from work as a registered nurse.

Provisional diagnosis of WE was entertained. Empiric therapy with intravenous thiamine was initiated. Remarkable clinical response was noted with resolution of dysdiadochokinesia, ophthalmoplegia and improved confusion and gait.

**Discussion:** Clinical findings and response to thiamine confirmed the diagnosis of WE. Gastric bypass and post-operative feeding intolerance predisposed her to malabsorption and thiamine deficiency. Poorly controlled diabetes was a unique aspect to this case. Acute correction of metabolic derangements in the setting of sustained hyperglycemia may have acted as a precipitating and aggravating factor for the development of WE. Increased thiamine requirements for glucose oxidation during DKA therapy further depleted endogenous thiamine stores.

**Conclusion:** With the increased incidence of obesity and popularity of weight loss surgeries, this case stresses the importance of heightened awareness of thiamine deficiency in this population. It also serves as a reminder that supplementation compliance must be questioned rather than assumed to reduce the risk of severe and potentially irreversible complications.
Abstract #615

INSIGHTS AND PERCEPTIONS OF OBESITY MANAGEMENT IN OLDER PEOPLE WITH OBESITY: RESULTS OF NATIONAL STUDY

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Objective: Continued obesity management challenges remain, especially among older persons who may have greater comorbidities. The ACTION (Awareness, Care, and Treatment In Obesity maNagement) study examined attitudes and behaviors related to obesity management among people with obesity (PwO). As a growing proportion of the population, this research examines results among people ages 65 and older.

Methods: This study consisted of a cross-sectional, US-based, stratified sampling of people with obesity (PwO). Inclusion criterion included: BMI ≥ 30 kg/m² based on self-reported height and weight. Adult PwO (n=3,008) completed online surveys. Of the total number of PwO, 946 (31%) were ages 65 and older. The instrument assessed attitudes, experiences and behaviors associated with obesity management. Descriptive statistics among older PwO and comparisons between PwO 65 years and older (“older PwO”) and 64 years and younger (“younger PwO”) are presented.

Results: Two-thirds (66%) of older PwO reported feeling that “obesity is a disease,” similar to younger PwO (64%). Of the PwO that have discussed “losing weight” or “being overweight” with a health care provider (HCP), a lesser proportion (56%) of older PwO report that they “seek support” from their HCP for weight loss (65% among younger). Similarly, fewer older PwO (50%) report having received a “formal diagnosis” of obesity as compared with younger PwO (56%). Older PwO report greater weight loss “success” in the past year (13%) compared with younger PwO (9%). As expected, older PwO report greater comorbidity prevalence (variable by condition, as much as twice the prevalence) such as high blood pressure, high cholesterol, and sleep apnea. A 33% greater proportion of older PwO (16%) reported that “a specific medical event” (heart attack, stroke, etc.) had a great influence on their desire to manage weight compared with younger PwO (12%).

Discussion: Considering their greater prevalence of comorbidities, older PwO may need more appropriate, attentive obesity management from HCPs. Greater morbidity and experiences with health-related life events may have also made their efforts to manage weight more serious and vigilant, which could be associated with greater self-reported weight loss success.

Conclusion: Although similar in many ways, older PwO show important statistical and proportional differences in obesity care and management compared with younger PwO. Older PwO more often report improvement in obesity management than their younger peers and, therefore, should be addressed by clinicians at least as well as younger PwO. Efforts at providing HCPs a better understanding of how older PwO perceive and manage their obesity may further improve outcomes in this group.

Abstract #616

EFFECT OF PHENTERMINE ON WEIGHT LOSS IN THE OBESE IN AN ACTIVE CLINICAL PRACTICE

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Objective: In view of the rising tide of obesity and the high cost of the newer anti-obesity drugs, we have carried out a retrospective analysis of the effect of phentermine, the oldest licensed anti-obesity drug in the pharmacopeia, in our clinical practice.

Methods: The study compared the magnitude of its effects in patients with and without diabetes and the occurrence of side effects like palpitation in active clinical practice. Out of 97 obese patients (Body weight=110±25 Kg) who were prescribed phentermine at a dose between 30-37.5 mg daily for about 6±1 months in our practice, 16 patients did not respond (<1Kg change).

Results: In the responders (n=81), the overall fall in body weight was 7.2±3.7 Kg or 6.4±3.1% (P<0.05) with a fall in systolic blood pressure (SBP) of 3.4±1.6 mmHg (P<0.05) and diastolic blood pressure (DBP) of 1.6±1.3 mmHg (NS). When patients were stratified according to their diabetes status, the mean weight loss in non-diabetics (n=32) was 10.4±5.4 Kg (P<0.001) while SBP and DBP fell by 6.2±3.3 (p=0.09) and 1.4±1.8 mm (NS) respectively. Among patients with diabetes, weight loss was 4.1±2.4 Kg (p=0.06) in those with HbA1c >6.5% (n=16), 3.2±1.6 Kg (p=0.09) in those with HbA1c between 6.0 to 6.5% (n=12) and 7.4±4 kg (p=0.01) in those with HbA1c <6% (n=21). Blood pressure did not change significantly in any of the diabetes subgroups. There was a slight and non-significant increase in the heart rate in obese patients without diabetes by <2±1 bpm and in patients with diabetes by 5±4 bpm. Two patients complained of moderate to severe palpitation
and had to stop the drug; one of them had a heart rate of 140 (sinus tachycardia). HbA1c levels did not change significantly with the use of phentermine.

**Conclusion:** We conclude that in a real life setting, the use of phentermine is associated with a significant weight loss and a fall in SBP without significant systemic side effects. The magnitude of fall is significantly lower in patients with diabetes. These results are important considering the fear of side effects currently in the minds of physicians, on the one hand, and the expense of the novel anti-obesity drugs on the other.

Abstract #617

**UNIQUE DIFFERENCES IN ADIPOKINES, MARKERS OF INFLAMMATION AND CIRCULATING GUT HORMONES AFTER BARIATRIC SURGERY BETWEEN OBESE NON DIABETIC, PREDIABETIC AND DIABETIC SUBJECTS**

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**Objective:** Bariatric surgery induces significant long-lasting weight loss and ameliorates obesity-associated co-morbidities. However, the exact mechanisms by which these interventions improve metabolic alterations are still under debate. Post-operative changes in circulating gut hormones, adipokines and inflammatory markers are thought to play a key role but results are still controversial. The aim of this study was to evaluate the impact of bariatric surgery on adipokines, inflammatory markers, glucagon like peptide (GLP)-1 and glucose-dependent insulinotropic polypeptide (GIP) levels in obese subjects with different levels of glycemic control.

**Methods:** Prospective study that included 102 obese subjects. Patients were evaluated at baseline, 4, 12 and 24 weeks after bariatric surgery. All subjects were assessed for adiponectin, leptin, Plasminogen Activator Inhibitor Type 1 (PAI-1) (multiplex analysis; Millipore, Billerica, MA), Interleukin (IL)-6 (HS ELISA), GLP-1 & GIP (RIA).

**Results:** Ninety-eight subjects completed 24-weeks of follow-up (30 non-T2DM, 34 pre-DM and 34 T2DM). Baseline demographic characteristics were similar between the groups with the exception of higher A1C, insulin, HOMA2-IR, PAI-1 and GIP-1 in T2DM patients. Adipokines improved significantly after 24 weeks in all groups. Adiponectin/leptin ratio improved significantly in pre-DM (p=0.01) and T2DM (p=0.04). PAI-1 improved significantly in pre-DM (p<0.0001) and DM (p=0.03). IL-6 improved significantly only in T2DM (0.97±0.15 to 0.52±0.12 pg/ml, p=0.04). At endpoint GLP-1 and GIP levels changed significantly in non-DM (GLP-1=33.81±1.69 to 48.68±3.35, p=0.0004; GIP=11.96±0.82 to 32.05±3.01, p=0.007) & pre-DM (GLP-1= 30.07±1.97 to 38.95±3.34, p=0.02; GIP=11.79±0.97 to 18.34±0.67, p=0.002) but not on DM (GLP-1=40.28±2.56 to 37.25±3.61, p=0.20; GIP=16.28±1.94 to 17.25±2.06, p=0.22). Changes in gut hormone levels after 24 weeks were associated with baseline A1C, insulin and HOMA2-IR in univariate regression analysis, but this relationship was lost in the multivariate model after adjusting for age and gender.

**Discussion:** This report shows that inflammatory markers and circulating gut hormones behave differently after bariatric surgery depending on baseline glycemic state. The lack of improvement on GLP-1 and GIP levels in the T2DM patients is surprising and need further exploration.

**Conclusion:** Bariatric surgery was associated with an improved Adiponectin/Leptin ratio in pre-DM and DM patients. GLP-1 and GIP levels improved in non-DM and pre-DM, but this was blunted in T2DM, contrasting with the improvement in PAI-1 and IL6. These data questions the role for GLP-1 and GIP in the rapid recovery of glycemic control in DM.
OTHER

Abstract #700

CLUBBING AS A PRESENTATION OF ANABOLIC STEROID USE

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Objective: To highlight a serious potential complication of anabolic steroid use

Methods: Case and literature review

Case Presentation: 45 year old man presented for evaluation of digital clubbing over 6 months. He initially underwent an evaluation including O2 saturation, PFTs, Echo and chest CT, which did not reveal any pathology. His reported use of exogenous anabolic steroids and acromegoid appearance prompted referral to us. The patient was otherwise asymptomatic; no weight loss, respiratory or gastrointestinal symptoms. The family history was non-contributory. The patient did not smoke or use mind-altering drugs. He was an avid exerciser and admitted to several illicitly obtained and self-administered medications to enhance muscle mass: testosterone cypionate 500mg IM QW, nandrolone (19-nortestosterone) 300mg IM QW, GHRP-6 (GH releasing peptide) 200mcg TID SC and tamoxifen 10mg PO BID. On exam, BP 152/94, HR 104, and BMI of 32.3 kg/m2. He was very muscular with normal male pattern hair growth, facial plethora, somewhat coarsened facial features, and mild frontal bossing. There were no other signs of acromegaly. Moderate clubbing of his fingers was evident. The chest was clear and the cardiac sounds normal. The patient declined a testicular examination. Labwork done 3 days after his last testosterone injection was notable for a total testosterone of 5721ng/dl, normal TSI, and Hgb/Hct 18.8g/dL/55.9%. Notable for a total testosterone of 5721ng/dL, normal TSI, and Hgb/Hct 18.8g/dL/55.9%, consistent with polycythemia.

Discussion: We herein describe a case of a man with anabolic steroid abuse, presenting as digital clubbing. The differential diagnosis of clubbing includes hypoxemic states, typically due to advanced cardiopulmonary diseases. It may also relate to conditions where blood flow to the terminal digits is impaired, such as in conditions associated with platelet aggregation (e.g., inflammatory bowel disease, malignancy), and Graves disease (“thyroid acropachy”), due to glycosaminoglycan accumulation and fibroblast proliferation. Our patient had none of the above conditions but did have polycythemia which has been linked to clubbing by increasing viscosity and reducing blood flow through terminal capillaries; as a result, vasodilation and endothelial growth factor release occurs, causing clubbing. Exogenous androgen use likely caused his polycythemia via increasing erythropoietin production and hemoglobin set-point, decreasing hepcidin resulting in an increase in free iron, and/or estrogen receptor-a-mediated bone marrow stimulation.

Conclusion: It is estimated that half a million Americans abuse anabolic steroids. Clinicians should be aware of the association between androgen excess, polycythemia and clubbing.

Abstract #701

BROWN TUMOR IN A PATIENT WITH PRIMARY HYPERPARATHYROIDISM

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Objective: To describe a case of primary hyperparathyroidism that presented with a brown tumor of the mandible.

Case Presentation: An 86 year old female presented with a two-month history of an enlarging left sided jaw mass. She was treated by her dentist with a course of antibiotics however the mass persisted. A biopsy was completed at an outside hospital, which demonstrated characteristics consistent with a benign Giant Cell Tumor. Upon presentation to our institution, physical exam revealed a 3.5 cm x 4 cm mass along the left lateral aspect of the mandible that was firm and non-tender. On laboratory evaluation PTH was 368 pg/mL (N: 11-51), calcium 12.0 mg/dL (N: 8.6-10.3), creatinine 1.2 mg/dL (N: 0.6-1.3), vitamin D-25 43 ng/mL (N: 20-50), vitamin D-1,25 93.1 (N: 19.9-79.3), alkaline phosphatase 184 U/L (N: 37-113). Parathyroid sestamibi scintigraphy and a neck ultrasound did not demonstrate parathyroid adenoma. Parathyroid 4D-CT Scan subsequently revealed a 7 mm left sided nodule just inferior to the thyroid consistent with parathyroid adenoma. Patient denied history of nephrolithiasis or other symptoms consistent with hypercalcemia. Bone densitometry demonstrated severe osteoporosis with a T-score of -5.9 at the right distal radius. The patient underwent left inferior parathyroidectomy. At the time of surgery a 650 mg left lower pole parathyroid adenoma was removed. Intraoperative PTH levels decreased from 259 pg/mL to 32 pg/mL. Her calcium normalized to 10.1 mg/dL post-operatively. At two months follow up her calcium remained normal at 9.4 mg/dL with a PTH of 27 pg/mL.

Discussion: Brown tumors are an unusual presenting manifestation of primary hyperparathyroidism. They are reported to occur in 0.8% of hyperparathyroid cases. Brown tumors result from increased osteoclastic activity and localized accumulation of vascular fibrous tissue in the setting of uncontrolled hyperparathyroidism. Management of Brown tumors generally involves treating the underlying hyperparathyroidism. Surgery can be considered if the lesion does not resolve after 1-2 years of proper medical treatment or if the lesion is causing physical impairment or disfigurement.

Conclusion: Due to routine screening of calcium levels,
it is rare, in recent decades, for patients with primary hyperparathyroidism to present with late stage bone loss. Browns tumor should be considered in the differential diagnosis for a patient with a benign jaw tumor and bone loss.

Abstract #702

EMERGING ENDOCRINOPATHIES RELATED TO PROGRAMMED CELL DEATH-1 INHIBITORS

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UTHSC

Case Presentation: A 65 year old Caucasian male was admitted to the hospital for suspected sepsis. His recent history was significant for lung cancer. Two months back his thyroid function tests (TFT) were consistent with subclinical hyperthyroidism. His free T4 was 1.6ng/dl and thyroid stimulating hormone (TSH) was less than 0.015 uIU/ml. On repeat TFT his TSH was found to be more than 100 uIU/ml and his free T4 had dropped to 0.28ng/dl. Phone call to his cancer center next day showed that he was started on Nivolumab, programmed cell death-1 (PD-1) inhibitor two weeks back. Clinically he was totally asymptomatic for hypothyroidism. He was started on low dose (50mcg) thyroid hormone replacement therapy and discharged to home as no sepsis was found on subsequent work up.

Discussion: Thyroid gland is the most common endocrine organ affected by the use of PD-1 inhibitors. The patient may manifest with either hypothyroidism or hyperthyroidism. Hypothyroidism is more common. The highest grade of this side effect was classified as grade 2 per Common terminology criteria for adverse events (CTCAE) criteria in checkmate 057 trial in which Nivolumab was assessed in treatment of non-squamous cell non-small cell lung cancer. But if these endocrinopathies are not captured and treated in time it could quickly progress to more severe side effects. This could require hospitalization and possibly increase mortality and morbidity associated with use of PD-1 inhibitors.

Conclusion: Awareness of the potential for severe endocrinopathies related to PD-1 inhibitors, and a team approach which includes endocrinologists could potentially prevent the failure to diagnose such potentially dire consequences. This could potentially reduce the morbidity, mortality and cost associated with treatment of metastatic malignancy.

Abstract #703

IDIOPATHIC HYPOPARATHYROIDISM ASSOCIATED WITH DEAFNESS, RENAL ANOMALY: AN INTERESTING CASE OF HDR (HYPOPARATHYROIDISM, DEAFNESS AND RENAL ANOMALY) SYNDROME

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Objective: Recognize HDR-syndrome as a cause of hypoparathyroidism.

Causes of non-surgical hypoparathyroidism include genetic (Di-George, HDR, Kenny-Caffey, Kearns-Sayre syndrome), autoimmune-polyglandular-syndrome type-1 (APS-1), and infiltration of parathyroid glands (Iron, copper etc.)

Case Presentation: A 62-year-old male with long-history of hypoparathyroidism, seizure-disorder, sensorineural hearing-loss, and chronic kidney-disease (CKD) presented to the hospital with shortness of breath secondary to heart-failure and severe-hypocalcemia. Endocrinology was consulted for severe-hypocalcemia. Initial laboratory-results revealed calcium-level of <5 mg/dl (8.5-10.5), PTH <6.3pg/ml (14-72), ionized calcium 0.69mg/dl (1.13-1.32), Phosphorus-7.5mg/dl (2.5-4.9), eGFR 39ml/min/1.73m2 and creatinine 1.82 mg/dl. There was no family history in parents or his 2 children. Home medications included calcium 1000mg QID, vitamin-D3 5000 units daily, sevelamer and antihypertensive medications. Calcium level normalized after he was started on intravenous-calcium-gluconate, and calcitriol 1 mcg BID. Serum 25-OH vitamin D, AM cortisol, LH, FSH, Anti TPO antibodies were within reference-range ruling out APS-1 syndrome. He was discharged on calcium-carbonate 1000mg QID and calcitriol 1 mcg BID.

On review of old-records and history from his family he had long-standing history of hypoparathyroidism, hypocalcemia, deafness since early childhood and chronic kidney disease. Abdominal-ultrasound showed small right-kidney with compensatory hypertrophy on the left. Genetic testing for DiGeorge syndrome (chromosome 22 q11.2) and Williams-Beuren-syndrome (Chromosome 7 q11.23) was negative in childhood. CT-head showed extensive-calcifications within basal-ganglia, thalami, subcortical and cerebellar white-matter consistent with long-standing hypoparathyroidism. Audiology-testing was positive for sensorineural-hearing-loss. The constellation of hypoparathyroidism, deafness and renal dysplasia raised the suspicion for HDR syndrome. A genetic test for GATA-3 was ordered and is pending.
**Abstract #704**

**IATROGENIC MILK ALKALI SYNDROME WITH SEVERE HYPERCALCEMIA AFTER TOTAL THYROIDECTOMY**

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**Objective:** Hypercalcemia, metabolic alkalosis and renal failure due to ingestion of large amounts of calcium and absorbable alkali are features of milk alkali syndrome (MAS). Historically, after the introduction of the protocol for treatment of peptic ulcer disease by Bertram Sippy with milk, cream and alkaline powders in 1915, several reports of MAS were described in literature. Calcium carbonate, commonly used as over the counter drug for treatment of peptic ulcer disease, is the predominant source of calcium and alkali in recent years. We present a unique case of severe MAS secondary to iatrogenic use of calcium carbonate after total thyroidectomy.

**Case Presentation:** A 55-year-old African American female underwent total thyroidectomy for multinodular goiter. Ten days after the surgery, labs showed undetectable PTH and total calcium of 8.4 (8.4-10.2 mg/dl). She was kept on calcium carbonate 4 grams per day, vitamin D 4800 IU daily and calcitriol 0.25 micrograms daily. A month after thyroidectomy, patient's mother referred intense pain in mid and lower back and at the right upper quadrant of the abdomen. Initial laboratories revealed calcium level at 8.0 mg/dl (nl 8-10.5), elevated phosphate 4.8 mg/dl (nl 2.5-4.3) and a calcium/phosphate product of 35, while using calcium carbonate 1200 mg product of 35, while using calcium carbonate. Patient’s PTH remains suppressed due to parathyroid injury during the thyroidectomy and she currently remains normocalcemic on calcium carbonate 600 mg twice a day and calcitriol 0.25 micrograms daily.

**Discussion:** Our patient had triad of hypercalcemia, metabolic alkalosis and renal failure consistent with MAS. Our case is very unique in that not only hypercalcemia was severe and iatrogenic but also that it was in setting of hypoparathyroidism after total thyroidectomy.

**Conclusion:** Severe hypercalcemia can occur in MAS even in setting of hypoparathyroidism. This case highlights the importance of taking good history regarding over the counter calcium supplements to appropriately prescribe calcium and vitamin D in these patients.

**Abstract #705**

**HYPERCALCEMIA OF MALIGNANCY IN A PATIENT WITH HYPOPARATHYROIDISM: A COMPLICATED BUT TREATABLE CONDITION**

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**Objective:** Hypercalcemia in a patient with primary hypoparathyroidism has rarely been described. Most of the cases reported have resulted from the treatment with excessive doses of calcium, vitamin D, or its derivatives.

**Case Presentation:** A 55-year-old male patient with primary hypoparathyroidism diagnosed when he was 12 years old, enucleation of the left eye due to retinal melanoma, hyperlipidemia, scoliosis, and Noonan’s syndrome (NS), was referred to the endocrinology clinics for follow up of hypoparathyroidism. During initial evaluation, the patient referred intense pain in mid and lower back and at the right upper quadrant of the abdomen. Initial laboratories revealed calcium level at 8.0 mg/d (nl 8-10.5), elevated phosphate 4.8 mg/dl (nl 2.5-4.3) and a calcium/phosphate product of 35, while using calcium carbonate 1200 mg and vitamin D3 600 IU daily. Calcitriol 0.25 mcg daily was added to therapy and calcium carbonate discontinued, although the patient was not compliant with treatment. Abdominopelvic CT scan and thoracolumbar MRI showed metastatic lesions to liver, pancreas, and pronounced osteolytic bone disease in vertebral bodies and ribs. Liver biopsy confirmed metastatic melanoma. Eight weeks after initial evaluation, serum calcium level increased to 12 mg/dl without calcium supplements. Parathyroid hormone (PTH), vitamin D 1,25-OH and PTHrP levels were within normal range.

**Discussion:** HDR is a genetic disorder characterized by hypoparathyroidism, sensorineural deafness, and renal anomaly caused by mutation of the GATA3 gene located at chromosome 10p. GATA3 is a transcription factor identified for embryonic development of the parathyroid glands, inner ears, kidneys, and thymus. Inherited in autosomal dominant pattern but de-novo mutations have also been identified. Diagnosis is usually based on clinical findings and confirmed by genetic test for GATA3 mutation.

**Conclusion:** Patients presenting with hypoparathyroidism, deafness and renal disorders should be tested for HDR syndrome.
the lower range of normal compatible with hypercalcemia of malignancy, most likely secondary to osteolytic disease. Chemotherapy with ipilimumab and nivolumab was started, and zoledronic acid added to treat hypercalcemia and bone pain. Calcium levels decreased to 7.4 mg/dl three days after bisphosphonate therapy. Calcium levels reached normal range (8.3 mg/dl) 4 days after a monitored calcium carbonate and calcitriol therapy. The patient returned to daily calcitriol therapy after stabilization of calcium levels.

Discussion: Hypercalcemia of malignancy can be successfully treated with bisphosphonates. However, in patients with hypoparathyroidism this can be challenging due to a higher risk of hypocalcemia. Our case report showed that patients with hypoparathyroidism presenting with increased plasma calcium levels should be assessed for malignancies and appropriate therapy given. An interesting fact is that even though patients with NS have an increased risk of cancer, it consists mostly of leukemia and certain solid tumors; melanoma is extremely rare in this condition.

Conclusion: Very few cases of hypercalcemia of malignancy have been reported in hypoparathyroid patients, and, to our knowledge, this is the first case secondary to osteolytic metastatic disease.

Abstract #706

GROWTH HORMONE THERAPY FOR A RARE CASE OF SHORT STATURE ASSOCIATED WITH AGGREGAN MUTATION

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Objective: The Aggrecan gene (ACAN) encodes aggrecan, the major proteoglycan component in the matrix of articular and growth plate cartilage. ACAN mutations result in a broad spectrum of phenotypes ranging from skeletal dysplasia to short stature. There is a dearth of literature pertaining to the management of short stature resulting from ACAN mutations.

Case Presentation: A healthy 21 month-old girl was referred to endocrine clinic for short stature evaluation. She was born full-term. From age 2 months, her height was noted to be well below the 3rd percentile with weight at 5-10th percentile. Review of systems was non-contributory, with no delayed milestones. Family history was notable for short stature in her father and paternal uncle. Both were treated with growth hormone for approximately ten years during childhood, resulting in adult heights of 68 and 70 inches respectively. Physical examination was only remarkable for significant short stature with height at 0.06th percentile (SDS -3.24) and weight at 9th percentile (SDS -1.34). Mid-parental height was at 10-25th percentile. Laboratory workup for short stature was unremarkable including normal thyroid function tests, growth factors, cortisol levels, celiac disease screen, PTH, karyotype and genetic testing for hypochondroplasia (FGFR3). Skeletal survey, bone age and brain MRI were also normal. Given her family history of short stature, whole exome sequencing (WES) was done that revealed a nonsense mutation in exon 7 (c.1443G>T) in ACAN. Her father and multiple family members bore the same mutation. She was started on growth hormone therapy at age 3 years. She has been on treatment for more than 15 months, and has shown good response with height improvement from pre-treatment SDS of -3.24 to present SDS of -2.36.

Discussion: In vivo animal models suggest that ACAN mutations alter the expression patterns of aggrecan mRNA and other extracellular matrix molecules alongside anomalous protein signalling, resulting in growth plate cartilage maldevelopment and spinal misalignment. ACAN gene mutations have been reported in multiple families with short stature and bone age advancement.

Conclusion: We here report a case of short stature associated with a novel ACAN mutation. She has no accelerated bone maturation. Her response to treatment highlights the potential role of growth hormone therapy for short stature resulting from ACAN mutations. Further research is warranted to determine the optimal treatment strategy for these patients.

Abstract #707

DEVELOPMENT OF SARCOIDOSIS AFTER TREATMENT OF CUSHING’S SYNDROME

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Objective: To review and contribute to the literature a rare case of the development of sarcoidosis after treatment of Cushing’s syndrome.

Case Presentation: 53 year old Caucasian woman was referred for follow up for a possible pituitary tumor. She had history of HTN, type 2 DM, fibromyalgia and OSA. She was obese with a cherubic face and had noticeably enlarged dorsal cervical fat pad. A positive overnight dexamethasone suppression test along with a high 24-hour urine cortisol and low ACTH supported diagnosis of Cushing’s syndrome. CT Abdomen/Pelvis showed a 3.7cm left adrenal mass. She underwent left adrenalectomy. Within two months after surgery she developed worsening
arthralgia along with non-tender subcutaneous nodules on her bilateral extensor surface of arms and legs. Biopsy of the nodule revealed granulomatous lesions consistent with sarcoidosis. Chest imaging showed no evidence of pulmonary involvement. She was started on prednisone 40mg daily and nodules resolved within 2 months.

**Discussion:** Chronically elevated corticosteroid levels cause the characteristic signs and symptoms of Cushing’s syndrome and can suppress the overt manifestations of autoimmune conditions. Normalization of serum cortisol after treatment of Cushing’s syndrome may exacerbate symptoms of a previously suppressed autoimmune condition. Review of the literature has shown less than 10 case reports of sarcoidosis after treatment of Cushing’s syndrome. Patients typically present with vague complaints of fatigue and arthralgias, with skin findings often prompting biopsy and subsequent diagnosis. In almost all the reported cases, subcutaneous nodules were the specific dermatological manifestation.

**Conclusion:** Development of sarcoidosis after treatment of Cushing’s syndrome is rare with most cases being diagnosed after the development and biopsy of subcutaneous lesions. Subcutaneous nodules have been characteristically seen in almost all the cases and thus the development of subcutaneous nodules in the post treatment phase of Cushing’s should raise suspicion of sarcoidosis. We acknowledge that without dermatological signs there is a diagnostic challenge in discerning symptoms of fatigue and arthralgia from steroid withdrawal versus onset of sarcoidosis or another autoimmune condition. However, we believe these rare cases bring forth the importance of considering alternative diagnoses in those patients who have other systemic complaints or persistent symptoms after treatment of Cushing’s.

**Abstract #708**

PARATHYROID CARCINOMA IS A RARE BUT IMPORTANT ETIOLOGY OF HYPERPARATHYROIDISM

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**Case Presentation:** A 53-year-old male was incidentally discovered to be hypercalcemic. On further evaluation, he complained of dry mouth, fatigue, anxiety, and diffuse skeletal pain. There was no family history of hypercalcemia. Dry mouth and hypertension were noted on examination. Serum calcium and intact parathyroid hormone (iPTh) were 18.9 mg/dL (8.5-10.5) and 1,247 pg/mL (12-88), respectively. Saline hydration, calcitonin, and denosumab improved serum calcium to 12.2 mg/dL. Parathyroid scintigraphy showed a focus of Tc-99m sestamibi uptake below the inferior aspect of the thyroid in the left tracheoesophageal space. A very large (3,800 mg) left parathyroid mass was removed en bloc with the left thyroid lobe and adjacent lymph nodes. Twenty minutes after resection, intraoperative iPTh fell from 1,606 pg/mL to 164 pg/mL. Two suspicious central compartment lymph nodes were biopsied, with frozen sections showing parathyroid tissue and prompting resection. Final diagnosis was parathyroid carcinoma (PC) metastatic to central compartment lymph nodes, and screening for a HRPT2 mutation was arranged.

**Discussion:** PC accounts for ~ 0.5-2.0% of primary hyperparathyroidism (PHPT) cases. In contrast to parathyroid adenomas, the incidence of PC is equal between genders, and PC is much more likely than adenomas to present with calcium > 14 mg/dL, iPTh ≥ 5-fold above the upper limit of normal, symptoms of hypercalcemia, and renal and bone disease. Tumors tend to be quite large, and in one PHPT series all PC patients had tumors ≥ 1,900 mg. Imaging does not reliably distinguish parathyroid adenomas from carcinomas but may assist surgical planning. Preferred management is en bloc resection of the tumor and ipsilateral thyroid lobe, paratracheal lymph nodes, and adjacent muscle and recurrent laryngeal nerve if involved by tumor. Analysis of 1,022 PC cases in the National Cancer Data Base revealed an 81% 5-year survival rate; positive lymph nodes and age > 57 years were associated with lower survival. Approximately 50% of patients experience recurrence, and death from PC is often due to severe hypercalcemia. Mutations of the tumor suppressor gene HRPT2, which cause hyperparathyroidism-jaw tumor syndrome, have been reported in two-thirds of sporadic PC cases, with nearly 20% of patients discovered to have germline mutations.

**Conclusion:** PC is a rare but significant cause of PHPT. Timely recognition of PC is essential to guide pre- and intraoperative management, and screening for HRPT2 mutations is indicated due to high prevalence and potential for germline mutations. Lifelong surveillance is required for early diagnosis and appropriate management of recurrence.
Abstract #709

A SINGLE CENTER TRANSGENDER CLINIC EXPERIENCE

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Objective: Cross-Gender Hormone Therapy (CGHT) is commonly utilized in the treatment of gender dysphoria. Most research is isolated to large US coastal cities or abroad and shows significant effects of CGHT on blood pressure, lipid profile, BMI, and depression and anxiety. The aims of this study were to analyze clinically relevant data from The Ohio State University’s Transgender Primary Care Clinic (OSUTPCC), a uniquely Midwestern transgender population.

Methods: Patients in this retrospective study were seen within the OSUTPCC’s first year. Demographic data were summarized for all patients. For those started on CGHT, changes in biometric and metabolic data were analyzed using a Wilcoxon Signed Rank Test. Depression and anxiety were tracked using the PHQ9 and GAD7 questionnaires. Clinical correlations were determined using a Spearman Correlation.

Results: The clinic saw 59 patients in the first year. Natal sex was 32 female, 27 male. Gender identity was 29 male, 25 female and 5 genderqueer. The mean age at the first clinic visit was 30 years; patients reported they began fully living as their identified gender at a mean age of 24 years. The majority of patients were self-referred (67.9%), white (84.7%), and reported dysphoria onset during early childhood (66.1%). Most were hormone naïve (62.7%), started on CGHT by the clinic (67.8%). Diastolic blood pressure increased for natal females placed on CGHT by an average of 3.4 mmHg (p=0.03). Several patients were smokers (39%), and 65% quit smoking prior to CGHT. A majority reported full (46.6%) or partial (27.6%) acceptance by their families. The PHQ9 and GAD7 scores after initiating CGHT suggested a trend toward significance.

Discussion: The clinic saw a relatively equal mix of transgender men and women as well as a few genderqueer individuals. Many were started on CGHT for the first time. There was a decline in tobacco use associated with CGHT and we find requiring smoking cessation prior to CGHT a useful clinical strategy for cessation. The authors were surprised at the magnitude of reported acceptance by family; this may be skewed by limited data and patients’ definition of “family”. There was a decrease in PHQ9 and GAD7 scores after initiating CGHT suggesting a trend toward significance.

Conclusion: The results of this study illustrate the clinical experience of a Midwestern Transgender Clinic and changes associated with CGHT. Further studies are warranted to analyze long term mental health outcomes and metabolic changes.

Abstract #710

ALWAYS ACTED AS PARAGANGLIOMA, ALWAYS READ AS SCHWANNOMA

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Objective: Head and neck paragangliomas (HNPGL) represent 0.6% of the head and neck tumors, up to 95% are non-secreting and up to 30% can be malignant. They often present as a cervical mass with compression or infiltration of adjacent structures or discovered on imaging. One of the differentials includes Schwannomas, which are rare benign tumors of nerve sheath origin that arise most commonly from the 8th cranial nerve. We present a case of secreting HNPGL, which was initially managed as a schwannoma.

Case Presentation: A 70-year old female, with history of uncontrolled hypertension, was diagnosed in 2010 with a right neck mass after presenting with ear pain. The MRI showed a 5.2x3.1 cm mass in the right carotid space extending up to the jugular foramen. The differential diagnosis included schwannoma and paragangioma, however the post contrast enhancement on subsequent MRI was interpreted as characteristic of a schwannoma. A conservative approach was chosen and the mass remained stable until 2012. She was lost to follow up for 3 years, continued to have uncontrolled hypertension and developed systolic congestive heart failure. In 2015 she presented with sudden onset right side neck and ear pain, dysphagia, dysphonia and paralysis of the right 10th, 11th and 12th cranial nerves. Repeated MRI showed that the mass had increased in size (6 cm), with peripheral rim like enhancement and central necrosis with local compression. Considering the clinical history the biochemical work-up for possible HNPGL was done: Normetanephrine were elevated in the plasma (2.42 nmol/l, ref. <0.89 nmol/l) and in the urine (3258 ug/g Cr, ref. <400 ug/g Cr). After preparation with phenoxybenzamine, the
An 88 yo male with CKD and left hip fracture was admitted for infected left hip hardware. He was treated with incision and drainage (I&D) by orthopedics. Despite this, he continued to have infection of his left hip. Orthopedics performed another I&D, along with resection arthroplasty and insertion of Stimulan beads (impregnated with Vancomycin), on 4/10. Beginning on 4/16, the patient became confused, agitated, and lethargic which he unfortunately experienced. Our patient was given a 40 cc mix of Stimulan beads containing 22 gm of elemental calcium. The large amount of calcium and the increased rate of dissolution of Stimulan beads, along with the patient’s dehydration and impaired kidney function, likely put him at increased risk for the development of hypercalcemia, which he unfortunately experienced.

A UK observational case study discovered that 3 of the 15 patients treated with Stimulan beads for PJI had transient hypercalcemia. Of those three, one developed symptoms and required treatment. As such, it is important to realize that hypercalcemia can be a potential complication for those treated with Stimulan beads.

Discussion: Both schwannomas and paragangliomas have low signal on T1-weighted images and an intermediate to high signal on T2-weighted MRI images. HNPGL are associated with a significant risk of malignancy and require pre-operative management; hence to differentiate them from benign tumors based on clinical manifestation, biochemical testing (although mostly are non-secretory), and imaging is imperative.

Conclusion: We present a case of normetanephrine secreting head and neck paraganglioma, which was initially interpreted as schwannoma on imaging. This case highlights the limitations of diagnostic techniques in the differential diagnosis of the complex neurovascular lesions.

Abstract #711

A MIND-ALTERING CASE OF HYPERCALCEMIA CAUSED BY ABSORBABLE ANTIBIOTIC BEADS

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Case Presentation: Stimulan is an absorbable calcium sulfate that is mixed with antibiotics into small beads to allow for the targeted delivery into a specified joint space. It fully absorbs into the local tissue 2-3 weeks after placement. It has become more common in the treatment of periprosthetic joint infections (PJI) as it offers the advantage of controlled release and local delivery of antibiotics. However, given its more recent use and limited follow up data, it is important to keep in mind the potential complications.

Clinical Case
An 88 yo male with CKD and left hip fracture was admitted for infected left hip hardware. He was treated with incision and drainage (I&D) by orthopedics. Despite this, he continued to have infection of his left hip. Orthopedics performed another I&D, along with resection arthroplasty and insertion of Stimulan beads (impregnated with Vancomycin), on 4/10. Beginning on 4/16, the patient became confused, agitated, and lethargic which was markedly different from his baseline. He was noted to have increasing serum calcium levels that began on 4/15 with the highest peak at 14.5 (8.4-10.4 mg/dL). Given the severity and slow resolution of the hypercalcemia, he was sequentially treated with IV fluids, calcitonin 300 units SQ x 5 doses, and pamidronate 60 mg IV. His serum calcium levels subsequently normalized in 7 days after initiation of therapy while his altered mentation resolved in 5 days.

Conclusion: The hypercalcemia was initially thought to be due to dehydration and AKI but didn’t resolve with IV fluids and improvement of renal function. Labs indicated that the hypercalcemia was non-PTH and non-PTHrP mediated. The following etiologies were ruled out: immobilization, hypervitaminosis D, malignancy, thyrotoxicosis, and adrenal insufficiency. In search of other explanations, we investigated a possible contribution of the Stimulan beads. Biocomposites representatives indicated that in-vitro trials have found that large amounts of Vancomycin mixed with Stimulan may cause the beads to dissolve faster. Our patient was given a 40 cc mix of Stimulan beads containing 22 gm of elemental calcium. The large amount of calcium and the increased rate of dissolution of Stimulan beads, along with the patient’s dehydration and impaired kidney function, likely put him at increased risk for the development of hypercalcemia, which he unfortunately experienced.

A UK observational case study discovered that 3 of the 15 patients treated with Stimulan beads for PJI had transient hypercalcemia. Of those three, one developed symptoms and required treatment. As such, it is important to realize that hypercalcemia can be a potential complication for those treated with Stimulan beads.
was presumptively diagnosed with sarcoidosis two years later at age thirteen but was not biopsy proven. At this time, Ca 15.7 mg/dL (9.8-10.2), phosphorus 3.7 mg/dL (2.5-4.5), iCa 8.8 mg/dL (4.5-5.6), PTH <7 pg/mL (15-65), PTHrP <1.1 pmol/L (<2), 1,25-dihydroxyvitamin D [1,25(OH)2D] 125 pg/mL (19.9-79.3), 24 hour urinary Ca 333.9 mg (100-300). She was started on prednisone 30 mg daily and admitted to the hospital. Tuberculosis Quantiferon test was indeterminant, and computed tomography of the chest, abdomen and pelvis with contrast showed no significant lymphadenopathy. During admission, Ca improved to 11.3 mg/dL after intravenous fluids and Lasix, and prednisone dose was increased to 60 mg daily. After discharge, she was seen by Endocrinology and started on a prednisone taper as well as ketoconazole 200 mg twice a day due to suspicion of CYP24A1 mutation as her Ca of 12 mg/dL did not normalize even with high dose prednisone. Four weeks later, patient noted improvement in symptoms with normalization of Ca to 9.9 mg/dL, iCa 1.29 mmol/L and 1,25(OH)2D 25 pg/mL (18-78) with total 25(OH)D 71 ng/mL. Testing done at Mayo Clinic in Rochester showed total 24,25-dihydroxyvitamin D [24,25(OH)2D] was 0.15 ng/mL and ratio of 25(OH) D to 24,25(OH)2D was 473 with ratio >80 suggestive of probable bi-allelic CYP24A1 mutation. Due to slight elevation of alanine aminotransferase, she was later switched to fluconazole 100 mg daily.

**Conclusion:** It is important to consider CYP24A1 mutation in a patient with persistent hypercalcemia, suppressed PTH and elevated 1,25(OH)2D in the absence of malignancy or granulomatous disease. Treatment with cytochrome P450 inhibitors like ketoconazole and fluconazole can help normalize calcium levels.

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**Abstract #713**

**DIFFUSE SYMMETRICAL LIPOMATOSIS: A CASE REPORT DEPICTING THE POTENTIAL FOR SEVERITY**

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**Objective:** Diffuse symmetrical lipomatosis, or Madelung’s disease, involves benign lipoma formation of the shoulder girdle, affecting quality of life immensely. As surgery is the mainstay for treatment, recognition of this condition is needed in medical literature to expand future treatment modalities. We present a case depicting the potential for severity, which is profoundly debilitating compared to those previously described.

**Case Presentation:** A 47 year old male with hypothyroidism, diabetes mellitus, and peripheral neuropathy presented with a two year history of recurrent lipomatous formations. Enlarging lesions were previously on his upper back, posterior left ear, and bilateral shoulders. Pathology showed benign lipomas in all resections. Rapid growth of similar lesions then occurred throughout his shoulder girdle, upper back, sternum, and submandibular regions. His quality of life had been affected, as the sternal mass caused recurrent pressure. Workup was negative for Cushing’s syndrome and acromegaly. Family history and social history were insignificant. On exam, there was gross enlargement of subcutaneous tissue in the submandibular regions bilaterally, with multiple masses in the upper back, bilateral shoulders, and anterior superior chest overlying his sternum (see Figures). Given his presentation, history of recurrent benign lipomatous formations, and associated endocrinopathies, the diagnosis of Madelung’s disease was clinically confirmed. To improve his quality of life, he was referred to plastic surgery for removal of his sternal lesion.

**Discussion:** Madelung’s disease involves lipoma formation in the shoulder girdle, giving a “horse collar” appearance. Ages 30-60 are most affected, with an incidence of 1 in 25,000, and male dominance of 30:1. In >90% of cases, there is associated alcoholism and predilection for Mediterranean descent. Neither were present in this case. Growth rate is variable, but fortunately malignant transformation is rare. Associated metabolic derangements include hyperinsulinemia, hypertriglyceridemia, altered glucose tolerance, and abnormal thyroid, adrenal, pituitary, or testicular function. Polyneuropathy is noted in 85% of patients. Long acting inhaled β2 agonists, intralesional enoxaparin injections, and subcutaneous deoxycholate have been used with limited success. The best management has been surgical excision, but no data suggests this will prevent recurrence.

**Conclusion:** The uniqueness of this case is his severity of lipomatous enlargement, non-Mediterranean descent, and lack of alcohol abuse. As quality of life can be severely impaired, future medical treatment options should be pursued to assist these patients after surgery, aiming to prevent recurrence.
Abstract #714

SPURIOUS TESTOSTERONE LABORATORY RESULT IN PATIENT TAKING ASFOTASE ALFA

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Case Presentation: Enzyme Replacement Therapies can catalyze competitive immunoassays, leading to a spurious lab result. Surprising lab results should prompt further investigation into laboratory techniques used for sample analysis. A 33 year-old male with hypophosphatasia and hypogonadism presented following initiation of a new medication, asfotase alfa, for treatment of hypophosphatasia. The patient reporting feeling more energetic after starting the new medication and denied any sexual dysfunction, no erectile dysfunction or decline in libido. Total testosterone had been within goal range on a stable dose of testosterone for years. Exam was unchanged and the patient was responding well to both therapies. Labs showed total testosterone <10ng/dL (175-781) on initial and repeat measurement. Free testosterone measured 6.7pg/mL (5.1-41.5). SHBG was 21nmol/L (11-80) and dihydrotestosterone was 200pg/mL (106-719).

Discussion: Hypophosphatasia is caused by mutation in the ALPL gene, which encodes the tissue non-specific alkaline phosphatase enzyme, leading to decreased activity of alkaline phosphatase (ALP). In 2015, the Food and Drug Administration approved asfotase alfa bone-targeted human recombinant TNSALP replacement therapy to treat hypophosphatasia. The Access Testosterone assay is a competitive binding immunoenzymatic assay. A sample is added to a reaction vessel with the mouse monoclonal anti-testosterone antibody, testosterone-ALP conjugate, and paramagnetic particles coated with goat anti-mouse polyclonal antibody. Testosterone in the sample competes with the testosterone-ALP conjugate for binding sites on a anti-testosterone monoclonal antibody. The antigen-antibody complexes are bound by the capture antibody. Materials bound to the solid phase are held in a magnetic field and unbound materials are washed away. Then, the chemiluminescent substrate is added to the vessel and the reaction is measured with a luminometer. The light production is inversely proportional to the sample’s concentration of testosterone. Consideration of the assay and the medication suggests that the exogenous asfotase alfa is interfering with the chemical reaction measuring total testosterone. This interference leads to spuriously lower lab results. Not surprisingly, serum free testosterone was normal because the free testosterone assay is a radioimmunoassay, unsusceptible to competition from ALP.

Conclusion: ALP is a common label for competitive immunoassays and the interference of this drug leads to a falsely low total testosterone. This interference was previously unreported. This case demonstrates the importance of understanding how laboratory studies are performed and correlating results to patient presentation.

Abstract #715

PSEUDOHYponATREMIA IN THE SETTING OF HYPERCHOLESTEROLEMIA

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Objective: The prevalence of hyponatremia is around 2% - 3%. It is important to differentiate between the different types of hyponatremia as management can differ. Unrecognized pseudohyponatremia that is aggressively treated can lead to increased morbidity and mortality.

Case Presentation: A 69 year old Caucasian gentleman initially presented with IgG-4 mediated pachymeningitis of his cervical spine that was treated with Rituximab, prednisone and trimethoprim/sulfamethoxazole (SMX-TMP). He subsequently developed drug induced liver injury that lead to SMX-TMP discontinuation. On follow up, he was found to have asymptomatic hyponatremia and was readmitted. Plasma sodium (Na) was 119 mmol/L (normal 136-144) and total protein 4.7 g/dL (normal 6.3-8). Serum osmolality was 283 mOs/kg (normal 275-295), urine osmolality was 332 mOs/kg and random urine Na was 45 mmol/L. Pseudohyponatremia was suspected and a lipid profile showed triglyceride: 281 mg/dl, cholesterol: 1340 mg/dl, HDL: 21 mg/dl, LDL: 1419 mg/dl. Direct ion-selective electrode (ISE) using blood gas analyzer was then used revealing a Na level of 132 mmol/L. Using Dimeski’s formula, the calculated corrected Na level was 131 mmol/L. Pseudohyponatremia was suspected and a lipid profile showed triglyceride: 281 mg/dl, cholesterol: 1340 mg/dl, HDL: 21 mg/dl, LDL: 1419 mg/dl. Direct ion-selective electrode (ISE) using blood gas analyzer was then used revealing a Na level of 132 mmol/L. Using Dimeski’s formula, the calculated corrected Na level was 131 mmol/L.

Discussion: Plasma is composed of 93% water and 7% proteins and lipids. Plasma Na concentration can be measured using direct or indirect ISE. With indirect ISE, the sample is diluted before analysis and the plasma Na is measured with the assumption that plasma is composed of 93% water. When hyperlipidemia or hyperproteinemia is present, the actual plasma water fraction is decreased. Using indirect ISE in these cases will result in falsely low plasma Na levels as the decreased plasma water fraction is not adjusted for. With direct ISE, the sample is analyzed without dilution and the plasma Na is measured directly irrespective of plasma water fraction and so is not affected.
by changes in plasma percentage concentration. Hypertriglyceridemia and hypercholesterolemia can both cause pseudohyponatremia. The plasma is lipemic with hypertriglyceridemia but not with hypercholesterolemia. While ultracentrifugation can be used to determine true plasma Na levels in patients with hypertriglyceridemia, it cannot always be used with hypercholesterolemia.

**Conclusion:** Around two thirds of laboratories in Unites States use indirect ISE. It is important to keep this in mind when evaluating patients with pseudohyponatremia to prevent inappropriate management that can cause increased morbidity and mortality. In such cases, direct ISE is recommended. Dimeski’s formulas can also be applied as an alternative. In addition to improving the quality of care, health care cost can be reduced by preventing unnecessary admissions and work up.

**Abstract #716**

**22 MONTH REVIEW OF IMMUNE CHECKPOINT INHIBITOR ASSOCIATED ENDOCRINE DISORDERS AT A SOUTHERN CALIFORNIA TEACHING HOSPITAL**

Lauren Clarine, D.O., Renil Rodriguez Martinez, MD, Matthew Levine, MD, Megan McGarvey, MD, Amy Chang, MD
Scripps Clinic

**Objective:** Immune checkpoint inhibitors (ICH), anti-PD1 monoclonal antibodies Nivolumab (Niv) and Pembrolizumab (Pem) and cytotoxic T lymphocyte antigen 4 antibody Ipilimumab (Ipi), are increasingly being used in treatment of metastatic melanoma, renal cell carcinoma, and lung cancer. These agents can induce rare severe endocrine immune-related adverse events that are inconsistently recognized. The incidence, presentation, and management of endocrinopathies following ICH therapy was reviewed.

**Methods:** A retrospective chart review (2015-2016) of patients who received ICH therapy and treatment at Scripps Green Hospital/Clinic was done. Demographic data, number of ICH doses, and data involving the development or progression of endocrine diseases was collected. Assessment of thyroid dysfunction, hypophysitis, adrenal insufficiency, and type 1 diabetes was done. Endocrine disorder severity was graded according to the NIH Common Terminology Criteria for Adverse Events.

**Case Presentation:** The study cohort was 103 patients. 68 (66%) were men and 35 (34%) were women. 23 patients received Pem, 23 patients received Ipi, 49 patients received Niv, 4 patients received Ipi/Niv, and 4 patients received Ipi/Pem. Hypophysitis was found in 5 patients (20%) on Ipi and 1 patient on Ipi/Niv. Of these 6 patients, 5 were treated for central adrenal insufficiency, 2 for central hypothyroidism, and 1 for SIADH. Type 1 diabetes was found in 2 patients (4%) on Niv. Primary hypothyroidism was found in 17 patients (35%) on Niv, 3 patients (13%) on Ipi, and 3 patients (13%) on Pem. Transient hyperthyroidism was found in 1 patient (4%) on Ipi and 1 patient on Ipi/Niv.

**Discussion:** It is known ICH therapy causes endocrinopathies, but a paucity of data regarding the incidence and course of diseases exists. There is a lack in standardized screening protocols for endocrine dysfunction before, during, and after ICH treatment. Thyroid dysfunction was the most common endocrinopathy. Hypophysitis was second most common. Hospitalization was required for management of severe endocrinopathies upon diagnosis (hypophysitis and type 1 diabetes). While most endocrinopathies were diagnosed within 2-4 months of starting therapy, a small number occurred after 1 dose and after the last infusion. Compared to other studies, hypophysitis incidence was similar but type 1 diabetes incidence was 3% higher. While few endocrinopathies were transient, most cause permanent dysfunction requiring long-term hormone replacement.

**Conclusion:** These findings suggest patients receiving ICH therapy should have baseline thyroid function tests and periodic monitoring of thyroid function, pituitary function and glucose levels for early recognition of and treatment of endocrinopathies.

**Abstract #717**

**AN X-TRAORDINARY CASE OF X-LINKED DIABETES INSIPIDUS**

DeAnna Henderson, MD, Saba Khayal
University of Tennessee Health Science Center

**Case Presentation:** Diabetes insipidus (DI) is a disorder of water homeostasis, presenting with polydipsia and polyuria of dilute urine. Inherited nephrogenic DI is a rare condition and can be x-linked, AD, or AR. X-linked DI is the most common form of congenital DI, presenting in male patients with mutations in the vasopressin receptor gene (AVPR2). This is an interesting case of a male with hypernatremia whose condition turned out to be more than it seemed. A 22 yo African American male with PMH of CHF, OSA, morbid obesity, and T2DM presented to the trauma ER with multiple gunshot wounds. He was stabilized and a CT scan of the chest, abdomen, and pelvis was negative for organ damage. However, he had hypernatremia with a serum Na of 165 mmol/L, creatinine of 1.1 mg/dL, BG of 152mg/dL, serum osmolality of 342 mOsm, and a urine
osmolality of 192 mOsm. He noted polydipsia, polyuria, and nocturia since childhood. Per his mother, he urinated almost every two hours nightly and drank four to five, 2 liter bottles of water daily. His T2DM was well-controlled at home with an A1c of 7.2. One year ago, he presented to another hospital with hyperglycemic crisis with a BG of 1152, a corrected Na level of 170, and a creatinine of 2.8. He was treated with volume resuscitation and an insulin gtt, and was discharged with multiple daily insulin injections and coreg. His Na at discharge was 148mg/dL and his creatinine was 1mg/dL. Endocrine was consulted. On physical exam, he was afebrile, 189kg, and alert and oriented. D5W was started at 150cc/hr due to CHF and free water po was encouraged. An ADH level was 3.1 pg/mL. Given his chronic hypernatremia, he was challenged with DDAVP over 2 days. During the challenge, the his urine osmolality (168-203 mOsm/kg) and specific gravity (1.003-1.007 NM) never showed a response and large volume urine output continued. Nephrology was consulted and HCTZ 25mg po qd was started and was increased to b.i.d dosing during his hospitalization, in addition to amiloride. Treatment resulted in improvement of his urine output, serum sodium (146mmol/L) and his urine osmolality (259mOsm/kg). Upon more inquiry, his mother revealed that her older son, who is a twin, presented with “water diabetes” but was lost to follow up. Her nephew also had polyuria and polydipsia as a child. With this pattern, X-linked nephrogenic DI was considered.

In conclusion, WCC adenomas pose a diagnostic challenge to clinicians on multiple levels. WCC should be considered if intraoperative frozen section histology from suspected adenoma suggests brown fat. Furthermore, both brown fat and parathyroid adenoma may appear on sestamibi scan as hot nodules, which can lead to misidentification of a WCC parathyroid adenoma. Finally, WCC can be sonographically silent, as in our case, posing a further barrier to diagnosis.

**Conclusion:**

In conclusion, WCC adenomas pose a diagnostic challenge to clinicians on multiple levels. WCC should be considered if intraoperative frozen section histology from suspected adenoma suggests brown fat. Furthermore, both brown fat and parathyroid adenoma may appear on sestamibi scan as hot nodules, which can lead to misidentification of a WCC parathyroid adenoma. Finally, WCC can be sonographically silent, as in our case, posing a further barrier to diagnosis.
misdiagnosis or excessive testing for type 2 diabetes and Cushing’s syndrome.

**Case Presentation:** 36-year-old Hispanic female was referred for evaluation of type 2 diabetes. She was diagnosed at age 20. She was initially treated with oral agents and transitioned to insulin after 12 years. On initial evaluation she was requiring 180 units of insulin daily. She had wasted extremities with increased abdominal and facial adipose tissue. BMI was 30 kg/m2. Changes to her appearance began at age 8. Multiple tests for Cushing’s syndrome were negative. HbA1C was 10.2%, triglycerides 4382, and she had hepatosteatosis.

46-year-old Hispanic male was referred for evaluation of type 2 diabetes. He was requiring 160 units of insulin daily. HbA1C was 9.9% and triglycerides were 1007. He had increased facial and abdominal adipose tissue relative to the extremities with acromegaloïd features. BMI was 38 kg/m2. Changes to his appearance started 5 years prior to presentation.

Both patients had physical exam notable for centripetal obesity with thin extremities. They had no striae, bruising, or any Cushingoid features. Both patients were eventually diagnosed with lipodystrophic diabetes. They were started on double-concentrated basal insulin, prandial insulin, liraglutide and metformin with remarkable improvement of their glycemic control. For hypertriglyceridemia, fibrate, high dose statin and low carbohydrate diet were started as well.

**Conclusion:** These cases highlight the importance of having a high index of suspicion for lipodystrophy syndromes. Lipodystrophic diabetes should be considered in the differential diagnosis of with diabetes with severe IR, hypertriglyceridemia and fatty liver. These patients should be tested for congenital causes of lipodystrophy.

**Abstract #720**

**RESECTION OF INSULINOMA THAT UNMASKED TYPE 2 DIABETES MELLITUS**

*Samuel Worsham, DO*

University of Kansas Medical Center

**Objective:** To present a case of Type 2 Diabetes Mellitus that was unmasked after Insulinoma resection.

**Case Presentation:** A 51 year old woman presents to the hospital for hypoglycemia and confusion with a 5 year history of persistent hypoglycemia, hyperphagia and more than a 180 lb. weight gain during that time. An infusion of 20% dextrose in water was required to maintain euglycemia. CT abdomen revealed a 2 cm mass in the distal pancreas. In a fasting state when the patient’s serum glucose reached 42 mg/dL (70-100 mg/dL) a laboratory investigation revealed serum insulin 21.3 mcU/mL (2-23 mcU/mL), C peptide 5.2 ng/mL (1.1-4.4), Beta hydroxybutyrate 0.1 (<0.3 mmol/L), and Hypoglycemic agent screen was negative. Exploratory laparotomy with partial pancreatectomy and splenectomy was performed, and a 2.5 x 2.4 x 2.2 cm tumor was resected. Histology was consistent with a well-differentiated, low grade, neuroendocrine tumor. Lymph node sampling was negative for metastasis. After resection of the insulinoma the patient became hyperglycemic and required insulin to maintain euglycemia after discharge.

**Discussion:** Insulinoma is a neuroendocrine tumor that is derived from the islet cells of the pancreas, with an incidence of 4 per million person-years. Patients generally present with fasting hypoglycemia (73%), sympathoadrenal and neuroglycopenic symptoms. Typically, insulinomas present as a single benign tumor (87%). The diagnosis of insulinoma is made by establishing an inappropriately elevated insulin level in the presence of hypoglycemia. After diagnosis, several modalities can be used to locate the tumor including: trans abdominal ultrasound, triple-phase spiral computed tomography, pentetreotide scintigraphy, endoscopic ultrasonography, and selective arterial calcium stimulation test. If a tumor cannot be located or the individual is not a surgical candidate, then medical management with diazepoxide or a somatostatin analog may be necessary. The median duration of symptoms before diagnosis is 1.5 years, but some persons may have symptoms for decades before diagnosis. For a benign solitary insulinoma the definitive treatment is resection of the tumor.

**Conclusion:** Insulinoma is a rare neuroendocrine tumor and the coincidence of Diabetes Mellitus masked by insulinoma is even more extraordinary. Weight gain from increased oral intake, due to hypoglycemic symptoms, may contribute to the development of Type 2 Diabetes Mellitus. Therefore, early recognition, diagnosis and definitive treatment of insulinoma may prevent development of secondary Type 2 Diabetes Mellitus.
Abstract #720

PRIMARY HYPERPARATHYROIDISM DUE TO LEFT SUPERIOR PARATHYROID ADENOMA AND ECTOPIC INTRATHYMIC PARATHYROID ADENOMA WITH IDIOPATHIC HYPOCALCIURIA

Ashley Hotz, MD, Ankur Gupta, MD, FACE
Wright State University

Objective: To describe a challenging case of primary hyperparathyroidism (PHPT).

Methods: We report a case of PHPT due to left superior parathyroid adenoma and ectopic intrathymic parathyroid adenoma associated with low 24-hour urine calcium excretion.

Case Presentation: A 68-year-old African-American man with stage 3 chronic kidney disease presented for evaluation of hypercalcemia for unknown duration but at least one year. He denied any history of kidney stones or bone fractures. He denied any family history of hypercalcemia. Physical exam was unremarkable. On labs, he was noted to have normal to high serum PTH level ranging from 36 to 127 pg/ml and elevated serum calcium ranging from 11.5 to 11.8 mg/dl. His serum albumin and 25-hydroxy vitamin D levels were both normal. His 24-hour urine calcium level was consistently below 100 mg with the lowest being 44 mg/day. Calcium sensing receptor (CASR) gene analysis test was performed and was negative for familial hypocalciuric hypercalcemia. His bone density at spine, hips, and left forearm was normal. Ultrasound neck failed to show enlarged parathyroid. Sestamibi scan with SPECT CT showed elevated uptake at the lateral margin of the left thyroid lobe and small focus of increased uptake with in mediastinum. The patient underwent exploratory neck surgery with removal of an enlarged left superior parathyroid adenoma. However, his blood calcium level remained elevated with high normal PTH after initial surgery. He then underwent mediastinal exploration with resection of mass that was consistent with an intrathyrmic parathyroid adenoma. His blood calcium level normalized after the second surgery.

Discussion: Ectopic parathyroids are most commonly found in the thymus or posterosuperior mediastinum. Mediastinal parathyroid adenomas (MPAs) incidence may be 1-2% of all parathyroid adenomas and have had a reported prevalence varying from 6 to 30%. MPAs may have higher presenting calcium levels and higher rates of bone disease. FHH needs to be ruled out when hypercalcemia is noted with hypocalciuria. Studies have demonstrated improved calcium retention in African-Americans compared to whites. This variation can sometimes explain lower urinary calcium levels. In a study of 96 patients investigating this difference in the setting of primary hyperparathyroidism, African American median calcium/creatinine ratios were nearly half that of white counterparts (122 mg/g vs. 214 mg/g respectively).

Conclusion: Urinary calcium levels may not always be reliable to differentiate FHH from PHPT especially in African Americans. Our case of PHPT is unique with double parathyroid adenomas including one ectopic and low 24-hour urine calcium excretion.

Abstract #722

AN ASSESSMENT OF EASE OF READABILITY OF ONLINE PATIENT EDUCATION MATERIAL ON THYROID CANCER TREATMENT: NOT SO READABLE AFTERALL

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Objective: Successful management of diseases largely depends on patient’s active participation in the medical care and having basic knowledge about the treatment options of the disease. Increased availability of online patient education material (PEM) has provided convenient means of perusal of medical information to the patients. Healthcare organizations such as the American Medical Association, National Institute of Health (NIH) and others recommend that the readability of online patient information material should be no higher than sixth-grade level, while the Centers for Disease Control and Prevention recommends the readability to be lower than eighth-grade level. Incidence of thyroid cancer tripled over past three decades in the United States leading to more patients searching for information online. Our aim is to assess the readability of the treatment options of thyroid cancer related PEMs and to determine whether they are at par with the recommendations.

Methods: PEMs from patient only section of websites like American thyroid association, Harvard medical school, NIH, Mayo clinic and others were collected. This text was analyzed by 6 commonly used readability tests - Flesch Reading Ease score (FRE), Gunning Fog (GF), Flesch-Kincaid Grade Level (FKGL), The Coleman-Liau Index (CLI), The Simple Measure of Gobbledygook (SMOG) Index, Automated Readability Index (ARI). Text from each article was pasted into Microsoft Word and analyzed using the 3 different online software Readability calculators. The average readability score was then calculated and compared for corresponding readability grade level.

Results: The mean FRE score is 50.2 (range 44.4-60) which corresponded to the level of education higher than ninth grade level, while the Centers for Disease Control and Prevention recommends the readability to be lower than eighth-grade level. Incidence of thyroid cancer tripled over past three decades in the United States leading to more patients searching for information online. Our aim is to assess the readability of the treatment options of thyroid cancer related PEMs and to determine whether they are at par with the recommendations.

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Abstracts – Other

ABSTRACTS – Other

EFFECTS OF SOMATROPIN (RECOMBINANT HUMAN GROWTH HORMONE) ON LIPID LEVELS IN ADULTS WITH GROWTH HORMONE DEFICIENCY: INTERIM ANALYSIS OF AN OPEN-LABEL, PHASE 3B, MULTICENTER TRIAL

Mohita Kumar, MD1, Bradley Miller, MD, PhD2, Alberto Pereira, MD, PhD3, Nitin Agarwal, MD4

1. Ferring Pharmaceuticals Inc., 2. University of Minnesota, Masonic Children’s Hospital, Pediatric Endocrinology, 3. Leiden University Medical Center, 4. Minnesota Epilepsy Group, P.A.

Objective: Growth hormone deficiency (GHD) in adults is associated with dyslipidemia. Somatropin is approved for pediatric GHD in the US. A long-term study was conducted to evaluate efficacy and safety of somatropin in adults with GHD. This interim analysis included data from up to 24 months of treatment to assess effect of somatropin on lipid concentrations.

Methods: This phase 3b, open-label, multicenter, observational, non-comparative study had a planned follow-up of 5 years. Patients aged ≥18 years with GHD confirmed by insulin-like growth factor 1 (IGF-1; ≤2 standard deviations of normal range for age/gender) or blood glucose (<2 mmol [36.0 mg/dL] on insulin tolerance test) and peak GH concentration (<9 mE/L on insulin tolerance, arginine, clonidine, or GHRH test) were enrolled and stratified by treatment experience. Somatropin was administered daily using the Zomah-JetTM needle-free injector. New patients (no somatropin treatment in previous 12 mo) were initiated on somatropin 0.17 mg/day, and this dose was titrated to the minimum required to achieve an IGF-1 within normal range; switch patients (previously treated) continued their current somatropin dose. Fasting total cholesterol (TC), low- and high-density lipoprotein cholesterol (LDL, HDL), and triglyceride (TG) levels were assessed every 6 months as secondary endpoints.

Results: Of 98 patients enrolled, 42 were new (mean age: 46.1 y) and 56 were switch (mean age: 46.3 y) patients; 89 (new, n=41; switch, n=48) who received treatment and had no major protocol violations were included in efficacy analyses. A lack of evaluable LDL observations did not allow this parameter to be analyzed. Baseline lipid parameters did not differ between new and switch patients. At 24 months, new patients had slight decreases (~4.9%) and switch patients had slight increases (3.5%) in TC levels (P=NS for both). HDL levels increased significantly in both groups; at 24 months, increases of 19.9% (mean level: 1.47 mmol/L [56.8 mg/dL]; P=0.003) and 11.1% (1.48 mmol/L [57.1 mg/dL]; P=0.002) were observed in new and switch patients, respectively. New patients had no significant changes in TG levels at any timepoint; switch patients had significant increases at the 6-month timepoint only (change from baseline: 7.6%; mean level: 2.31 mmol/L [204.4 mg/dL]; P=0.0148).

Discussion: Effects of somatropin on lipid parameters, besides HDL, were difficult to interpret from the current analysis, especially without LDL data.

Conclusion: Somatropin significantly increased HDL levels at 24 months in adult patients with GHD; effects on other lipid parameters remain inconclusive.

Abstract #724

CARDIOVASCULAR AUTONOMIC FUNCTION ONE MONTH POST- PARATHYROIDECTOMY

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1. University of Delaware, 2. Nemours Children’s Specialty Care, 3. Christiana Care Health Services

Objective: Hypercalcemia due to elevated parathyroid hormone levels may affect autonomic control of the heart in primary hyperparathyroidism (PHPT). The etiology of autonomic dysfunction is multifactorial with potential metabolic and inflammatory parameters. Components of the metabolic syndrome (e.g., insulin resistance (IR)) are prevalent in PHPT and patients manifest signs of subclinical inflammation. We examined potential associations of cardiovascular autonomic function (i.e., heart rate variability [HRV]), markers of inflammation, and IR before and one-month after parathyroidectomy.

Methods: Power spectral analysis, with and without...
respiratory analysis, provided frequency domain measures of HRV: high frequency (HF) [parasympathetic measure], low frequency (LF), LF/HF ratio [may mirror sympathovagal balance], HF and LF in normalized units (nu) [normalized with respect to total spectral power], respiration frequency area (RFA), low frequency area (LFA), and LFA/RFA ratio. HOMA-IR and markers of inflammation such as interleukin-6 (IL-6) and lipocalin-2 (LCN-2) were also measured.

**Results:** Thirty participants (27 females), age=60±9 years and BMI=29±5 kg/m2 were studied. With the exception of heart rate (67±7 vs. 69±8 bpm, p<0.01), there were no significant changes pre- to post-surgery for measures of HRV. Post-surgical LCN-2 levels increased (p<0.01), whereas IL-6 and HOMA-IR did not change significantly. Spearman correlations of post-surgical HOMA-IR with HRV parameters were: LF/HF ratio (r = 0.42, P<0.05), HFnu (r=-0.39, p<0.05), and LFnu (r=0.39, p<0.05). LCN-2 and IL-6 were also correlated (r=0.58, p<0.01). Using HOMA-IR>1.8 as a cut-off value to indicate increased IR, sympathovagal measures were higher for those with an elevated HOMA-IR (e.g., LF/HF ratio 2.2±1.2 vs. 1.3±1.1, p<0.05). Regression analysis for post-surgical HFnu and LF/HF ratio as outcomes with HOMA-IR, calcium, and LCN-2 as potential independent variables revealed significant associations with HOMA-IR (p<0.05) (LF/HF model R2=0.53, p=0.001; HFnu model R2=0.34, p=0.017).

**Discussion:** One month post-parathyroidectomy did not result in an improvement in HRV. Post-surgical LCN-2 levels were higher, possibly due to tissue damage from surgery. IR is often associated with low-grade systemic inflammation. Thus it is possible that HOMA-IR was influenced by LCN-2. Nonetheless, HOMA-IR was independently associated with measures of HRV whereas LCN-2 was not. Whether altered HRV preceded IR or vise-versa is not clear.

**Conclusion:** One month post-parathyroidectomy appears to be insufficient time to impart improvements in HRV. HRV may be influenced by metabolic syndrome/inflammation.

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**Abstract #725**

**SUCCESSFUL MEDICAL MANAGEMENT WITH MIFEPRISTONE IN A PATIENT WITH OCCULT ECTOPIC CUSHING’S SYNDROME**

Saima Farghani, MD, FACE1, Michele Lamerson, RN, MS, CPNP2

1. Midatlantic Diabetes and Endocrinology Associates, 2. Corcept Therapeutics

**Objective:** Tumor localization is a challenging & lengthy process when a tumor producing Cushing’s syndrome (CS) is occult. Managing CS manifestations in the interim is necessary.

We present a complex case of suspected ectopic CS successfully treated w/ a glucocorticoid receptor antagonist, mifepristone (MIFE, Korlym®, Corcept Therapeutics).

**Case Presentation:** 63y/o woman presented via the ED w/ severe weakness & recent mental status changes. She c/o polyuria, polydipsia, and weight gain (~40lbs. in 3mos.) w/o hx of DM. She was emotionally labile, irritable & depressed.

PE: BP 160/81mmHg; 185lbs (BMI 31.6); Cushingoid features (moon facies, facial plethora, hirsutism); edema of the lower extremities; thin skin.

Labs: K 2.9mEq/L, Glucose 512mg/dL, A1C 10.6%, cortisol AM 74.60µg/dL; PM 62.9µg/dL, UFC 1201µg/d, DST 33.39µg/dL, ACTH 132pg/dL.

Imaging: Neg pituitary MRI; R adrenal adenoma (3.1 X 2.9cm) on CT; neg octreoscan.

Meds: Lasix 40mg QD, Metoprolol 50mg BID, Nifedipine 90mg QD, Ramipril 15mg QD

In ED: 20U insulin STAT & was started on insulin therapy (84U TDD), labetalol 200mg TID, continued nifedipine & ramipril, hydralazine 10mg TID, KCL, heparin (for DVT risk). Discharged to rehab center.

W/in 1wk, re-admitted to the ICU w/ suspected infection. She was increasingly depressed & confused. Insulin TDD increased (84U to 146U) to maintain glucose in the mid-200s.

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MIFE 300mg was initiated for hypercortisolemia w/ spironolactone 100mg BID for persistent hypokalemia. W/in 24hrs, BP decreased (160/90 to 100/70mmHg), increased (100/70mmHg), insulin TDD reduced (48U). She became alert & awake, & remained hemodynamically stable. She returned to the rehab facility w/ plan for IPSS for localization of the ACTH producing tumor.

6wks after ED visit: MIFE titrated to 600mg w/ control of BP, A1C improved to 5.5%.

At 2mos: re-admitted w/ hypotension & altered mental status, related to urosepsis. During this hospitalization, she required intubation and mechanical ventilation. MIFE was interrupted and IV dexamethasone given. 2 wks later, MIFE was restarted at 300mg/d and w/in 6wks, she looked...
& reported feeling better. At 6mos: 57lbs weight loss; normotensive w/only spironolactone; euglycemic w/o insulin. She regained activities of daily living, ambulating independently w/ improvements in depression & hirsutism while taking MIFE 300mg/d & spironolactone 100mg BID. Repeat octreoscan remained neg. 

Conclusion: MIFE therapy led to significant improvements in CS manifestations (appearance, muscle weakness, glycemic control, BP & weight) w/ elimination of all anti-diabetic & reductions in anti-hypertensive meds, making MIFE a viable option when an ACTH secreting tumor cannot be localized.

Abstract #726

A CASE OF FIBROUS VARIANT OF HASHIMOTO’S THYROIDITIS

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Rutgers-NJMS

Case Presentation: The patient is a 38 year old male who presented to our clinic with a 1 year history of neck swelling. The patient reported that neck swelling started initially on the left side and within 3 months had affected the entire neck. Neck swelling was accompanied by increasing hoarseness of his voice and mild dysphagia to solids. This prompted him to present to ENT. Evaluation included laryngoscopy which showed the larynx was medialized to the right, right vocal cord was difficult to visualize as a result, but the left vocal cord appeared mobile. A CT neck was then obtained and showed a large mass infiltrating the thyroid gland that circumferentially surrounded the right common carotid, right internal and external carotid, with encroachment upon the tracheal esophageal groove, and slight medialization of the right vocal cord. Lab studies showed elevated TSH of 69 μIU/mL, T4 < 1.0 μg/dL, and T3 0.27 ng/dL, and a thyroid peroxidase level of 470 Iu/mL. A fine needle aspiration of the thyroid was attempted but found to have insufficient cells for interpretation. He then underwent an open thyroid biopsy; pathology showed a fibro-inflammatory lesion with vasculitis consistent with fibrosing variant of Hashimoto’s thyroiditis or Riedel’s thyroiditis.

The patient was initially treated with levothyroxine therapy with no improvement in symptoms. He was then started on tamoxifen for presumed diagnosis of Riedel’s thyroiditis. However on further histologic evaluation, patient’s diagnosis was found to be more consistent with fibrosing variant of Hashimoto’s thyroiditis given IgG4 negative staining on histology. Patient was then started on Prednisone 40mg daily for one month with stabilization of but no improvement in symptoms. At present, we increased prednisone to 60mg daily and started patient on mycophenolate 1 gram daily based on a single case study which showed dramatic improvement in symptoms after 1 month on this regimen.

Conclusion: Fibrosing variant of Hashimoto’s thyroiditis is a rare disease entity and can be clinically and histologically difficult to differentiate from Riedel’s disease. Treatment of both of these conditions is difficult and further studies should be performed to evaluate optimal treatment of each condition.

Abstract #727

IMPACT OF METRELEPTIN ON HEPATOMEGALY IN PATIENTS WITH GENERALIZED LIPODYSTROPHY

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Objective: Lipodystrophy syndromes are clinically heterogeneous, inherited or acquired, and often life-threatening disorders. The underlying pathogenesis of generalized lipodystrophy (GL) is the irreversible widespread deficiency of adipose tissue leading to low leptin levels. Due to lack of adipocytes, excess calories accumulate as triglycerides (TG) in ectopic locations such as the liver. Ectopic liver fat can progress to hepatomegaly, steatohepatitis, portal hypertension, cirrhosis, and liver failure. This study examined the effect of leptin replacement therapy (metreleptin, ML) on liver volume (LV) and key metabolic parameters in patients with GL.

Methods: This is a post hoc analysis of an open label, prospective study of ML in patients with GL conducted at the NIH. LV by MRI, was assessed for all available patients enrolled from 2000–2008. Normal LV was calculated as 25 mL/kg of body weight. Mild, moderate, and severe hepatomegaly were defined as ≤1.25 multiple of normal (MN), 1.25–2.5 MN, and >2.5 MN, respectively. TG, hemoglobin A1c (A1c), AST, and ALT were measured at baseline and after ML treatment.

Results: Among the 34 evaluable patients with GL enrolled through 12/31/2008, 22 had baseline liver volumetric measurements. At baseline, all had enlarged liver with a mean ± SD LV of 3467 ± 1208 mL, ranging from 1.1–6 times the normal. The majority of patients were female (68%), 59% had congenital GL, and the mean age was 23 ± 16 years. At baseline, 95% had diabetes, 91% had
hypertriglyceridemia, and 2 patients had autoimmune hepatitis. For patients assessed within a year after initiating ML (n=21, mean treatment duration of 9.8 ± 2.8 months), LV decreased by 24.5 ± 16.6% (95%CI –32% to –17%). Patients (n=14) with longer exposure (46.7 ± 24.4 months) appeared to have a larger decrease in LV relative to baseline of 34.7 ± 18.9% (95%CI –45.6% to –23.7%). Treatment with ML for one year resulted in significant reductions in A1c [n=19, –2.1 ± 1.2% (95%CI –2.7% to –1.5%)], AST [n=19, –46.8 ± 63.0 U/L (95%CI –77.2 to –16.4 U/L)], ALT [n=19, –69.1 ± 101.68 U/L (95%CI –118.7 to –20.7 U/L)], and TG [n=15, geometric mean decrease of 47.2%, 25th percentile –79.5%, 75% percentile –23.5%]. The most commonly reported adverse event was abdominal pain.

Discussion: Moderate to severe hepatomegaly, usually due to hepatic TG accumulation, is a common feature in patients with GL. ML was generally well tolerated.

Conclusion: In addition to its metabolic effects, these data provide additional evidence that ML has a significant and sustained effect in reducing LV in patients with GL.

Abstract #728

PRIMARY CARE USE OF FRAX: TO ASSESS OSTEOPOROSIS RISK SCORE AMONG BANGLADESHI MALE & FEMALE SUBJECTS.

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Objective: This study was designed to assess the effectiveness of use of FRAX as risk assessment tools for osteoporosis risk score sheet among Bangladeshi subjects and how the results of the tools correlate with each other.

Methods: The observational descriptive study was conducted with ethical permission among randomly sampled 600 Bangladeshi subjects; both male & female, who attended outpatient department (OPD), Medicine, MARKS Medical College & Hospital, Dhaka, from January to August, 2016. With written informed consent, a questionnaire was designed to complete the osteoporosis specific risk score sheet. The cases with past history of major trauma, vertebral surgery, and those with suspected vertebral metastasis lesion caused by malignant tumor were excluded . BMI (kg/m2) was determined. The subjects had not a BMD score. We calculated major osteoporotic and hip fracture incidence to 10 years as a function of the FRAX probability. Statistical analysis was carried out to find the correlation between various variables.

Results: A total of 600 subjects [Male, 353(58.30%) & Female; 247 (40.80%)] were included. Mean age of the subjects were 52.16±7.96 (Mean±SD). The mean body height, weights, BMI presented significant differences between male & female [p<0.05].The mean FRAX 10-year Risk Scores, both Major Osteoporotic Fracture and Hip Fracture were more in female subjects [p=0.019 & p 0.588 respectively]. Risk Scores, both Major Osteoporotic and Hip Fracture showed significant association in post menopausal women [P< 0.05]). Risk Assessment Factors for Risk Scores among male and female did not significantly differ except smoking [p <0.05]. Among risk assessment factors, H/O Parent Fractured Hip, Glucocorticoids, Rheumatoid arthritis showed strong association with presence≥ 20% Risk scores for Major Osteoporotic Fracture & ≥ 3% for Hip Fracture [p<0.05] . And subjects having H/O Previous Fracture & Secondary Osteoporosis showed significant association with ≥ 20% Risk scores for Major Osteoporotic Fracture.[p<0.05]

Discussion: The public health burden of fractures will fail to decrease unless the subset of patients who are at increased risk for fracture are identified and treated. Ten-year fracture risk assessment with FRAX scoring system is increasingly used to guide for treatment decisions. With the help of such scoring systems; health resources can be judiciously utilized.

Conclusion: FRAX is an effective tool, particularly in developing countries like Bangladesh, where most of the patients cannot afford expensive DEXA scans for BMD assessment. By noting down the risk factors, we can screen out the subjects both male & female who require further evaluation and management.

Abstract #729

FACTORS INFLUENCING FAILURE OF GLYCEMIC CONTROL AMONG BANGLADESHI ADULTS WITH TYPE 2 DIABETES

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Objective: The study was conducted to explore the factors which influence failure of glycemic control among adult patients with type 2 diabetes in Bangladesh.

Methods: A cross sectional study was conducted among adults with type 2 diabetic patients in the outpatient departments of 9 urban diabetes care centres in Bangladesh. Data were recorded in a semi-structured questionnaire by face to face interview. Diabetes Knowledge (DK) questionnaire, Diabetes Self-efficacy (DSE) score, Hospital Anxiety and Depression scales (HADS) were used.

Results: Out of 11575 respondents with type 2 diabetes, schooling ranged from primary to post graduation levels. The largest group patients (33.1%) aged between 50 - 59
years and most of female respondents were housewives and majority of males were service holders; around 18% were smoker and 24.1% smokeless tobacco consumer. About 21.4% of the respondents could attain good glycemic control in terms HbA1C (HbA1C <7%) and 28.5% in terms fasting plasma glucose [FPG < 6.7 mmol/L (120mg/dl)].

Smokeless tobacco consumption (OR 1.3, CI 1.04, 1.97) increases the probability of having uncontrolled fasting plasma glucose, whereas, higher DSE score (OR 0.99; CI 0.98, 0.99) and lower age of onset of diabetes (OR 0.99 CI 0.98, 0.99) seem to have protective effect. Women are found to have better HbA1C control than men (OR 0.53 CI 0.36 – 0.77). Educational attainment of the patients (OR 0.95, CI 0.91, 0.98), DSE score (OR 0.98, CI 0.97, 0.99), age of onset of diabetes (OR 0.98, CI 0.96, 0.99) and treatment with basal bolus insulin (OR 0.76, CI 0.66, 0.89) showed to have protective effect on HbA1C control. 

**Discussion:** HbA1C showed to have better control with increasing family income level and level of education seems to have significant relation with diabetes control status which is similar many other studies. Women are found to have better HbA1C control than men. Educational attainment, DSE score and age of onset of diabetes showed to have protective effect on HbA1C control. Treatment with basal bolus insulin kept highest percent of people with good glycemic control, secretagogues and premixed insulin, medical nutrition therapy and sensitizer and premixed insulin followed that. No significant association was found between glycemic control with duration of diabetes, residence, smoking and nonsmoker tobacco consumption, family income.

**Conclusion:** Solvency, higher education and female gender helps good glycemic control. DSE score and age of onset of diabetes showed to have protective effect on HbA1C control. Treatment with basal bolus insulin kept highest percent of people with good glycemic control.

**Abstract #730**

**INTERVENTIONAL ENDOCRINOLOGY. A NEWER FUTURE IN ENDOCRINE PRACTICE**

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**Objective:** Current shortage of endocrinologists and fading role of endocrinology as a subspecialty are of concern and are partly attributed to lack of financially rewarding procedures. The aim of this presentation is to demonstrate that integration of endocrine treatment with in-office laser procedures provides the endocrinologist with newer tools for comprehensive management of endocrine disorders.

**Methods:** For the purpose of this presentation, a comparative study was carried out to compare overall treatment results in patients with documented PCOs receiving anti-androgen therapy combined with laser-assisted treatments (Group 1) versus other patients receiving either laser therapy (Group 2) or endocrine treatment (Group 3).

**Case Presentation:** The integration of endocrine treatments with applications of in-office laser procedures achieved optimal results in shorter times. Group 1 patients received 2-4 laser therapies per year as compared to yearly 6-10 laser sessions in group 2 and 3 patients. While all patients in group 1 achieved a minimum of 50% hair reduction in 6 months time, only 40% of patients in group 2 achieved 50% hair reduction in six months time and only 24% of patients in group 3 noticed significant hair reduction in 6 months.

Examples of combined treatments will be demonstrated to show-case the effectiveness, simplicity and safety of various laser technologies when combined with pharmacologic therapies.

**Discussion:** The endocrinologist is well suited to develop the skills to provide laser assisted procedures as a part of integrated medical care for PCOs and other endocrine disorders. Interventional endocrinology has been proposed by other investigators as a futuristic prospect in endocrine management by integrating diagnostic and therapeutic procedures. The present study demonstrates the feasibility and effectiveness of laser assisted treatments when conducted by the endocrinologist in combination with pharmacologic treatment.

**Conclusion:** In conclusion the author proposes the establishment of a newer discipline, Interventional Endocrinology, which would include the application of diagnostic, therapeutic and a multitude of in–office procedures to provide a larger spectrum of management for the endocrinologist and perhaps opens the door for a newer practice of aesthetic endocrinology.
Abstract #731

PERCEPTIONS ABOUT TRAINING DURING ENDOCRINOLOGY RESIDENCY PROGRAMS IN INDIA OVER THE YEARS: A CROSS SECTIONAL STUDY

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Objective: Perception on quality of endocrinology training in India is not known. This study aimed to evaluate the perceptions about endocrinology residency programs in India among current trainees as compared to practicing endocrinologists.

Methods: Trainees attending a preconference workshop at the annual conference of Endocrine Society of India (ESICON) were given a questionnaire designed to evaluate their perceptions on their training. This evaluated the reasons for choosing endocrinology, their experiences during residency and career plans. Practicing endocrinologists, attending ESICON with at least 5-years experience were evaluated as controls.

Results: Questionnaires from 63 endocrine trainees and 78 practicing endocrinologists were analyzed. Endocrinology is perceived to be the super-speciality with best quality of life (QOL) but fair with regards to financial remuneration. Among current trainees 61.89%, 31.74% and 34.91% are satisfied with training in clinical endocrinology, laboratory endocrinology, and clinical/translational research respectively. The corresponding figures for practicing endocrinologists are 71.78%, 25.63% and 30.75% respectively. Exposure to national endocrinology conferences during their endocrinology residency is adequate. However exposure to international endocrinology conferences, research publications, project writing, grant application is limited. Laboratory endocrinology is rated as the most neglected aspect during endocrine residency. Most of the trainees want to establish their own clinical practice in the long run. Very few doctors [trainees (17.46%) and practicing endocrinologists (12.82%)] wish to join the medical education services.

Conclusion: There is a good perception of QOL in endocrinology, in spite of average financial remuneration. There is dissatisfaction with quality of training in laboratory endocrinology, and clinical research. Very few endocrinologists consider academics as a long term career option in India.

Abstract #732

PREOPERATIVE NECK ULTRASOUND AS AN ADJUNCT TOOL IN DIAGNOSIS OF PARATHYROID CARCINOMA

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Objective: To report a case of primary hyperparathyroidism (PHPT) which preoperative neck ultrasound (US) was used to differentiate parathyroid carcinoma (PC) from parathyroid adenoma (PA).

Case Presentation: A 72-year-old man presented with dysphagia for 3 days along with polyuria, fatigue and hoarseness of voice for 6 months. Physical exam revealed a firm mass in the left side of the neck just above sternocleavicular area, measuring 3x4 cm which moved on swallowing. Laboratory data: serum calcium 17.3 mg/dL (8.6-10), PTH 4,564 pg/ml (15-65), phosphorus 4.3 mg/dL, creatinine 2.7 mg/dL. Provisional diagnosis was PHPT. 99mTc sestamibi scan showed an increased tracer uptake focus in the lower pole of left thyroid lobe. Neck US demonstrated an extrathyroidal, encapsulated, solid heterogeneous mass, posterior to the lower pole of left thyroid lobe measuring 3.6x3.1x2.8 cm with irregular margin, peripheral vascularity and peri-lesional penetration through the capsule. Since US findings were suggestive of PC, surgical consultation was expedited. Patient underwent en-bloc resection of left inferior parathyroid gland and left thyroid lobectomy. Pathological report showed PC, size 4x3.3x2.8 cm, weight 30 g with extensive vascular invasion, capsular invasion, absent perineural or thyroid gland invasion, mitotic rate 0/50 HFP, Ki67 0.5-1%. PTH level decreased to 124.2 pg/mL. Patient developed hungry bone syndrome 3 days after surgery.

Discussion: PC accounts for 0.5-5% of PHPT. Mean age of diagnosis is the 5th decade of life. PC usually occurs sporadically however it is present in 15% of patients with hereditary hyperparathyroid jaw tumor syndrome. It is prudent to distinguish PC from PA in order to determine operative strategy. Complete en-bloc resection of the tumor is the only curative approach for PC. Recurrence, resulting in repeated operations and surgical complications is quite common in patients whose initial operation is inadequate. Although some clinical features such as palpable neck...
mass, severe hypercalcemia, extremely high PTH level may suggest PC, these features can overlap with PA. Multiple studies have shown the role of neck US in assisting diagnosis of PC. By reviewing US characteristics of PC in comparison to PA, the suspicious features of PC are heterogeneous echotexture, irregular shape, non-circumscribed margin, calcification and soft tissue infiltration. Large size is also suggestive of PC. Although there is no specific size cut-off, one study reported that a mass of < 1.5 cm was unlikely PC. Depth-width ratio of > 1.0 was proposed as a predictor of PC in one study but was not reproducible in others.

Conclusion: Neck US is a useful tool in aiding diagnosis of PC and planning operative strategy.

Abstract #733

KNOWLEDGE AND ATTITUDE OF ENDOCRINE TRAINEES TOWARDS THE MANAGEMENT OF ENDOCRINE DISORDERS IN PEOPLE LIVING WITH HIV IN SINGAPORE

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Objective: Advances in the treatment of HIV infection has resulted in the life expectancy of people living with HIV (PWH) approaching that of the general population. Endocrine and metabolic disorders such as diabetes mellitus and osteoporosis occur more frequently in PWH than in the general population. While HIV Endocrinology is increasingly recognised as an emerging field within Endocrinology, little is known about the attitudes and practice patterns of HIV Endocrinology care among endocrinologists. This pilot study endeavours to assess the knowledge, practice patterns and confidence levels among endocrinology trainees in Singapore in managing endocrine disorders in PWH.

Methods: An anonymous survey was administered to 23 endocrinology trainees in Singapore. 4 domains were assessed, namely (1) Previous exposure to endocrine disorders in PWH; (2) Attitudes towards treating PWH; (3) Case studies in Endocrinology designed to assess for differences in treatment philosophy between a PWH and a non-infected counterpart; and (4) Knowledge and confidence in managing endocrine disorders in PWH. Trainees were also asked if they would consider HIV Endocrinology as a subspecialty in the future.

Results: The participation rate was 73.9%, with the majority of trainees (88.2%) having managed less than 5 PWH with endocrine disorders. 94.1% of the trainees had little or no hesitation in treating PWH, but more than half (58.8%) felt inadequate in managing endocrine disorders in this unique population. 82.4% deemed it as an emerging field and were open to the idea of pursuing it as a subspecialty in the future, but felt that more attachments to a specialised clinic would bolster interest and confidence. Through the 14 case studies given to the trainees, it was reassuring to note that most trainees would not compromise medical treatment in any way for a PWH if it was indicated (e.g. initiating bisphosphonates in osteoporosis or arranging for continuous glucose monitoring in a patient with diabetes mellitus). More than half were, however, ambivalent about prescribing cross-hormonal therapy to transgender individuals. In addition, some trainees were hesitant about offering surgery (eg, thyroidectomy for Graves disease) for HIV patients, preferring medical therapy such as thioamides or radioactive iodine instead.

Conclusion: While HIV Endocrinology is an emerging field with the promise of being recognised as a subspecialty, many trainees felt that they lack training in this area. Increasing exposure from regular case discussions as well as structured attachments to a joint HIV-Endocrinology specialised clinic can further fuel interest in this field.

Abstract #734

PREGNANCY IN A MALE: A DISASTER OF MIS-TAKEN SEX/GENDER ASSIGNMENT

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Objective: Gender/sex assignment is a crucial process in patients with genital ambiguity. This is a case report of a patient who had an anatomical anomaly and was mislabeled with indeterminate sex and wrongfully assigned male sex for rearing.

Case Presentation: A 22 year old unmarried male presented via the Surgery Department with progressively enlarging mass in the abdomen and vague abdominal discomfort. Examination revealed female secondary sexual characteristics and lack of facial/body hair. Radiological investigations revealed a pregnancy of 26 weeks gestation. Karyotyping confirmed “46 XX”. Gender re-assignment was done immediately in accordance with the patient’s wishes, with gender-appropriate modification in attire and phenotypic appearance. The pregnancy was followed routinely with elective Caesarian Section as a mode of delivery prior to term. Considering the societal norms and safety of the patient, the diagnosis disclosed to the extended family was that of an “abdominal tumour”,
which would be operated in due course. After delivery, the baby was handed over to the biological father, in accordance with the mother’s wishes. Her diagnosis was confirmed to be bladder extrophy with associated genital abnormalities, with the vaginal opening being just inside a large, single opening through which urine would dribble freely. The bladder extrophy was repaired by skin grafting at the age of 1 year. A futile attempt to localise the testis was made by exploratory laparotomy and bilateral inguinal exploration at age 4. The family was then informed about indeterminate sex and was advised to raise the child as a “boy”.

Discussion: The case described is the first case of pregnancy in a male reported in literature. It reflects how flawed assessment and management of sexual ambiguity can be, even in cases handled in large tertiary care hospitals, despite the absence of clear sexual ambiguity. Careful handling of the social issues with regards to the gender change and the fate of the baby may have saved lives in this case.

Conclusion: A multi-disciplinary conference of specialists interested in gender issues, should be held in all cases of gender ambiguity, so that mistakes like this do not happen.

Abstract #735
ABNORMAL FIBROBLAST GROWTH FACTOR23-MEDIATED CRITICAL HYPOPHOSPHATEMIA AND KRAS MUTATION IN A PATIENT WITH COLON CARCINOMA.

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Objective: FGF-23 is a recently identified bone-derived hormone. It principally acts in kidney to induce PO4 excretion. It binds to its cognate FGFR 1 (FGFR1) in the presence of its co-receptor Klotho. Several neoplasms associated with hypophosphatemia causing oncogenic osteomalacia (OSM) have been reported. However, FGF23 levels were not measured in most. We report a case of colon cancer with genetic mutation in KRAS, who had very high serum FGF23-mediated hypophosphatemia.

Results: A 57-years-old pt. with metastatic colon carcinoma had critically low PO4 , 0.27-0.4 mmol/l (RR: 0.8-1.45) throughout hospital course, despite large PO4 replacement (60 mmol IV plus 1500 mg oral/day), inappropriately high urine PO4 69 mmol/day, abnormal fractional excretion PO4 26% (>5% indicates renal wasting), normal renal functions (creatinine 50 umol/l:RR 46-96, e-GFR>60), abnormal FGF23 11,750 RU/ml (normal<180), suppressed PTH 6.7 ng/l (RR: 15-65), high serum calcium 3 mmol/l (RR; 2.1-2.55), normal PTHrP 1.5 pmol/l (normal <2), high AlkPase 971 IU/l (46-122), normal vitamin D3 64 nmol/l (RR: 50-250), tumor genotype gly12Asp (GGT>GAT). Immuno-staining of tumor for FGF23 is pending. Bone scan did not show OSM possibly related to hypercalcemia & short-lived course of disease resulting in death.

Discussion: Patient had selective renal PO4 wasting causing critical hypophosphatemia. FGF23 is a potent phosphaturic agent and was singularly responsible for hypophosphatemia, since PTH and PTHrP were not abnormal. The case underscores a dynamic interaction between, FGF23, PTH, and calcemia as well. Suppressed PTH was related to combined effect of hypercalcemia and high FGF23. FGF 23 inhibits PTH synthesis & secretion. It does so by multiple mechanisms. These include increased expression of parathyroid Ca++ sensing & Vitamin D receptors, reduced parathyroid cell proliferation, & influencing FGFR-Klotho complex. Normal serum vitamin D is not too surprising as it has been reported before in OSM(3), and metabolic bone disease was attributed to low 1,25 Vitamin D3 , that we did not measure in our case. It is intriguing to speculate that the somatic mutation of the tumor was responsible for ectopic tumor production of FGF23. Such an association has been reported before (4). Only positive immunostaining can confirm the idea in our patient. All other causes including renal failure have been ruled out to explain abnormal FGF23.

Conclusion: Exploration for the cause of hypo-phosphatemia in patients with colon malignancy helps understand tumor biology and patient management.

Abstract #736
A CASE OF CARBIMAZOLE-INDUCED PLEURAL EFFUSION

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Objective: Carbimazole is the pro-drug of methimazole. We report a case of a carbimazole-induced pleural effusion.

Case Presentation: A 35-year-old woman, with Graves’ disease treated with carbimazole 40 mg/day, presented with dyspnea for 3 days. She had tachypnea, goiter and non-audible breath sounds with dullness on the right side of the chest. A chest x-ray (CXR) showed a massive right side pleural effusion. Laboratory results revealed normal leukocytes, normal serum electrolytes and creatinine, serum LDH 215.5 U/L (125-220), protein 71 gm/L (64-83), albumin 37 gm/L
(35-50), ESR 31 mm/hr (2-37) and CRP 6 mg/L (0-5). TSH was < 0.01 mIU/L (0.45-4.5), FT3 5.6 pmol/L (2.6-5.7) and FT4 7.5 pmol/L (9-20). ANA, ANCA and hepatitis B and C antibodies were negative with normal serum complement. Pleural fluid aspiration showed a clear fluid with leukocytes 230/uL (neutrophil 32%, lymphocytes 11%, monocyte 1% and eosinophil 56%), erythrocytes 68/uL, pH 7.829, LDH 95.7 U/L, protein 47.9 gm/L, albumin 30 gm/L, negative bacterial and fungal cultures, negative acid fast bacilli and negative mycobacterial DNA. Based on Light’s criteria, this was an exudative eosinophilic effusion. Therefore, a thoracoscopic pleural biopsy with drainage of 1600 ml of the pleural fluid was performed. The biopsy indicated mild non-specific chronic pleuritis in the absence of granuloma and negative mycobacterial DNA. A chest CT scan showed right moderate hydro-pneumothorax with partial lower lobe collapse/consolidation. Thus, carbimazole was considered the reason of her reactive pleural effusion and we switched it to propylthiouracil (PTU). The patient tolerated PTU and she received radioactive iodine therapy. After 3 months, a CXR showed no reaccumulation of the pleural fluid.

Discussion: There are 3 previously reported cases of exudative unilateral or bilateral pleural effusions after using carbimazole for 3 to 27 months. Infectious and vasculitic conditions were excluded and this indicated that carbimazole is most likely the cause of the effusion. The absence of effusion recurrence after 3 months from fluid drainage and a substitution with PTU substantiated that it was carbimazole related. Pleural effusions were commonly described with PTU, which is known to alter myeloperoxidase configuration causing ANCA positivity while carbimazole does not do the same. Carbimazole-induced pleural effusion may be secondary to local pleuritis or leukocytoclastic vasculitis, however, the exact mechanism is still unknown.

Conclusion: In the very rare situation of carbimazole-induced pleural effusion, carbimazole should be changed to an alternative. Our case demonstrated no reaccumulation of the pleural fluid.

Abstract #737

SERUM TRACE ELEMENTS LEVELS IN TYPE 2 DIABETES MELLITUS AND THEIR RELATIONSHIP WITH GLYCEMIC STATUS

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Objective: The study was conducted to estimate the serum levels of serum magnesium, zinc, chromium and copper and in type 2 diabetic patients and their association with age, glycemic status and duration of diabetes.

Methods: A comparative observational study was conducted in 6 diabetes care centers in Dhaka city, Bangladesh during April to December 2015. Data were collected by trained research physicians with the help of pretested case record form. Duration of diabetes, presence of chronic complications, glycemic control status were recorded from the patients’ guided book provided the centers. A total of 1935 subjects were selected randomly, 890 had type 2 diabetes and one or more chronic complications of diabetes and 1045 did not had. Serum trace elements were estimated by atomic absorption spectrophotometer.

Results: Among the respondents, 52.3% were male, the largest age group was 40-59 years (35.1%) and most of them were rural dwellers (59.6%). Hypozincemia was seen in all patients with type 2 diabetes, but the decrease in levels was more in the group with chronic complications of diabetes (80.11+21.31 vs. 92.03 + 20.15; p<0.05). Serum copper level was higher among cases with diabetic complications (164.05± 9.32) than the patients without diabetes related complications (161.45 ± 6.41) and controls (130.88 ± 8.01). No statistically significant difference (P value is 0.37) in the mean copper level was observed between (88.4±40 µg/dl) among patients with diabetes related complications and in uncomplicated diabetes patients (101±39 µg/dl). Serum Zn (P value <0.05) (510±89 µg/dl), serum chromium (1.99±0.8 µg/dl) and serum level of magnesium were significantly lesser (P value is <0.05) (17.76± 0.66 µg/dl) levels were significantly lesser in patients with complications. HbA1C was higher among the trace element deficient group (P value <0.05).

Discussion: The study found serum zinc, magnesium and chromium levels be lower in patients of type 2 diabetes with complications than those without these complications. Similar results were reported by other studies. As seen in this study, magnesium levels were lower in patients of type 2 diabetes mellitus with chronic complications of diabetes. In this study, the copper level was higher in type 2 diabetes mellitus patients with complications than patients without these complications which almost similar to many other studies. But serum copper level was higher
among the patients.

**Conclusion:** Serum magnesium, chromium and zinc were found to be significantly lower in patients with diabetes type 2 with complications as compared to uncomplicated diabetes patients. The good glycemic control of the patients had positive impact on the serum levels of trace elements.

**Abstract #738**

**UTILIZATION OF A PHARMACIST TO PROVIDE DIABETES MANAGEMENT DURING SHORT TERM MEDICAL LEAVE OF AN ENDOCRINOLOGIST**

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**Objective:** What happens to patient care when a physician assumes a short-term medical leave? Medical literature summarizes a host of strategies to cover medical leave of physicians mostly in a hospital practice setting. These include hiring a short-term physician, utilizing a permanent part-time physician, managing coverage with other physicians in the hospital system and contracting with a company that offers locum physician coverage. There are no reports in the literature detailing the strategies of practice coverage when a physician takes short-term leave in an outpatient practice having no other like specialist in the hospital system. Our endocrinology practice chose to pursue a different approach. The objective of this research is to assess the effectiveness of a doctor of pharmacy (PharmD) providing clinical services during short-term medical leave of an endocrinologist.

**Methods:** During the 12 week medical leave of the endocrinologist, patients previously seen by the endocrinologist for a diagnosis of diabetes were scheduled to see the PharmD. Progress notes with interventions, written by the PharmD, were accepted via electronic signature of the endocrinologist off campus. Data analysis was completed with paired t-test, Χ² and linear regression.

**Results:** One-hundred and fifteen patients were seen over the 12 week medical leave of the endocrinologist for a total of 176 consults (91 office, 85 telephone). The mean age of participants was 68 years old with an average duration of diabetes of 17 years. Hemoglobin A1c (HbA1c) was reduced significantly from 8% to 7.6% (-0.4%, p=0.017) following the appointment and intervention by the PharmD. The percentage of patients meeting goal HbA1c improved from 34.9% to 53.5% (18.6%, p=0.082). No models in the linear regression, duration of diabetes or medication change, were significant in regards to achieving goal HbA1c.

**Discussion:** The results reveal that the PharmD improved glycemic control of patients during the short-term medical leave of the endocrinologist over a 12 week duration.

Collaborative practice, established between the PharmD and endocrinologist prior to the medical leave, was seen to be a crucial agreement in this medical leave arrangement. Although the small sample size limits the extrapolation of data, the results are favorable and warrant this as an additional strategy for patient care in the absence of an endocrinologist.

**Conclusion:** Utilization of the PharmD was a successful alternative strategy to cover medical leave for an endocrinologist in an outpatient setting to manage patients with diabetes. This model could be considered when planning for medical leave of a physician to augment or substitute current strategies.

**Abstract #739**

**SCREENING IN A YOUNG PATIENT WITH PRIMARY HYPERPARATHYROIDISM**

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**Objective:** To describe a young patient with primary hyperparathyroidism who had elevated urinary catecholamines and metanephrines on routine follow-up.

**Case Presentation:** A 19-year-old student with no past medical history, presented with a 2-day history of worsening abdominal pain. Examination revealed generalized epigastric tenderness with voluntary guarding. It was noted that he had an adjusted calcium level of 3.55 mmol/L (Reference Index 2.15-2.58), with a parathyroid hormone level of 110.5 pmol/L (RI 0.8-6.8) a 25-hydroxy vitamin D level of 16 ug/L, creatinine of 85 umol/L (RI 60-105) and phosphate of 0.6 mmol/L (RI 0.8-1.6). Serum amylase and lipase were raised respectively at 820 U/L (RI 28-85) and 400 U/L (RI <160). A skeletal X ray demonstrated lytic lesions in multiple sites, suggestive of brown tumours.

As such, a diagnosis of acute pancreatitis precipitated by hypercalcemia from primary hyperparathyroidism. He was started on analgesia, intravenous hydration, bisphosphonates and calcitonin. An ultrasound of the thyroid demonstrated a 4.8 x 2.0 x 1.8 cm left lower pole mass with increased vascularity, suggestive of a parathyroid tumour. A pituitary panel and thyroid function tests were normal, as were 24-hour urinary catecholamines and metanephrines. He denied any diarrhea, flushing or rashes, and further history and investigations were not suggestive of gastric ulcers, hypoglycemia or diabetes mellitus. There was no family history of hypercalcemia, and no jaw tumours on physical examination. He improved with medical treatment and was discharged with close Endocrine and Surgery follow-up. He subsequently underwent surgical removal of the
parathyroid adenoma 1 month later. As he had declined genetic testing, he was monitored in the Endocrine clinic with annual calcitonin and urinary catecholamine and metanephrine levels.

During a routine visit, his 24-hour urinary catecholamines and metanephrines were elevated beyond twice the upper reference limits [(noradrenaline 520 nmol/day (RI 72-505), dopamine 3862 nmol/day (RI 253-2575), normetanephrine 5132 nmol/day (RI 480-2424)]. Further history excluded any concurrent sickness or medications. He was thus sent for a computed tomography scan of the adrenal glands to evaluate for a pheochromocytoma.

**Conclusion:** It is important to regularly screen for the development of MEN-associated conditions such as pheochromocytoma or medullary thyroid cancer in young patients with primary hyperparathyroidism, if genetic testing has not been done. Earlier detection would allow intervention before symptoms present. Family genetic screening should also be offered for the same purpose.

**Abstract #740**

**ADENOMA WEIGHT IS NEGATIVE ASSOCIATED WITH HDL LEVELS IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM**

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**Objective:** To investigate the relationship between adenoma weight and serum HDL levels in patients with primary hyperparathyroidism (PHPT). We hypothesize that patients with PHPT may have higher prevalence of dyslipidemia.

**Methods:** This was a retrospective case control study. Patients’ laboratory results were documented. Intraoperatively, the resected parathyroid adenomas were weighed and recorded. We considered 165 PHPT patients aged from 24 to 83 years (mean ± SD, 57.7 ± 11.5) from both genders with a BMI ranging from 18 to 66.47 (mean ± SD, 30 ± 6.2). The sample was divided into two aged matched groups by median adenoma weight (more or less than 0.61 gram). Each group was subdivided by BMI: 103 patients had a BMI ≥ 30 kg/m2 and 62 had a BMI ≥ 30 kg/m2. Multivariate regression analyses were performed to investigate the association between adenoma weights, iPTH with serum HDL levels.

**Case Presentation:** A total of 165 PHPT patients, including 31 men (18.8%) and 134 women (81.2%) were evaluated in this study. A significant inverse correlation was found between adenoma weight and high density lipoprotein (HDL) in the entire group (r = -0.2, P = 0.008). In non-obese patients (BMI < 30 kg/m2) HDL levels tended to be higher with adenoma weight ≤ 0.61 gram compared with >0.61 gram (P < 0.001). In contrast, in obese patients (BMI ≥ 30 kg/m2), there was no significant difference in HDL levels between patients with adenoma weight ≤ or > 0.61 g (P = 0.6). Adenoma weight remained as independent predictor of HDL cholesterol levels in a multivariate regression analyses after adjustment for age and body mass index (β = -2.96, P = 0.01).

**Discussion:** Previous studies have suggested that PTH may have hyperlipimic properties that increase the risk of morbidity and mortality in individuals with PHPT. Our study has demonstrated that PHPT patients with larger adenoma weight had higher plasma levels of Ca and iPTH, and lower values of HDL cholesterol than those with smaller adenomas. The present study has failed to show any association between iPTH and HDL cholesterol. The results of this study indicate that hyperparathyroid patients may exhibit unfavorable alteration in metabolic variables associated with increased risk of cardiac diseases.

**Conclusion:** PHPT patients had larger parathyroid adenomas at the time of surgery had low HDL levels. Due to a higher risk of dyslipidemia in non-obese PHPT patients with large adenoma size, physicians may have to lower the threshold for Parathyroidectomy in this group of patients.

**Abstract #741**

**SINGNIFICANCE OF AN ELEV ATED VIP IN A MEN 1 PATIENT WITH INSULINOMA**

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**Objective:** Multiple endocrine neoplasia type 1 (MEN 1) is a rare autosomal dominant inherited endocrine disease comprised of pancreatic, parathyroid, and anterior pituitary tumors. Pancreatic islet tumors occur less frequently, among them gastrinomas and insulinomas are the most prevalent.

**Case Presentation:** A 38-year-old Caucasian male presented with abdominal pain and frequent hypoglycemic episodes. Patient had a past history of MEN-1 with heterozygous nucleotide change c.1078delC which is reported as a dominant mutation associated with MEN. He developed recurrent nephrolithiasis at age 20. At that time he was diagnosed with hyperparathyroidism and had partial parathyroidectomy. During a routine follow up, he complained of hypoglycemic episodes and abdominal pain. He reported capillary glucoses as low as 20 mg/dL associated with lightheadedness and confusion. Radiologic imaging revealed a stable 0.8 cm area of calcification in the distal body of the pancreas. Octreotide scan showed no focal
increased radiotracer uptake. A serum VIP was elevated to 96.3 pg/mL with no symptoms of diarrhea. Serum Insulin level was 25.9 uIU/mL and C-Peptide was 5.7 ng/mL. A 72 hour fast resulted in a Glucose of 53 mg/dL and corresponding insulin level of 25.6 uIU/mL, proinsulin of 5.2 pmol/L, c-peptide of 5 ng/mL and low B-hydroxybutyrate. In response to glucagon, plasma glucose improved to 83 mg/dL (>25 points) concerning for Insulinoma. A calcium stimulation test to localize the Insulinoma was performed. Basal insulin level in the splenic artery was 65 uIU/mL and C-peptide was 10.9 ng/mL, on stimulation with calcium 30 minutes later the insulin level increased to 154.5 uIU/mL and c-peptide to 20.1 ng/mL, both continued to increase at 90 and 180 minutes. Splenic artery lesion peak was suggestive of Insulinoma lesion in the tail of the Pancreas. Distal Pancreatectomy was performed and patient came off Diazoxide. Histopathology confirmed the lesion from tail of the pancreas to be a well differentiated neuroendocrine tumor (Insulinoma).

Discussion: Insulinomas are the most common cause of hypoglycemia resulting from endogenous hyperinsulinism. Patients with symptoms of Neuro-endocrine tumors, especially in the setting of MEN1, require diagnostic testing even if radiologic imaging is inconclusive. Approximately 90-95% of insulinomas are benign, and long-term cure is achieved with resection of the insulinomas.

Conclusion: We report a case with an insulinoma less than a centimeter in size with a marginal elevation of VIP levels, undetectable on nuclear imaging. Ongoing surveillance for symptoms of VIPoma will be key. It also highlights the limitations of imaging techniques in the diagnosis of complex neuroendocrine tumors.

Abstract #742

TESTICULAR SEMINOMA PRESENTING AS ACUTE UNILATERAL GYNECOMASTIA

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Objective: Testicular cancer is one of the most common malignancies in young males. Gynecomastia, defined as benign proliferation of male glandular tissue, has been reported as the sole initial clinical finding in up to 5-15% of these patients. This association is often unrecognized.

Case Presentation: Clinical Case

During a routine visit for type 1 diabetes, a 36 year old male expressed concerns of a 4 month history of right breast enlargement, with an associated 40lbs unintentional weight loss (BMI 18). Enlargement was non-tender without nipple discharge. No relevant systemic illness, medications or alcohol abuse were noted. No symptoms to suggest hypogonadism or pituitary disease. A 2cm subareolar right breast mass was palpated. A firm and enlarged left testicle without discrete nodules or regional lymphadenopathy was appreciated.

Total testosterone and estradiol levels were 8.57nmol/L (N 4.56-28.2) and 73 pmol/L (N 50-218) respectively. Alpha-fetoprotein (AFP), b-HCG, LH, FSH, prolactin, free T4, liver and renal functions were normal. Testicular ultrasound revealed an enlarged left testicle with suspicious 1.4cm hypoechoic focus. Left orchiectomy was performed. Pathology revealed a 4.8 cm classical seminoma, stage 2b confined to testis with lympho-vascular invasion. Tumour stained positive for germ cell tumor markers, equivocal for hCG and negative for AFP. CT scans were negative for metastatic disease.

Post-orchiectomy, his gynecomastia resolved within 6 months and he remains under surveillance protocol without adjuvant therapy, at the local cancer center.

Discussion: The etiology of gynecomastia can be complex, including physiological and pathological causes. Germ cell tumors are the most common testicular lesions in young males. These tumors can lead to gynecomastia by increasing circulating estrogen levels. Upon initial glance, no discrete testicular masses were palpated and biochemical investigations seemed to be within normal limits. However, calculation of the estradiol to testosterone ratio of 1:120 indicated a state of relative hyperestrogenism, most likely stimulating breast development (normal peripheral ratio 1:300). As well, in this context, the asymmetry and abnormally firm consistency of the testicular gland should prompt further imaging as these lesions are often only identified with ultrasound.

Conclusion: This case report stresses the importance of careful clinical assessment, including testicular examination in men presenting with isolated breast enlargement. Gynecomastia coupled with testicular abnormalities and hyperestrogenism should raise high suspicion for testicular malignancy, which requires prompt diagnosis for favorable prognosis.
Abstract #743

GRANULOMATOUS HEPATITIS AND HYPERCALCEMIA ASSOCIATED WITH INTRAVESICAL BACILLUS CALMETTE-GUERIN THERAPY

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Objective: Bladder cancer is the fourth most prevalent cancer in men. The most effective adjuvant therapy used in the treatment of bladder cancer is intravesical Bacille Calmette-Guérin (BCG). Although normally well tolerated, there are infrequent instances of life threatening complications.

Methods: An 82-year-old man presented with worsening generalized weakness, fatigue, and weight loss for two years. He was treated for carcinoma in situ two years prior with transurethral resection and 12 cycles of BCG. His symptoms had begun soon after initiation of BCG. Therefore, an extensive assessment was initiated.

Case Presentation: Labs revealed elevated alkaline phosphatase, liver function tests, and calcium with suppressed parathyroid hormone (PTH). Important normal labs included PTH-related peptide, thyroid stimulating hormone, free kappa/lambda ratio, serum protein electrophoresis, and urinalysis. His 25-hydroxyvitamin D level was low, but 1,25-dihydroxyvitamin D and angiotensin-1 converting enzyme levels were elevated, raising concern for granulomatous disease. Imaging suggested against sarcoidosis and biliary, metastatic, or intrinsic/post-renal disease. A cystoscopy was uneventful. A liver biopsy revealed granulomatous hepatitis with negative Ziehl Neelsen and Grocott’s methenamine silver stains, suggesting against the presence of acid-fast bacilli or fungal organisms.

Discussion: Despite the lack of evidence on liver biopsy, the patient’s hepatic granulomatous disease and resulting hypercalcemia were concluded to be due to a Mycobacterium bovis infection from BCG therapy. This deduction was based on the temporal relationship of the BCG therapy to the onset of symptoms and abnormal lab findings. Thus, empiric treatment for a Mycobacterium bovis infection with isoniazid, rifampin, and ethambutol was started.

Conclusion: The patient’s hypercalcemia trended down and remained normal after anti-mycobacterial therapy. Literature on granulomatous-induced hypercalcemia suggests glucocorticoids as an effective component of treatment. With the wide-spread prevalence of in situ bladder carcinoma and the strong propensity to use BCG immunotherapy as part of the treatment plan, there lies a high potential for more physicians to encounter life-threatening complications from BCG therapy.

Abstract #744

MEDICAL MANAGEMENT BETTER TOLERATED THAN PARATHYROIDECTOMY IN PATIENTS OVER AGE 85 WITH PRIMARY HYPERPARATHYROIDISM

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Objective: To determine if medical management versus surgery was better tolerated among primary hyperparathyroidism (PHPT) patients aged 85 and older.

Methods: In this retrospective chart review of PHPT patients evaluated at Robert Wood Johnson University Hospital Endocrinology outpatient clinic from January 2000 to December 2013, there were 15 patients aged 85 and above. Data including patient demographics, baseline characteristics, clinical presentation and overall clinical picture at 1 month follow-up were examined.

Case Presentation: The mean age of 88 ± 2.5 years, 80% were female, and 86% white with a mean iPTH level of 266 ± 399 pg/mL and a total serum calcium of 11.1 ± 0.84 mg/dL. 12 (80%) of the patients were medically managed (with bisphosphonates, cinacalcet, emphasis on increased hydration, and removing thiazides) while 3 (20%) of the patients underwent parathyroidectomy. Of the medical treatment group 3/12 (25%) were treated with cinacalcet, and only 1/12 (8%) was treated with augmented hydration. There were no post-operative complications in the surgery group, and no hospitalizations for the patients in the medical management group. However, 2/3 (67%) of the surgeries failed to lower PTH back to the normal range and symptomatic therapy had to be initiated. Of the medically managed group, Cinacalcet had to be stopped in 1/3 (33%) patients for GI intolerance.

Discussion: We found that parathyroidectomy was likely inferior to symptomatic management for PHPT. Symptomatic treatment resulted in controlled disease with all 12/12 (100%) of patients. Comparatively only ⅓ (33%) of the surgeries resulted in a clinical cure, the remainder had to be medically managed. When we reviewed the literature, there was a paucity of data comparing symptomatic management versus surgery for patients over age 85 with PHPT. It has been suggested in a limited case series that medical management is acceptable and even preferable to surgery in patients over 90 years old. One other case series published in the Netherlands of 4 patients from age 79-87 indicated satisfactory treatment and low incidence of sequelae from PHPT with non-surgical management. Our expanded case series supports this growing body of literature that medical management
Abstracts – Other

Abstract #745
SURGEON PERFORMED ULTRASOUND FACILITATES SINGLE QUADRANT FOCUSED PARATHYROIDECTOMY

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Objective: Background: Single-quadrant focused parathyroidectomy for primary hyperparathyroidism is dependent on accurate pre-operative image localization. While localization has traditionally been performed using 99mTc-sestamibi scan (SM) and radiology department-performed ultrasound, surgeon-performed ultrasound (SPU) has been shown to provide similar sensitivity in localizing parathyroid adenomas.

Methods: A database of patients with primary hyperparathyroidism who underwent parathyroidectomy from August 2011- May 2015 was reviewed, and results of pre-operative imaging modalities were assessed.

Results: A total of 74 patients with primary hyperparathyroidism underwent both Sestamibi scan (SM) and surgeon performed ultrasound (SPU). SM and SPU were concordant for quadrant (superior vs inferior; left vs right) in 50 patients, facilitating single-quadrant focused parathyroidectomy in 49/50 (98%) patients. SM and SPU were discordant in 16 patients, with 11/16 (68.7%) of patients undergoing single-quadrant focused parathyroidectomy. Both modalities were non-localizing in 8 patients with only 4/8 (50%) of patients undergoing single-quadrant focused parathyroidectomy.

Conclusion: When SPU and SM scan localize to the same quadrant, nearly all patients can successfully undergo focused single-quadrant parathyroidectomy. However, when imaging is discordant or non-localizing, the rate of successful focused single-gland parathyroidectomy decreases.

Abstract #746
PRIMARY HYPERPARATHYROIDISM, REDEFINING CURE

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Objective: Primary hyperparathyroidism is the most common cause of hypercalcemia in the outpatient population. The classic diagnosis is established by the presence of hypercalcemia with an inappropriately elevated PTH level, in the absence of other causes of hypercalcemia. Cure rate for primary hyperparathyroidism has been reported to be 93–100% and has been defined as normocalcemia at 6 months. The follow up to confirm normal calcium postoperatively and at 6 months is resource intensive and costly. The aim of this study was to determine if there is a subset of patients who can be defined as cured earlier than 6 months.

Methods: This was a retrospective study of patients who underwent parathyroidectomy between January 1, 2012 and March 31, 2014. Patients with history of MEN syndrome, secondary or tertiary hyperparathyroidism where excluded. Patients with normal preoperative calcium, normal PTH, and those without 6 months follow up were excluded. Patients were divided into two groups, cured and not cured. Preoperative sestamibi scan was correlated to intraoperative findings, and labeled as concordant (TP), wrong location (FP) or negative (FN) for each group. Comparison analysis was performed between the two groups, examining age, gland weight, imaging concordance, preoperative PTH, intraoperative PTH, intraoperative cure (decrease of baseline PTH by 50% to normal or near normal PTH level), and 6 months cure rate.

Case Presentation: A total of 509 patients were screened, 214 met our inclusion criteria; 202 cured and 12 not cured (94% cure rate). 205 of 214 (96%) had intraoperative cure. There was no significant difference between cured and not cured in age (62 years vs 62 years, p = 0.48), gland weight (753 mg vs 478 mg, p= 0.15) or preoperative PTH (133 pg/ml vs 123 pg/ml, p=0.33). There was a statistically significant difference between cured and not cured in final intraoperative PTH (37 pg/ml vs 55 pg/ml, p=0.008) and percent PTH decrease (69% vs 43%, p < 0.0001). Fischer exact test revealed significant difference between cured and not cured in intraoperative cure rate (p < 0.0006), imaging concordance (p=0.012) and solitary vs multiglandular disease (p=0.015). Subgroup analysis in patients with concordant imaging, solitary parathyroid adenoma and intraoperative PTH decrease by 50% to normal or near normal correlated with a 6 months cure rate of 98%.
Conclusion: Patients with primary hyperparathyroidism who have concordant imaging, single adenoma pathology, and intra-operative PTH decrease by 50% to normal or near normal (15-65 pg/ml) can be considered cured, and may not need further laboratory follow up.

Abstract #747
THE ROLE OF EXCEPTIONAL PARENTAL LONGEVITY, NUTRITION, AND LIFESTYLE IN CARDIOVASCULAR DISEASE RISK
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Objective: To test whether individuals with parental longevity have lesser burden of cardiovascular disease independent of dietary patterns, socioeconomic status and lifestyle habits.
Methods: The subjects are participants of the LonGenity study, an on-going longitudinal study that recruits community dwelling Ashkenazi Jewish adults of age 65-94 years. The LonGenity cohort consists of two groups (1) offspring of parents with exceptional longevity (OPEL; n=395, 58.7% female, mean age 74.8 ± 6 years), defined as individuals with at least one parent living past the age of 95 years, and (2) offspring of parents with usual survival (OPUS; n=450, 49.6% female, mean age 76.4 ± 7 years), defined as individuals whose parents died before the age of 95 years. Medical and demographic information was obtained using standardized questionnaires. Socioeconomic status was defined based on validated classification scores. Dietary intake was evaluated with the Block brief food frequency questionnaire in a sub-group of the study population (n=234; OPUS=89, 65.2% female and OPUS n=145, 56.6% female).
Results: At baseline, there were no significant differences noted in the body mass index (BMI), obesity, smoking, daily physical activity, years of education and the social strata scores between OPEL and OPUS. Compared to OPUS, OPEL had higher daily consumption of alcohol (2.4g vs. 1.2g, p=0.018), even after adjustment for age and sex, but this difference was unlikely to be of clinical significance. The daily consumption of other foods, including total calories, fats, carbohydrates, proteins, and fiber, were similar between the two groups. OPEL demonstrated a lower prevalence of hypertension (41.6% vs. 51.4%, p=0.006), coronary artery disease (CAD; 10.4% vs. 16.1%, p=0.02), and stroke (1.5% vs. 5.4%, p=0.003). The baseline prevalence of cardiovascular disease, defined by a history of CAD or stroke, was also lower in OPEL compared to OPUS (11.5% vs. 19.9%, p=0.001) and remained significant after adjustment for age, sex, and BMI.
Discussion: Studies have shown that dietary composition, socioeconomic status and lifestyle factors are important risk factors for cardiovascular disease. Our results demonstrate that compared to OPUS, OPEL did not exhibit healthier dietary or lifestyle habits, nor higher socioeconomic status; yet, OPEL were less likely to manifest cardiovascular disease. These results suggest that exceptional parental longevity confers certain genetic advantages that provide protection against cardiovascular disease.
Conclusion: Parental longevity is associated with lower cardiovascular disease prevalence in the offspring that is independent of dietary patterns, socioeconomic status and lifestyle habits.

Abstract #748
RETROSPECTIVE REVIEW OF PATIENTS TREATED WITH CLOMIPHENE CITRATE FOR MALE CENTRAL HYPOGONADISM
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Objective: The prevalence of hypogonadotropic hypogonadism is rising and it is estimated that 40% of males over the age of 65 have hypogonadism. Central hypogonadism is most common among obese, metabolic syndrome and type 2 diabetic patients. Clomiphene has been used to treat hypogonadism in these patients, however, this is not an FDA approved indication. Clomiphene has been used in the setting of male infertility and has shown its effectiveness in preservation of testicular volume and spermatogenesis. Both clomiphene and its isomer, enclomiphene, have been demonstrated to be effective treatment for male central hypogonadism.

Methods: This is a retrospective case series analysis of 23 patients treated with clomiphene for central hypogonadism in an endocrinology clinic. Baseline data was gathered include patients’ ages, baseline total testosterone (TT), free testosterone (FT), SHBG, LH, FSH, albumin, TSH and FT4. Patients’ were initially started on 25 mg of clomiphene citrate daily for four weeks. After four weeks of daily clomiphene, TT and FT were reassessed. If there was an initial adequate response to clomiphene, patients were then placed on 25 mg every other day. Repeat TT and FT were then obtained to assess the patients’ continuous response to clomiphene.
Case Presentation: The average age of the patients in the
study was 51.26 years old with an average BMI of 33.04. The baseline mean total testosterone and free testosterone was 216.91 ng/dl and 42.64 ng/dl, respectively. The TT and FT after 4 weeks of 25 mg daily of clomiphene citrate therapy were 556.74 ng/dl and 97.07 ng/dl, respectively. After a minimal of an additional 4 weeks of treatment on the lower dose of 25 mg clomiphene every other day, the TT and FT were 486.58 ng/dl and 88.39 ng/dl, respectively. 

Discussion: Clomiphene has been studied in male infertility and in the setting of androgen deficiency. In several reported short-term studies, it has been efficacious with a safe side effect profile. In our series, no significant adverse side effects were noted. Clomiphene was initiated at 25 mg daily resulting in a significant rise in testosterone concentrations. The dose was lowered to 25 mg every other day and the testosterone concentrations remained within normal limits. Only 2 of 23 patients failed to respond. The gold standard treatment of hypogonadism is traditional testosterone supplementation. However, cost and potential adverse side effects of exogenous testosterone is a cause for concern. Clomiphene may provide a safe, inexpensive and effective treatment for male central hypogonadism.

Conclusion: Clomiphene is effective for treating males with central hypogonadism. However, long-term studies are needed.

Abstract #749

THE ADDED MORBIDITY OF MALNUTRITION WITH AGING IN MULTIPLE ENDOCRINE NEOPLASIA TYPE 1

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Objective: Due to concern for inoperable tumor, patients with Multiple Endocrine Neoplasia (MEN) type 1 sometimes undergo surgery for pancreatic mass over 2cm. The following case illustrates a chronic complication that can result from these surgeries.

Case Presentation: A 43 year old man with MEN type 1 underwent exploratory laparotomy for 2.5 cm mass in the pancreatic head 14 years earlier. At the time, he had enucleation of the pancreatic mass, distal pancreatectomy, splenectomy. The surgery was complicated by pancreatic duct resection and required treatment with Roux-en-Y pancreaticojejunostomy, duodenotomy, cannulation of ampulla of vater. Two months later, he was found with left upper quadrant abscess. He had repeat exploratory laparotomy, debridement of the abscess, pyloric exclusion and gastro-jejunostomy.

Additional Medical History: Primary hyperparathyroidism, osteoporosis, gastrinoma, four gland parathyroidectomy Disease course: The patient developed progressive weight loss and fat soluble vitamin deficiencies. 14 years post-op, he weighed 67.5 kg (BMI=20.4 kg/m2), in contrast to 121 kg before the surgeries. His laboratory results 14 years post-op were: Vitamin A level=4 (reference range 36-120 mcg/dl), Vitamin E <2.0 (ref range 5.5 – 17 mg/l), 25 hydroxy vitamin D=5 (ref range 10-80 ng/ml). Prealbumin=8 mg/dL and total cholesterol= 54 mg/dL — both low; serum vitamin B12= 677 pg/mL and folate=14.5 ng/mL—both normal; Hemoglobin/ Hematocrit=11.4 g/dl / 36.4%; Gastrin= 4628 (ref range <100 pg/ml). DEXA scan revealed osteoporosis (Lumbar spine Z-score= -3.0). Ionized calcium=1.38 (ref range 1.12-1.32 mmol/L) PTH=85 (ref range 15-65 pg/ml)

His malnutrition was determined to be from a combination of 1) bacterial overgrowth 2) pancreatic insufficiency and 3) altered bowel motility. He was determined to have a blind bowel loop that functioned as a sink for ingested food predisposing him to bacterial overgrowth. He regained some weight on a trial of rifaximin for bacterial overweight. However, he failed to follow up for continued therapy. He also could not afford long term multivitamin treatment of his fat soluble vitamin deficiencies. He declined reparative bowel surgery and any associated pre-operative nutrition therapy. 14 years post op, he could still partake in all of his independent activities of daily living.

Conclusion: Although rare, chronic malnutrition can occur as a result of surgical treatment of neuroendocrine tumors of the gastrointestinal system. Nutrition therapy is not typically covered by insurance and can be financially burdensome for the patient. Endocrinologists and surgeons need to advise patients pre-operatively of this potential complication.
Abstract #800

CYSTIC PROLACTINOMA: A SURGICAL DISEASE?

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**Objective:** Prolactinomas have long been considered a medically treatable disease. First line therapy, in most cases, are dopamine agonists. Indications for surgical treatment of prolactinomas include failure to respond to or intolerable side effects to dopaminergic therapy, rapidly progressing neurological deficits, and CSF leak with fistula formation. However, conflicting recommendations exist on whether a pharmacologic versus surgical approach be used to manage patients with predominantly cystic prolactinomas. We present one such case of a cystic prolactinoma in which surgery was selected as first line therapy.

**Case Presentation:** A 26-year-old African American man presented to an outside hospital with complaints of dull right-sided headaches for 1 week. He first noticed the headache on waking, after drinking heavily the night before. The headache worsened over the next few days, which prompted him to go to the Emergency Room. The evaluation included a head CT which demonstrated a 4 cm solid/cystic pituitary mass with possible hemorrhagic conversion and compression of the optic chiasm. He was transferred to University of Maryland Medical Center for neurosurgical evaluation. He denied symptoms of pituitary hormone excess or deficiency including galactorrhea. He denied visual symptoms though formal visual field testing demonstrated temporal hemianopia. Hormonal evaluation revealed hyperprolactinemia (prolactin=1627 ng/mL) and central hypothyroidism (TSH=2.72 uIU/mL; FT4=0.5 ng/dL). The patient was started on Levothyroxine. Because of the large cystic component of the prolactinoma and clinical evidence for compression of the optic chiasm, the patient underwent transsphenoidal resection of the mass. Post-operatively, the patient was started on Bromocriptine 2.5 mg PO daily for suppression of residual prolactinoma tissue. Notably, the patient developed DI on post-operative day 3 requiring DDAVP for the rest of his hospitalization and on discharge.

**Conclusion:** It has been theorized that cystic prolactinomas may not respond well to dopamine agonists due to a possible lack of dopamine receptors in the cystic part of the tumor. However, some small studies show favorable responses to medical therapy alone. Surgical outcome studies show comparable remission rates and prolactin normalization as medical therapy. Although morbidity and mortality of transsphenoidal surgery is low, outcomes are highly dependent on the skill and experience of the neurosurgeon. While larger randomized studies are needed to compare medical versus surgical outcomes, for now, each patient should be considered on a case-by-case basis before deciding on a treatment modality.

Abstract #801

CONSERVATIVE MANAGEMENT OF PITUITARY APOPLEXY

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**Objective:** To describe a case of pituitary apoplexy.

**Methods:** Case presentation and literature review.

**Case Presentation:** 71 year old male with past medical history of hypertension, obesity, and pre-diabetes presented to the emergency department with three days of sudden onset worst headache of his life, diplopia, nausea and vomiting. The CT scan head was unremarkable. He was hydrated and discharged with diagnosis of dehydration and heat stroke. In about a week, he felt worse and got readmitted with unsteadiness, generalized weakness, persistent diplopia and syncope. Physical examination including the visual field test was unremarkable except low BP of 76/54 mmHg. MRI brain revealed 1.7 cm x 1.3 cm x 1.1 cm lobulated enhancing mass within sella turcica with minimal deviation of the pituitary stalk to the left without any suprasellar extension or optic chiasm impingement, and post contrast sequence with possible extension into left cavernous sinus. Laboratory data was consistent with secondary adrenal insufficiency, central hypothyroidism, central hypogonadism with normal electrolytes. Treatment with high dose steroids and levothyroxine was initiated, which led to significant improvement in symptoms. Later, he was transitioned to physiologic dose of hydrocortisone. He has been asymptomatic since then.

**Discussion:** Pituitary Apoplexy (PA) is a rare clinical syndrome manifested by sudden hemorrhage or infarction of pituitary gland often into existing pituitary adenoma, (80% of which are not previously diagnosed). PA complicates about 2-12% of pituitary adenomas, especially non-functioning tumors. It clinically presents with sudden onset severe headache (95%), nausea/vomiting (69%), visual disturbances (60-70%), ocular palsies (70%), change in mental status (24%) and hypopituitarism with secondary adrenal insufficiency (70%), central hypothyroidism (50%), and central hypogonadism (75%). Secondary adrenal insufficiency can be life threatening if left untreated. Although there are not any randomized controlled trials in the literature to compare surgical and conservative approach, several case series and
case reports have reported excellent outcomes in terms of visual function, ocular palsies, and subsequent tumor growth with conservative approach.

**Conclusion:** PA is a life threatening condition that can be missed if not recognized early. PA was previously considered a neurosurgical emergency, is now managed conservatively in cases without significant visual field defects and loss of consciousness.

**Abstract #802**

SEVERE RHABDOMYOLYSIS ASSOCIATED WITH ADIPSIC CENTRAL DIABETES INSIPIDUS IN A PATIENT WITH NEUROSARCOIDOSIS

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**Case Presentation:** 40 year old African American male with pulmonary and neurosarcoidosis who presented with generalized weakness. Medical history included ventriculo-peritoneal shunt for hydrocephalus, seizure disorder, congestive heart failure and pulmonary thromboembolism. He was neither hungry nor thirsty and could not recollect time of last fluid intake. Records showed prior episodes of hypernatremia, which required hospitalization and intravenous hydration. Physical examination revealed tachycardia (118 /min), tachypnea (31/min), and blood pressure of 115/84 mmHg. He was lethargic and dehydrated. Laboratory data revealed a serum Na- 175meq/L (135-145); BUN- 87mg/dl(7-18); serum creatinine- 10 mg/dl (0.7-1.3); serum osmolality- 412 mosm/kg ( 270-290); urine osmolality- 384 mosm/kg (293-1093); urine specific gravity 1.020 (1.003-1035), eGFR- <15.0 and CPK- > 20,000 units/ml (35-232); calculated free water deficit was 17 Liters. Imaging showed a hyper-dense mass in the basal ganglia, and a functional left-sided VP shunt. He developed acute hypoxic respiratory failure from volume overload which required mechanical ventilation and hemodialysis for oliguric renal failure. He was treated with intravenous hydration and subcutaneous DDAVP 0.1mg daily. Serum Na improved to 149 meq/L after 3 days when CPK was 2,971 units/ml. He was extubated after cardio-pulmonary stabilization. At the time of discharge, renal function had recovered fully with serum creatinine- 0.81mg/dl, eGFR- > 60 mls/min and serum Na- 143 meq/L. After a year, with adherence to desmopressin and scheduled water intake, frequency of hypernatremia, has decreased significantly.

**Discussion:** Adipsic diabetes insipidus (DI) is a rare disorder characterized by impaired vasopressin secretion and absence or decreased thirst response to hyperosmolality. It can occur after extensive intracranial surgery, head injury, toluene exposure, septo optic dysplasia, neurosarcoidosis, as well as rupture or clipping of aneurysms of the anterior communicating artery of the circle of Willis. Patients may present with polyuria, hypernatremia, dehydration, renal failure, encephalopathy or seizure. Common comorbidities are thromboembolism, obstructive sleep apnea, obesity, cognitive deficits and thermoregulatory dysfunction. Rhabdomyolysis as in our case is very rare. Management includes adequate hydration with adjustment of water consumption based on weight, DDAVP and monitoring of serum sodium.

**Conclusion:** Adipsic DI is a rare but severe metabolic complication of neurosarcoidosis; prompt recognition and adequate treatment of this condition is vital to prevent undue morbidity and mortality.

**Abstract #803**

HYPONATREMIA AS THE INITIAL PRESENTATION OF A SELLAR MASS

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LSUHSC

**Objective:** A sellar mass is low in the differential for patients with hyponatremia. Sellar masses are a common cause of secondary adrenal insufficiency, which may cause hyponatremia via cortisol deficiency. We present a case of euvolemic hyponatremia that failed to respond to fluid restriction and oral salt tablets. Final diagnosis was cortisol deficiency due to sellar mass.

**Case Presentation:** A 67 year old white female with a history of hypertension, depression on paroxetine, and nicotine patch presented with generalized fatigue, headache, and nausea. A year earlier she had been hospitalized with hyponatremia attributed to water drinking and blood pressure medication. Current serum sodium was found to be 121 mmol/L and she was admitted. She was restricting salt on her daily diet secondary to her hypertension. However, there was no evidence of volume depletion or poor cardiac function. Urine osmolality was high at 520 mosm/kg, suggesting SIADH. Paroxetine was discontinued. She was started on salt tablets and fluid restriction. Sodium remained low and endocrinology was consulted. The primary team had performed an ACTH stimulation test showing a baseline cortisol of 3.4 mcg/dL and a stimulated cortisol of 17 mcg/dL. Given this suboptimal stimulation, free T4, TSH and LH were ordered to screen her pituitary reserve. Her freeT4 was low at 0.71 ng/dL (normal = 0.76-1.46) and TSH was 1.28 mU/L (normal = 0.36-3.74), suggesting central hypothyroidism. LH was also low at <2.0 mIU/mL (normal for post-menopausal female = 8.6 – 61.8). These
results prompted a pituitary MRI showing a lesion of the pituitary stalk measuring 12 x 9 x 16 millimeters. She continued on fluid restriction and salt tablets 2 gm three times a day, but sodium remained below 126 mmol/L. Cortisol replacement (15 mg in the AM and 5 mg PM) was initiated. After a single day of cortisol treatment sodium improved to 134 mmol/L. A follow-up check 2 weeks later showed sodium of 141 mmol/L.

**Conclusion:** This patient presented with symptomatic hyponatremia of a euvolemic type. Given her general medicine condition and history, the leading etiologies were medication side effect, voluntary water intoxication, or ectopic ADH syndrome. Hypopituitarism was not clinically evident. Similar cases have been described previously but are nonetheless still easily missed. Evaluation of the HPA axis should be considered in any hyponatremic patient who does not have an evident cause or who responds poorly to usual measures. Replacement cortisol in ACTH deficient patients can improve sodium levels as quickly as a day or two.

**Abstract #804**

**GRANULAR CELL TUMOR OF THE NEUROHYPOTHYSIS**

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**Objective:** Granular cell tumors (GCTs) can present in different parts of the body, but frequently in the subcutaneous soft tissue of the head, neck or the skin. GCTs of the neurohypophysis are uncommon, and mostly presents in the adult age. They account for less than 0.1% of all primary brain tumors. To date, approximately 70 case reports have been described in the literature.

**Methods:** A case report

**Case Presentation:** This is the case of a 38-year-old Hispanic man who presented with symptoms of intermittent headache, dizziness, and vision loss for 4 months, but no other specific neurological or hormonal symptoms. Brain Magnetic resonance imaging (MRI) revealed enlargement of pituitary gland, measuring 2.1 x 1.8 x 1.2 cm with heterogeneous diffuse contrast enhancement extending up to left side toward sphenoidal sinus and having contact with the left third cranial nerve. Nevertheless, these findings were inconclusive, and the differential diagnoses included pituitary macroadenoma, lymphoma, and metastases. Hormonal work up revealed a normal pituitary function. Transsphenoidal surgery was performed, and pathological findings revealed a granular cell tumor of the infundibulum. Immunohistochemistry profile examination was focally positive for CD-68 in a few cells, and strongly positive for S-100 in tumoral cells, confirming the diagnosis of a GCTs of the infundibulum. The patient developed diabetes insipidus (DI) immediately post-surgery and was consulted to Endocrinology Service at our institution. Hormonal workup post-procedure, was consistent with normal anterior pituitary function. A persistent DI required intranasal Desmopressin therapy with adequate response.

**Discussion:** GCTs of the neurohypophysis are difficult to diagnose preoperatively due of the absence of specific imaging and clinical features. The tumors are commonly small solitary lesions with no mass effect, but in some situations, the tumor can be large and result in compressive symptoms such as visual impairment, headaches, and endocrine problems. This case was not associated with hormonal symptoms, nevertheless showed ophthalmologic symptoms owing of the tumor size. Most GCTs are benign with slow growth, however, sometimes are associated with invasion or recurrence. Complete surgical resection is the treatment of choice, as in our case.

**Conclusion:** We report an unusual case of GCT of the infundibulum presenting with compressive symptoms suggestive of a mass effect at the pituitary gland. Imaging studies cannot differentiate from other pituitary lesions and a pathological confirmation is needed for diagnosis. Early diagnosis, extensive tumor removal and hormonal profile are the keys to managing these cases.

**Abstract #805**

**ISOLATED PITUITARY METASTASIS FROM RENAL CELL CARCINOMA IN A HORSESHOE KIDNEY**

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**Objective:** Pituitary metastases from renal cell carcinoma (RCC) are extremely rare. Less than 1% of resected pituitary lesions are found to be metastases, with RCC accounting for only 2.6% of these cases. We report a case of RCC in a horseshoe kidney with an isolated pituitary gland metastasis.

**Case Presentation:** A 56-year-old man presented in July 2016 for the evaluation of a sellar mass. He had been experiencing fatigue, severe weight loss, anorexia, constipation, and nonspecific abdominal pain for about three months. Initial blood work found central hypothyroidism with TSH 0.07 mIU/L (0.4-4.5) and freeT4 0.6 ng/dL (0.8-1.8). MRI was contraindicated due
to retained bullet fragments, but CT head showed a 2.6 x 1.8 x 2.5 cm sellar mass with some cavernous sinus involvement and bony destruction of the hypophyseal fossa but no suprasellar extension. Remainder of his pituitary function revealed panhypopituitarism, with FSH 1.5 mIU/mL (1.6-8), LH 0.2 mIU/mL (1.5-9.3), GH 0.1 ng/mL (low <7.2), though only borderline low AM cortisol of 9.6 µg/dL (4-22). Prolactin was mildly elevated at 78.8 ng/mL (2.0-18). AM testosterone level was deferred due to clinical irrelevance at the time. TSH and total testosterone levels were normal in 2014. On presentation, he had no visual complaints, and no visual field defects were detected on exam. He denied polyuria and polydipsia. Hydrocortisone and levothyroxine led to cessation of weight loss, but unmasked diabetes insipidus requiring desmopressin therapy.

Imaging for his abdominal pain revealed a 12.1 cm mass arising from the right renal moiety of a horseshoe kidney. Open heminephrectomy was performed in Sep 2016. Pathology showed clear cell RCC, Fuhrman grade 2, confined to the kidney, with negative surgical margins, pT2a. CT head at that time found no significant change in the sellar mass.

Four weeks later, he complained of progressively worsening headache and visual disturbance such that he could no longer drive. Interval CT head found that the sellar mass was now 3.6 cm and included a 1.0 cm suprasellar extension that abutted the optic chiasm. Pathology from urgent trans-sphenoidal hypophysectomy revealed renal cell carcinoma.

Discussion: Symptomatic pituitary metastasis from RCC are rare. To our knowledge, only 28 cases have been reported in the literature, and most of those occurred in the setting of diffuse metastatic disease. They typically mimic signs and symptoms of non-functioning macroadenomas. They can be synchronous, metachronous or even the presenting lesion of the primary tumor.

Conclusion: A pituitary mass in the setting of malignancy should raise suspicion for metastatic disease even though it is extremely rare.

Abstract #806

ADRENAL INSUFFICIENCY AS MAIN CLINICAL FEATURE OF PANHYPOPITUITARISM IN A PATIENT WITH A PITUITARY MACROADENOMA

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Objective: With the exception of iatrogenic HPA axis suppression by exogenous glucocorticoids, Adrenal Insufficiency is rare, and most cases are now due to deficiencies of the ACTH secretion from the Pituitary. The diagnosis should be considered in any patient with unexplained weight loss or hypotension

Case Presentation: 72 year old male with history of Hypothyroidism and Hypogonadism presented to our clinic for evaluation of Adrenal Insufficiency. He had a 3 year history of nausea, vomiting and a 100 pounds weight loss followed by a year of stable weight. Now generalized weakness is his most prominent symptom. He also had a long history of erectile dysfunction, he was offered Testosterone replacement in 2014 but he refused. He was started on Levothyroxine 25 mcg in 2010, he did not have significant complaint and labs were consistent with mild subclinical Hypothyroidism at the time, over the years he continued to have persistent low FT4 and normal TSH. During our visit, BP was normal at 116/66m, negative Orthostatics. Physical exam is significant for generalized weakness and dry skin but otherwise normal. Laboratory studies revealed a Na level 141 mEq/L (135-145), K 4.5 mEq/L, FT4 0.56 ng/dL (0.66 -1.7) with an inappropriately normal TSH 2.83 (0.48-4), a significantly low Testosterone level of 8 ng/dL (241 – 827), low AM Cortisol 1.7 ug/dL (4.5-22.7) with an inappropriately low normal ACTH 13 pg/mL ( 6-50). A Pituitary MRI showed a 1.4 x 1.8 x 1.5 cm pituitary with abutment of the optic chiasm without displacement. We started glucocorticoid therapy, increased the Levothyroxine dose and referred him to Neurosurgery

Discussion: The clinical manifestations of hypopituitarism is dependant upon the cause, the type, and degree of hormonal insufficiency. Many of the symptoms of secondary or tertiary adrenal insufficiency are the same as those for primary adrenal insufficiency, and are presumably due to glucocorticoid rather than mineralocorticoid deficiency. These include weakness, fatigue, myalgia, and arthralgia. Gastrointestinal symptoms are less common but can also be present and result in weight loss if very severe, as seen in this patient.

Conclusion: The probability of Adrenal Insufficiency is extremely low in the absence of specific clinical features such as hyperpigmentation, hypotension, hypoglycemia, vitiligo, known Pituitary disease, anorexia and weight loss, in the presence of any of them, one must exclude Adrenal Insufficiency. This patient underwent an extensive work up for unexplained weight loss of 100 pounds over the course of 2 years. One needs to have a high index of suspicious for AI when dealing with a presentation similar to this.
Abstract #807

PITUITARY STALK INTERRUPTION SYNDROME

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UMASS

Objective: Pituitary stalk interruption syndrome (PSIS) is a rare disease with an estimated incidence rate of 0.5/100,000 births. On imaging, it is characterized by a triad of findings: 1-absent or thin pituitary stalk (PS); 2-ectopic posterior pituitary; and 3-anterior pituitary hypoplasia. The most common presentation in children with PSIS is short stature associated with growth hormone deficiency with up to 40–100% of reported cases also having multiple anterior pituitary hormone deficiencies. The function of the posterior pituitary is usually intact.

Case Presentation: A 42 year old female, from Dominican Republic was referred to the endocrine clinic for “premature menopause”. She did not have regular pubertal development, had minimal breast development, and no hair growth in the pubic or axillary area. She recalled only one menstrual period at age 17. She reported decreased appetite with 20 lb weight loss over 2 years, and for few months prior to presentation, dizziness and blurry vision. She denied galactorrhea, headaches, polyuria or polydipsia. There was no similar history in the family including her fraternal twin sister. She denied previous hospitalizations or surgeries.

On exam her height was 4’11”, weight 87 lb. BP 97/63, heart rate 71/ min. She looked younger than her stated age. She had no visible axillary or pubic hair. Breasts were Tanner stage II. External genitalia pre-pubescent Labs: Follicle Stimulating Hormone: 0.5 mIU/ml, Luteinizing Hormone: 1.2 mIU/ml, Estradiol: <20 pg/ml, Insulin Like Growth Factor 1: 17 ng/ml, Thyroid Stim Hormone: 10.12 uIU/ml, Free T4: 0.45 ng/dl, am Cortisol: 2.0 mcg/dl, ACTH: 18 pg/ml, Prolactin: 10.4 ng/ml, Sodium: 137 mmol/l, ACTH Stim test: Cortisol: at 0 min: 1.6 mcg/dl, at 30 min: 5.5 mcg/dl, at 60 min: 8.5 mcg/dl. Bone density: Osteoporosis. Bone age: adult.

MRI: Posterior pituitary ectopia with a partially empty sella, absence of the pituitary stalk and small adenohypophysis.

She was treated with Hydrocortisone followed by Levothyroxine and birth control pills.

Discussion: Pituitary stalk interruption syndrome was first described in 1987 by Fujisawa et al. in 1987. The pathogenesis has not been fully understood yet. The theories are: 1-perinatal injury to the PS; 2-X-linked inheritance due to the male predominance; 3-mutations of certain genes; 4- aberrant embryonic development. Multiple anterior pituitary hormone deficiencies are more common in adults than in children. The absence of a visible pituitary stalk on imaging appears to predict more anterior pituitary deficiencies.

Conclusion: We present a rare case of pituitary stalk interruption with multiple anterior hormone deficiencies.

Abstract #808

A LETHAL CONSEQUENCE OF RADIOTHERAPY: RADIATION-INDUCED SARCOMA IN A PATIENT WITH GIANT PROLACTINOMA

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Objective: Radiation-induced sarcoma (RIS) is a rare (<0.3%) but devastating consequence of radiotherapy. We present a case of a giant prolactinoma resistant to medical therapy that subsequently underwent radiation therapy, unfortunately resulting in RIS.

Case Presentation: A 52-year-old male with a history of aggressive, resistant giant prolactinoma underwent tumor debulking in 2007. He was on cabergoline for 1 year but his prolactin remained >5000 ng/mL and the residual tumor persisted. In 2008, he received 50.4 Gy of intensity-modulated radiation therapy (IMRT). In 2016, he had rapid progression of his proptosis, ptosis and extra-ocular muscle deficits. MRI showed a 4.8 cm enhancing solid mass within the radiation field, extending into the right cavernous sinus, middle fossa and infratemporal masticator space, which had increased 20 times in volume since 2015. Partial resection of the lesion revealed a high-grade sarcoma with features of fibrosarcoma after immunohistochemical and cytogenetic testing excluded other diagnoses. He started adjuvant radiotherapy but died due to increased intracranial pressure within 4 months of diagnosis.

Discussion: RIS diagnosis was made in our case using Cahan’s criteria: 1) the sarcoma was within the irradiated field, 2) it was histologically distinct from the index lesion, and 3) there was a latency period between the time of radiation exposure and diagnosis. Factors that increase the risk of RIS include higher radiation dosage, younger age at the time of exposure, exposure to chemotherapy for the primary tumor, genetic tendencies, and use of IMRT. In sellar RIS, the median radiation dosage is 44.14 Gy and the mean latency period is 10 years, with a range of 5-20 years. Prognosis is significantly worse than stage-matched de novo sarcomas. The mean time between diagnosis and...
death is 6.5 months (range 0.5-15 months) and there is 40% survival at 6 months. Treatment options are limited. When possible, surgical resection with clear margins is curative. For sellar lesions, it is impossible to perform complete resection due to confining anatomy. The goal of surgery is to confirm the diagnosis, relieve mass-related symptoms, and aid in developing targets for adjuvant therapy. Adjuvant radiotherapy is often used to slow further growth. However, no treatment modalities have been able to stop the progression of these neoplasms. Neoadjuvant or post-radiation chemotherapy is controversial. **Conclusion:** Radiotherapy may be used as an adjuvant treatment in aggressive pituitary adenomas, but it is associated with significant morbidity and mortality. RIS is a fatal adverse effect of radiotherapy with no effective treatment. Patients should be informed of this rare, yet lethal risk.

**Abstract #809**

**A CASE OF POSTOPERATIVE PERMANENT DIABETES INSIPIDUS**

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**Objective:** Discussion of atypical presentation of diabetes insipidus as a complication of trans-sphenoidal surgery

**Case Presentation:** 56 year old woman with history of Diabetes Mellitus Type 2 presented for routine visual field exam. She was found to have visual field defects but no other neurologic or endocrine symptoms. A Pituitary MRI revealed a contrast-enhancing mass, occupying the sellar and suprasellar space, 2.6 x 1.8 x 1.6 cm with compression of the Optic Nerve. Endocrine evaluation revealed no hormone abnormalities. Endoscopic endonasal transsphenoidal resection was performed; pathology was consistent with Rathke Cleft Cyst. The patient was followed closely for two weeks post operatively and reported no complications; no significant lab abnormalities were found during this time. 2 months after surgery, she developed polyuria, polydipsia, nocturia and nausea. Evaluation for diabetes insipidus was performed. Labs were drawn at 0, 1, 2 and 3 hours showing persistent hypernatremia, high serum osmolality, low urine osmolality, consistent with Diabetes Insipidus. She was started on desmopressin 0.1mcg intranasal, 1 spray at bedtime with resolution of the symptoms and normalization of sodium levels.

**Discussion:** Postoperative and Posttraumatic DI classically present with a triphasic response to Pituitary Stalk damage. The first phase of DI begins in the first 24 hours and lasts 5-7 days, followed by a second antidiuretic phase of SIADH where urine becomes concentrated and urine output markedly decreases. The duration is variable and can last from 2 -14 days. After AVP stores are depleted from the degenerating posterior pituitary tissue, the third phase of chronic DI often, but not always manifests. **Conclusion:** Following a Pituitary surgery, if present, DI typically follows a triphasic pattern that most of the times is transient. The literature suggests that one can use Na levels during this period to predict the presence of permanent DI, a level of >145mEq/L has a higher predictive value for permanent DI development, and patients with Na levels <145 mEq/L in the first five days will rarely if ever develop permanent DI. Our patient presented in atypical fashion with no initial electrolyte abnormalities and symptoms starting two months post operatively, suggesting the need for serial follow up evaluations post pituitary surgery.

**Abstract #810**

**TRIPHASIC RESPONSE OF DIABETES INSIPIDUS: A CASE OF WATER BALANCE DISORDER FOLLOWING PITUITARY SURGERY**

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**Objective:** To present an interesting case of triphasic pattern of Diabetes Insipidus (DI) following endoscopic removal of a large non-functioning pituitary macroadenoma.

**Case Presentation:** A 31-year-old man with no significant medical history presents to the endocrine clinic after being evaluated by an ophthalmologist for bitemporal visual field loss and headache. MRI demonstrates a 3.2 x 2.5 cm pituitary macroadenoma with mass effect on the optic chiasm. Preoperative hormonal workup was consistent with a non-functioning adenoma. He underwent endoscopic transsphenoidal resection of the pituitary macroadenoma. Post-operatively, he developed secondary hypothyroidism and adrenal insufficiency requiring hormone replacement. Polyuria started on the 2ndpostoperative day (POD), with negative fluid balance and hypernatremia consistent with DI. He was then started on intravenous Desmopressin (DDAVP). On the 6th (POD), the patient developed hyponatremia with a serum sodium of 124 mmol/L with a urine osmolality of 809 mOsm/kg, concerning for SIADH. He remains clinically euolemic. DDAVP was then discontinued and patient was started on fluid restriction. Although gross symptoms of hyponatremia such as alteration in mental status or seizure were absent, the patient had headaches and dizziness. Sodium level further trended down to 123 mmol/L the following day and hypertonic saline infusion was started. After discontinuing hypertonic saline at 125 mmol/L, fluid restriction increased serum sodium further to 135 mmol/L and was subsequently
discontinued. He was discharged with normal sodium level. On one month follow up, the patient again started producing hypotonic polyuria with hypernatremia for which DDAVP 0.05 mg daily was started. The patient continues to do well on this regimen.

**Discussion:** Central DI has been reported to complicate about 30% of the pituitary surgeries. Most of the time, the disease is transient and relatively benign. Only in 1-15% of the cases, chronic post-operative DI develops. The course can be transient, permanent or triphasic. In triphasic response, the first phase of DI lasts 5-7 days followed by a second phase of SIADH. This SIADH phase is due to uncontrolled release of AVP from the posterior pituitary or the remaining magnocellular axons. Once the AVP stores are depleted, the third phase of chronic DI follows although not always. Therefore, signs of recovery from DI after few days should be treated with caution, as it could herald a triphasic response.

**Conclusion:** Detailed reports of Triphasic Response of Diabetes Insipidus are scarce. It is important for clinicians to familiarize themselves of this water balance disorder following neurosurgery, as management can be very challenging.

**Abstract #811**

**A CASE OF PAPILLARY CRANIOPHARYNGIOMA: AN UNCOMMON SUPRASELLAR MASS**

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**Objective:** Craniopharyngiomas are typically benign tumors of the sellar or parasellar region and have a bimodal distribution. Papillary craniopharyngioma accounts for approximately 10% of cases in adults and they are associated with substantial long-term morbidity.

**Case Presentation:** A 55-year-old Asian male presented to Ophthalmology with complaints of progressive vision loss. Visual field testing found a bitemporal hemianopsia. He was sent for an MRI, which showed 1.7 x 2 x 1.6 cm ring-enhancing cystic mass in the suprasellar cistern which was close to the pituitary stalk, but appeared to be separate from the pituitary gland. There were small nodular areas of enhancement that were seen in the periphery of the cystic mass. The patient underwent modified right-sided pterional craniotomy for resection of the mass. Pathology revealed papillary neoplasm covered by well-differentiated monomorphic squamous stratified epithelium without evidence of atypia which is consistent with papillary craniopharyngioma. The specimen was sent for BRAF mutation determined by PCR, which was positive for BRAF V600E mutation. He developed diabetes insipidus within 24 hours after surgery which resulted in a prolonged ICU course. Post-operatively, he developed panhypopituitarism and diabetes insipidus. He is maintained on Prednisone 5 mg daily, levothyroxine 100 mcg daily, desmopressin 0.1 mg twice a day and testosterone gel 1% 3 pumps daily. His symptoms are controlled on his current regimen and his vision has improved. Recurrence is being monitored with serial MRIs.

**Discussion:** Papillary craniopharyngioma is an unusual suprasellar tumor in adults. Papillary craniopharyngiomas are rare compared to adamantinomatous craniopharyngiomas. Adamantinomatous craniopharyngioma occur in children and adults, while papillary craniopharyngioma predominantly occur in adults. Papillary craniopharyngiomas are solid tumors made of sheets of squamous epithelial cells with prominent scattered papillae made of fronds of squamous epithelial cells that overlie fibrovascular cores.

Adamantinomatous craniopharyngiomas have mutations of β-catenin (CTNNB1) gene. Papillary craniopharyngiomas carry a BRAF mutation, which are typically BRAF V600E. Targeted therapy to inhibit BRAF and mitogen-activated protein kinase kinase (MEK) has been used to treat papillary craniopharyngioma with dramatic response and improved treatment course. Drugs such as Dabrafenib or Vermurafenib, alone or in combination with Trametinib, have been shown to decrease the solid and cystic portion of tumor in patients with papillary craniopharyngioma.

**Conclusion:** This approach may help to prevent morbidity from papillary craniopharyngiomas in the future.

**Abstract #812**

**A RARE PRESENTATION OF COEXISTING PAPILLARY THYROID CARCINOMA, PRIMARY HYPERPARATHYROIDISM AND NERVE SHEATH TUMORS**

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**Objective:** Primary Hyperparathyroidism, a common disorder with an incidence of 1 in 80 in the general population. The incidence of papillary thyroid cancer is close to 14.9 per 100,000. Therefore, it is not uncommon to see these two endocrine diagnoses together in one patient. Comparatively, malignant peripheral nerve sheath tumors are extremely rare with incidence of less than 0.001 in the general population. Review of literature suggests that neural sheath tumors can occasionally be found in patients with parathyroid adenoma or papillary thyroid cancer. However, concurrent presence of papillary thyroid carcinoma, parathyroid adenoma and nerve sheath tumors
has not been previously reported in the literature and may represent a novel underlying syndromic genetic mutation.  

**Case Presentation:** A previously healthy 43-year-old male presented initially for an annual health examination. Past medical history and physical exam were only remarkable for hyperlipidemia. Family history was significant for glioblastoma in mother. During routine lab work he was noted to have an elevated serum calcium level of 11.1 mg/dL (ref 8.6 – 10.2 mg/dL) with an intact parathyroid hormone level of 90 pg/mL (ref 15 – 65 pg/mL). While undergoing surgical evaluation for treatment of primary hyperparathyroidism, a thyroid nodule was discovered on ultrasound. Biopsy of the thyroid nodule confirmed a diagnosis of papillary carcinoma with potential involvement of adjacent lymph nodes. Subsequent biopsy of these lymph nodes suggested the presence of neural tissue based tumors. Subsequent biopsy of these lymph nodes suggested the presence of neural tissue based tumors. MRI of the neck showed innumerable nerve sheath tumors concerning for a systemic disorder. PET scan was also significant for possible malignant transformation of neural tissue in several other areas of the body. Laboratory work up for other pituitary, adrenal or thyroid disorders including pheochromocytoma and Cushing’s disease was negative.  

**Conclusion:** This rare presentation of papillary thyroid carcinoma, parathyroid adenoma and nerve sheath tumors may represent a novel underlying genetic syndrome. A few case reports have previously described neural sheath tumors with papillary thyroid carcinoma and others have described neural sheath tumor with parathyroid adenoma but literature review has not revealed the presence of all three occurring concurrently. While this presentation appears to be related to other known multiple endocrine neoplasia syndromes (MEN), it does not precisely follow any of the known MEN presentations raising the possibility of a yet unknown genetic syndrome.

**Abstract #813**

**MIMIC OF AN ENDOCRINE TUMOUR: SPINDLE CELL ONCOCYTOMA OF THE ADENOHYPOPHYSIS**

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**Objective:** Spindle cell oncocytomas (SCO) are defined as an oncocytic non-endocrine neoplasms of the anterior pituitary that manifests in adults. We are presenting a case in which a presumed pituitary adenoma was in reality a SCO.

**Case Presentation:** A 46 year old female with a known non-functional pituitary lesion that was stable for eleven years presents after she developed visual symptoms. Imaging showed a 10.2 x 15.4 x 11.8 mm suprasellar mass with minimal superior deflection of right optic nerve. She has history of primary hypothyroidism, endometriosis and infertility. Preoperative she had normal free T4, TSH, prolactin, somatomedin, 24 hour urinary free cortisol, low estrogen and elevated FSH. She underwent transsphenoidal resection of the mass. Pathology showed a tumor composed of a mildly cellular population of oval or spindled nuclei within loose fascicles and an eosinophilic background. Histologic examination ruled out normal neurohypophysis and low grade tumors such as pilocytic astrocytoma and granular cell tumor. Immunostains supported SCO over the other differential of pituicytoma. SCO are considered WHO grade 1, although they have not been thoroughly characterized. The patient’s post-operative course was complicated by transient secondary adrenal insufficiency and diabetes insipidus.

**Discussion:** SCO was initially described in 2002 and to our knowledge, there have been a total of 26 published case reports in addition to this case. In 2007 SCO was added to the WHO classifications of tumours of the central nervous system. The clinical presentation mimics non-functional pituitary adenomas, and is thus only diagnosed in cases where resection is warranted. SCO tends to have a mixture of intra and suprasellar components; however radiological findings are non-specific and cannot differentiate SCO from pituitary adenomas. SCO arise from adenohypophysis, and is suspected to be derived from folliculostellate cells, which are spindle cells that are postulated to act as supporting elements in regulating activity of endocrine cells. Immunohistochemical markers include S-100 protein, vimentin and epithelial membrane antigen, and is negative for hormones markers. Treatment of SCO is surgical resection. Unlike pituitary adenomas, SCO tend to be highly vascular and thus have a higher risk of bleeding intraoperatively. Patients often have pituitary hormone deficits post-operatively. Some cases have reported early recurrences, although overall prognosis is good, thus corresponding to WHO grade 1.

**Conclusion:** This case illustrates a rare tumor that mimics non-functional pituitary adenomas that endocrinologists and neurosurgeons should include in their differential diagnosis when investigating pituitary lesions.
Abstract #814

INCIDENTAL RETROPERITONEAL MASS - CAN IT BE A PARAGANGLIOMA?

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Objective: Paragangliomas are rare neuroendocrine tumors that arise from extra-adrenal chromaffin tissue. It is not uncommon for these tumors to go undiagnosed for a long time or mismanaged when they manifest with an unusual presentation. We present a case of a 22 year old woman who was incidentally discovered to have an intra-abdominal sympathetic paraganglioma.

Case Presentation: We present a case of a young female patient, 22 years old, who was admitted for severe acute abdominal pain. CT scan revealed ruptured ovarian cyst and incidentally discovered 6 cm right retroperitoneal mass. Her medical history included prediabetes, hypertension and “unexplained” episode of cardiogenic shock while studying abroad. Abdominal MRI showed well encapsulated retroperitoneal lesion adjacent to the superior pole of the right kidney measuring 4.3 x 5.2 x 5.4 cm. FDG PET/CT done for further evaluation showed intensely hypermetabolic right retroperitoneal mass consistent with the patient’s known paraganglioma and no evidence of metastatic disease. In retrospect she has had intermittent symptoms suggestive of catecholamine excess for years. Core needle biopsy done after imaging (unaware of the diagnosis of paraganglioma) revealed chromogranin and S100 positive paraganglioma which was further confirmed on surgical pathology. Fortunately she did well after the biopsy. Hormonal evaluation after biopsy revealed elevated urinary norepinephrine and normetanephrines, with mainly increased normetanephrines (5747 ug/24 h). Plasma norepinephrine and normetanephrins were also elevated (3350 pg/ml and 21.95 nmol/L). Patient underwent open resection of the functional paraganglioma without any complications and did well after the surgery. Considering young age of presentation, she was referred for genetic mutation testing.

Conclusion: Our case demonstrates the need to consider paraganglioma of the retroperitoneum in the differential diagnosis of retroperitoneal masses. Functional paraganglioma presents with symptoms of catecholamine excess that includes hypertension, flushing, diaphoresis, etc. These lesions should never be biopsied given the risk of inducing a catecholamine crisis. Increasing awareness of these rare presentations and correct management is important so that these patients can have positive outcomes. Early diagnoses of functional paraganglioma is important because their removal is often curative and leads to complete resolution of symptoms.

Abstract #815

VISUAL FIELD DETERIORATION WHILE ON MEDICAL TREATMENT IN A PATIENT WITH GIANT PROLACTINOMA

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Objective: To describe visual field (VF) loss in a patient with giant prolactinoma due to rapid decrease of tumor size from dopamine agonist therapy resulting in traction on the optic chiasm.

Case Presentation: A 58 year old male was referred to our Endocrinology department after he had been evaluated for bitemporal hemianopsia by his ophthalmologist. MRI brain showed a 6.2 x 4.4 x 3.4 cm infiltrative sellar mass with supra-sellar extension and cavernous sinus involvement more on the left. Initial workup showed prolactin level of 16,887 (2.0-14 ng/ml), testosterone 76 (220-1000 ng/dl), FSH 2.9 (1-10 mU/ml), LH 1.5 (1-7 mU/ml), TSH 2.16 (0.4-5.5 uU/ml) and free T4 0.8 (0.7-1.8 ng/dl). IGF-1, ACTH, AM cortisol and corticotropin stimulation tests were normal. Patient had low libido but no galactorrhea and had grown children at the time of presentation. Patient was started on cabergoline 0.5 mg twice a week. Testosterone replacement was not started initially due to concern for secondary elevation in prolactin levels and possible increase in tumor size. Within 2 months of being on the above dose of cabergoline, patient’s visual symptoms resolved. VF testing showed significant improvement returning to almost normal, prolactin level dropped to 5,900 and MRI showed shrinkage of tumor to 4.4 x 3.8 x 3.3 cm with improvement of mass effect on chiasm. As his prolactin levels were still very high, cabergoline was increased in a step-wise manner over the next 3 years to a total of 7 mg/week. Prolactin continued to drop progressively to a nadir of 804 but did not normalize. His pituitary MRI, 3 years out showed complete resolution of tumor with small residual pituitary along the margin of an enlarged sella. Patient had insidiously developed blurriness of vision with no clear subjective field deficits by this time, 3 years into treatment. VF testing showed significant worsening of VFs, this time in a patchy pattern unlike his initial bitemporal hemianopsia. His MRI images showed marked tenting of the optic apparatus without any mass effect.

Conclusion: Large prolactinomas could lead to delayed visual deterioration during therapy due to chiasmal intrasellar prolapse caused by a shrinking macroadenoma. It is important to perform follow-up MRIs and VF testing in these patients periodically even when prolactin levels are dropping to look for early signs of traction on the optic chiasm. Early detection of chiasmal herniation can
be reversed with medication dose adjustments preventing permanent sequelae or the need for corrective surgery.

**Abstract #816**

**DIARRHEA IN A HYPERthyroid PATient SECONdARY TO A VIPOMA**

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University of Arizona

**Objective:** VIPomas are rare endocrine tumors capable of causing debilitating large volume secretory diarrhea. Patient’s diarrhea could exceed 3 L/day which can be life threatening. It is important to consider secondary causes of diarrhea, as this issue can be debilitating, embarrassing, and even fatal.

**Case Presentation:** A 56 year-old male presented to the hospital multiple times in a two-month period for uncontrolled large volume watery diarrhea. His medical history was significant for Graves’ disease. Initial suspicion was that his diarrhea was caused by his hyperthyroidism, for which he was started on methimazole and anti-diarrheal medication. Despite optimal pharmacologic therapy, his diarrhea continued to relentlessly persist. This lead to his final admission where he was admitted to the Intensive Care Unit (ICU) for severe dehydration, acute kidney injury (AKI), and marked hypokalemia.

In the ICU the patient was aggressively rehydrated and work-up was initiated for secondary causes of his diarrhea (stool pathogen panel). Stool osmolality studies indicated a secretory diarrhea. Clostridium difficile, ova and parasites, HIV, and hepatitis serology all returned non-significant. Autoimmune work-up was also non-contributory. Due to lack of significant laboratory findings in conjunction with mildly elevated Liver Function Tests (LFTs), a contrast-enhanced computed tomography (CT) of the abdomen/pelvis was ordered that revealed an 8x6cm mass in the pancreatic body. Serum gastrin and vasoactive intestinal peptide (VIP) were measured that found a significantly elevated VIP level of 1065 pg/ml (normal <75pg/ml). Serum gastrin was normal. An Octreotide scan yielded only a localized tumor with significant improvement in his diarrhea. His stools became formed with a decrease in frequency of stooling. The patient continued to improve and was eventually discharged home in stable condition. He was referred to surgical oncology for further work-up and treatment.

**Conclusion:** Chronic diarrhea can have multiple causes. Hyperthyroidism typically causes hyperdefecation rather than watery diarrhea. In this case study, VIPoma was discovered after a patient’s third hospitalization with severe watery diarrhea. Prior admissions solely attributed his symptoms to hyperthyroidism without considering other causes. This case teaches us the heuristics bias providers tend to make in the setting of premature closure and anchoring. Considering alternative diagnoses could have led to an earlier correct diagnosis, thus improving mortality and/or complications.

**Abstract #817**

**CENTRAL SEROUS RETINOpathy: AN UNCOMMON SIGN OF AN UNCOMMON DISEASE**

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**Case Presentation:** Central serous retinopathy (CSR) is characterized by fluid accumulation under the retina and visual distortion. It is thought to be idiopathic but exacerbated by stress or steroids.

History: A 43-years old male presented with excessive hair growth, low libido and erectile dysfunction for 2 years. He had gained weight despite caloric restriction. No increase in ring or shoe size. His past medical history consisted of male infertility, hypertension, hyperlipidemia, and depression. He had a uvulo-palato-pharyngoplasty in the past for sleep apnea. No relevant family history.

Examination: BP was 143/95mmHG, weight 241lb, BMI 31.8 kg/m2. Exam of all other systems were normal. Breast exam showed bilateral lipomastia. He had an abdominal girth of 55 inches. The testes were abnormal at 15ml in volume. Skin showed no bruising, striae or thinning. Laboratory tests showed a mildly elevated insulin like growth factor-1 level 290 (101-267), SHBG 11, testosterone 143 ng/ml. Gonadotropin level, thyroid indices and prolactin were normal. His adrenocorticotropic hormone was elevated at 80 but a 24-hour urine free cortisol level was normal at 29. 1 mg overnight dexamethasone suppression test demonstrated cortisol suppression to 4.8. An oral glucose tolerance showed minimal suppression test of growth hormone. Pituitary MRI showed a 3-4 mm microadenoma. Over 3-4 years his urine free cortisol remained normal and his IGF-1 level remained above normal. He was started on Somatuline treatment for suspected acromegaly. The patient decided to stop somatuline and decided to follow yearly with no therapy. He then developed a blind spot in the right eye which the retinal specialist concluded it was CSR. There was progressive weight gain and depression along with development of type 2 diabetes. The patient went on to develop a 2nd blind spot consistent with CSR. We
considered the possibility of a diagnosis of Cushing’s disease. Repeat ACTH levels continued to be elevated with borderline high cortisol levels. Trial of Mifepristone was instituted, his HbA1C improved from 8.2% to 6.9% on no diabetes therapy. Patient eventually had a resection of his pituitary adenoma. His diabetes resolved, there was dramatic weight loss, his depression resolved and he could have a child.

**Conclusion:** The purpose of this abstract is to highlight an obscure finding of hypercortisolemia that led to the diagnosis of Cushing’s disease. The patient did not have overt signs but the development of CSR prompted a re-examination of the condition which led us to the correct diagnosis. Mifepristone therapy helped reveal the nature of this condition. Dramatic results were achieved after adenoma resection.

**Abstract #818**

**IMPORTANCE OF THE PRE-OPERATIVE ACTH STIMULATION TEST IN EVALUATING NON-FUNCTIONAL PITUITARY MACROADENOMA**

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**Objective:** To assess if an adrenocorticotrophic hormone (ACTH) stimulation test performed during the pre-operative evaluation of non-functional pituitary macroadenoma can aid in the identification of ACTH staining pathology.

**Methods:** A retrospective chart review was conducted on 148 patients with histopathological confirmed pituitary macroadenoma who underwent a pre-operative ACTH stimulation test. From 148 patients, 14 (9.5%) showed diffuse ACTH staining, 75 (50.6%) showed other-staining (diffuse staining for anterior pituitary hormones other than ACTH), and 59 (39.9%) were non-staining (no staining for any anterior pituitary hormones). Patients with rare or focal staining were excluded. Pre-operative ACTH stimulation tests were reviewed and the delta total cortisol (mg/dL) at 30 and 60 minutes from baseline were calculated. Normality was evaluated using a histogram and the Shapiro Wilk test. The basal and maximal delta cortisol (mean+/-SD) were compared between the ACTH staining pituitary macroadenoma and the non-ACTH staining (N=134), other-staining (N=75) and non-staining (N=59) tumors individually using two-sample t-tests and presented as means and standard deviations.

**Results:** The mean basal cortisol level in the ACTH staining group (13.9 ± 4.2) was higher vs. the non-ACTH staining (10.6 ± 4.8, P=0.012), other-staining (10.7 ± 4.9, P=0.018) and the non-staining (10.5 ± 4.6, P=0.012) tumors. The maximal delta cortisol in the ACTH staining group (17.3 ± 8.6) was not statistically significantly different, vs. the non-ACTH staining (16.3 ± 5.8, P=0.67), other-staining (15.6 ± 5.5, P=0.47) or non-staining (17.3 ± 6.1, P=0.97) tumors.

The mean basal and maximal delta cortisol levels in the other-staining group were not statistically different compared to the non-staining group (P=0.77 and P=0.10, respectively).

**Discussion:** While the basal cortisol levels in the ACTH staining group were statistically significantly higher vs. the other-staining and non-staining groups, the large variability in values did not allow clinical utility. No observed differences were found in the maximal delta cortisol level between groups. Our study is limited by the small sample size of ACTH staining macroadenoma, as well as by the larger variability in the delta cortisol response among the ACTH staining group.

**Conclusion:** In our study, basal cortisol levels were higher in patients with ACTH-staining pituitary macroadenoma. A multicenter study, affording a larger number of ACTH-staining tumors, may determine if the ACTH-stimulation test can be useful in pre-operatively identifying ACTH-staining pathology.

**Abstract #819**

**HYPERCORTISOLISM AND HYPOGONADISM INDUCED BY CALORIC RESTRICTION AND A RIGOROUS WORKOUT ROUTINE**

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**Case Presentation:** Background: Excessive exercise and caloric deficiency can result in reversible hypogonadotropic hypogonadism (HGHG), but can also cause reversible ACTH-dependent hypercortisolism (pseudo-Cushing’s syndrome). Clinical Case: A 23-year-old man with no medical history and on no medications reported fatigue, low libido, and abrupt gain of 15 pounds. Labs were consistent with HGHG. Prolactin was normal. AM serum cortisol (26.5 mcg/dL, n 3.7-19.4 mcg/dL) and ACTH (48 pg/mL, n 6-50 pg/mL) were high-normal. Two 24-hour urine collections contained elevated free cortisol (UFC) levels (225.9 mcg/24h and 381.8 mcg/24h, n 4.0-50.0 mcg/24h); all collections contained appropriate amounts of creatinine and volume. A 2-day, low dose (2 mg) dexamethasone test did not suppress the serum cortisol (25.1 mcg/dL) or ACTH (35 pg/mL). There were no other abnormalities in pituitary function.
Physical exam revealed normal vital signs. BMI was 23.6. Besides some facial fullness and mild plethora, no other cushingoid features were present. No pituitary adenoma was seen on MRI. Administration of CRH resulted in elevated and increasing concentrations of ACTH in the right petrosal sinus (peak at 20 minutes, 336 pg/mL). ACTH in the left petrosal sinus and periphery remained less than 30 pg/mL. Some suspicious pituitary tissue was removed trans-sphenoidally, but pathology was normal. The patient had gained 11.4 kg (BMI 27.1) in the month between initial evaluation and surgery. In the 3 days post-operatively, serum cortisol showed physiologic nadir and diurnal variation. The patient was voraciously eating double portions of meals and eating in the hospital cafeteria between meals. No glucocorticoids were required. Three weeks post-operatively, a 2-day, low dose dexamethasone test suppressed the serum cortisol (< 0.8 mcg/dL). Midnight salivary cortisol (0.21 mcg/dL, n < 0.09 mcg/dL) and 24-hour UFC (133.0 mcg/24h) were elevated 2 months post-operatively. He lost 8.7 kg (BMI 24.3) in the 2 months after surgery. He stated that, besides during the peri-operative period, he regularly and strenuously exercised. He typically ate two small meals of only meat and vegetables daily. He was asked to consume 2000-2500 calories daily, withhold strenuous exercise for 1 week prior to lab testing, and keep a log of diet and exercise. Two months later, the patient’s log showed compliance with the above diet and exercise modifications. He had gained 11.2 kg (BMI 27.9). Improvement was seen in midnight salivary cortisol (0.03 mcg/dL) and 24-hour UFC (83.0 mcg/24h).

Conclusion: Chronic caloric deprivation and rigorous exercise must be considered in the differential diagnosis of ACTH-dependent hypercortisolism.

Abstract #820

ENDOCRINE MANIFESTATIONS OF SOLITARY MEDIAN MAXILLARY CENTRAL INCISOR SYNDROME

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Objective: Solitary median maxillary central incisor syndrome (SMMCIS) is a rare congenital disorder that leads to a spectrum of midline developmental defects. It has been associated with multiple endocrine abnormalities. We describe 2 cases of SMMCIS, one with hypopituitarism and the other with delayed puberty.

Case Presentation: 41 year old female was seen for fatigue. She was diagnosed with hypothyroidism and growth hormone (GH) deficiency at 3 years of age and was started on levothyroxine and GH. She had primary amenorrhea and oral estrogen and progesterone were started. She did not have hyperprolactinemia, adrenal insufficiency or diabetes insipidus. Physical examination was significant for a single median incisor and hypopituitarism. She had run out of medications for 1 year and lab investigations confirmed secondary hypothyroidism, hypogonadotrophic hypogonadism and GH deficiency. Brain magnetic resonance imaging showed a small anterior pituitary, ectopic posterior pituitary and dehiscence of sellar floor. She was restarted on levothyroxine, GH and oral contraceptives with improvement in the fatigue and weight loss.

21 year old male was seen for small genitalia. He had small penis and testes since birth. He had delayed puberty and received injectable hormonal therapy with some penile and testicular development. He did not have a syndromic diagnosis. On exam he had normal stature, syndromic facies: low implanted ears, hypopituitarism and a single median incisor. Genital exam revealed micropenis and normal testes. Lab investigations showed normal hypothalamic pituitary axis.

Discussion: SMMCIS syndrome occurs in 1 of 50,000 live births and gives variable phenotypes. It was first described in association with short stature as “Monosuperoinscisivodontic dwarfism” in 1976. SMMCIS is associated with short stature in 50% of cases, 33% have GH deficiency. Other endocrine manifestations include hypopituitarism and delayed or precocious puberty. Deviant sella turcica and pituitary abnormalities were described in 10-50% of cases. It is associated with cranio-facial anomalies such as choanal atresia, cleft lip/palate, holoprosencephaly, cardiac malformations, spine abnormalities and ambiguous genitalia. 25% of cases have a family history of similar midline defects. Sonic Hedgehog (SHH) gene mutations at 7q36 have been associated with SMMCIS. Diagnosis can be made via prenatal ultrasound at 16-22 weeks gestation or after teeth eruption at 8 months age.

Conclusion: Presence of syndromic hallmarks such as SMMCIS can aid in early diagnosis of hormonal deficiencies in childhood. Awareness to the syndrome is needed as some patients present undiagnosed into adulthood.
Abstract #821

RECURRENT PITUITARY APOPLEXY IN COWDEN SYNDROME: A CASE REPORT

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Objective: Pituitary apoplexy is an uncommon complication of pituitary tumors; recurrent apoplexy is rare with few reported cases. It is caused by hemorrhage and/or infarction of a tumor within the pituitary gland and presents with neuro-ophthalmic signs in patients with pre-existing pituitary tumors. In this case report, we present a patient with recurrent pituitary apoplexy with history of Cowden syndrome (CS).

Case Presentation: A 62 year old female was admitted with headache and double vision with examination findings of complete CN III palsy with partial CN II, IV, V1 and V2 palsies. MRI showed pituitary apoplexy with large intrasellar mass involving left cavernous sinus with a small intrasellar hemorrhage. She has history of pituitary macroadenoma with apoplexy 4 years ago which was resected. She also has history of carcinoid of the appendix, multifocal papillary thyroid carcinoma, right renal cell carcinoma, B/L invasive lobular ER/PR positive breast CA, multiple GI polyps and uterine fibroids. Physical examination showed vascular lesions in buccal and mucocutaneous oral surface, skin lipomas, oral papillomas and macrocephaly. Cancer genetics confirmed that she met clinical criteria for Cowden’s syndrome. She was stabilized hemodynamically and was treated with intravenous steroids. She underwent endoscopic pituitary resection, had good recovery and had outpatient follow up. Pathology confirmed pituitary macroadenoma with apoplexy and elevated Ki-67 proliferation.

Discussion: Pituitary apoplexy is an endocrine emergency necessitating urgent stabilization and steroid replacement with consideration of surgical management vs conservative treatment. It manifests as a sudden, severe headache and neurologic and hormonal dysfunction. Urgent biochemical and endocrine assessment is vital. As our patient also had Cowden syndrome, we researched on association with pituitary adenoma. CS is an autosomal dominant multiple hamartoma syndrome in a spectrum of PTEN hamartoma syndromes. There is high risk for benign and malignant tumors of the thyroid (usually follicular), breast, genitourinary, gastrointestinal and brain, vascular malformations and cutaneous melanoma. Affected individuals usually have macrocephaly, facial trichilemmomas and oral papule. Pituitary adenoma is suspected as not a true manifestation of CS.

Conclusion: We report a case of recurrent pituitary apoplexy in a patient with Cowden syndrome. High index of suspicion, hemodynamic stabilization and steroid replacement are pivotal in management. There is no confirmed relationship of CS with pituitary adenoma or apoplexy.

Abstract #822

DIAGNOSIS OF GROWTH HORMONE DEFICIENCY IN CHILDHOOD CANCER SURVIVORS: A SYSTEMATIC REVIEW

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Objective: Clinical manifestations of growth hormone deficiency (GHD) can be very subtle, particularly in adults or children who attained adequate height. Overall accuracy of hormonal testing is highly variable. Low serum levels of IGF-1 or IGFBP3 in adults seem to be suggestive of the diagnosis; and, in children with structural abnormalities or known hypopituitarism or underlying genetic causes, can be used to diagnose GHD. There remains, however, very limited literature on the diagnostic tests of GHD in individuals who underwent hypothalamic/pituitary radiation for treatment of childhood malignancies. Recently, the Pediatric Endocrine Society published guidelines on diagnosis and treatment of GHD in children and adolescents; it is unknown, however, whether the same recommendations apply to childhood cancer survivors (CCS).

Methods: We performed a systematic review evaluating GHD through IGF-1 and/or IGFBP3 measurements compared to GH dynamic testing, and diagnosing GHD by various GH dynamic tests. A comprehensive search of several databases was conducted from each database’s inception to 2016. In addition, the references of the studies obtained from the original search were screened by the reviewers for additional inclusions.

Results: A total of 211 citations were retrieved, from which 14 studies were included. IGF-1 was evaluated in 8 studies and IGFBP3 in 7. The comparator tests, however, varied widely among the studies. Overall, both IGF-1 and IGFBP3 had suboptimal diagnostic accuracy but strongly correlated. The use of both tests simultaneously in the same cohort did not add to the diagnostic accuracy of either test alone.

Despite high variability in testing protocols, dynamic tests remained the most accurate in appropriately identifying patients with GHD. Insulin tolerance test (ITT) seems to be the most accepted reference test, alone or in combination with arginine; although standardization of the testing strategy among practice groups is absent. Growth hormone releasing hormone (GHRH) and/or arginine stimulation
performed almost similarly to ITT, although in one study GHRH with arginine stimulation had 66% sensitivity and 88% specificity in comparison to ITT. There were insufficient data available to assess the accuracy of serial GH testing, whether nocturnal or over a 24-hour period.

**Conclusion:** Based on the review of the available data, the diagnostic accuracy of different dynamic tests for GHD in CCS seems to follow the same pattern as in the adult population. Although IGF-1 and IGFBP3 may be useful screening tools, they performed poorly when used to diagnose GHD.

**Abstract #823**

**DELAYED ONSET OF CENTRAL ADRENAL INSUFFICIENCY WITH ANTI PD-1 ANTIBODY THERAPY**

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**Objective:** Immune checkpoint receptors such as programmed cell death 1 (PD-1) are expressed in T cells and mediate suppression of T cell activation. Many human tumors express PD-1 ligands and avoid immune destruction by binding PD-1 receptors. Checkpoint inhibitors, approved for the treatment of a number of malignancies, including melanoma, are associated with life threatening hypopituitarism in less than 1% of patients. Here, we report a rare case of severe central adrenal insufficiency occurring five months after discontinuation of pembrolizumab, a PD-1 inhibitor used for the treatment of malignant melanoma.

**Case Presentation:** A 65 year old man presented to the hospital complaining of one week of generalized weakness, severe fatigue, poor oral intake and decreased urination. His medical history included right cheek melanoma diagnosed six years prior to presentation, treated with surgical resection and neck lymph node dissection. Due to disease recurrence in the cervical lymph nodes, he was treated with ipilimumab for 4 doses two years prior to presentation, but treatment was stopped due to development of Guillain Barre Syndrome. When his disease recurred in the neck, he was treated with fifteen months of pembrolizumab at 2 mg/kg every 3 weeks without significant toxicity. His medical history included right cheek melanoma diagnosed six years prior to presentation, treated with surgical resection and neck lymph node dissection. Due to disease recurrence in the cervical lymph nodes, he was treated with ipilimumab for 4 doses two years prior to presentation, but treatment was stopped due to development of Guillain Barre Syndrome. When his disease recurred in the neck, he was treated with fifteen months of pembrolizumab at 2 mg/kg every 3 weeks without significant toxicity. Patient achieved complete remission and finished treatment five months prior to hospital admission. On hospital presentation blood pressure was 84/51, and pulse 82/minute. Patient was somnolent but oriented to time, person and place. Admission laboratory data was remarkable for creatinine 5.01 mg/dl, sodium 135 mmol/l, potassium 3.8 mmol/l, baseline cortisol 0.2 ucg/dl and ACTH <0.5pg/ml. Patient received hydrocortisone 50mg IV q 8 hours with rapid improvement of symptoms. Hormonal workup revealed low gonadotropins but unremarkable thyroid and prolactin levels. MRI of the pituitary did not show evidence of hypophysitis or adenoma. After resolution of symptoms and improvement of kidney function, patient was discharged home with hydrocortisone replacement.

**Conclusion:** With a half life of 26 days, pembrolizumab should be eliminated in 130 days. A median time to development of severe endocrinopathy is 2-3 months while patients receive the treatment. To the best of our knowledge there are no case reports of new development of hypopituitarism months after discontinuation of the treatment. In our case, the patient presented with severe central adrenal insufficiency five months after discontinuation of therapy, with no other clear explanation for the acute central adrenal insufficiency, suggesting that immune-related endocrinopathy induced by PD-1 inhibitors can develop months after discontinuation of therapy.

**Abstract #824**

**NEW ONSET CARCINOID SYNDROME AFTER INITIATION OF A SELECTIVE SEROTONIN REUPTAKE INHIBITOR IN A PATIENT WITH PELLAGRA**

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Mount Sinai Beth Israel

**Case Presentation:** An 85 year-old female with a history of depression and metastatic neuroendocrine carcinoma presented with failure to thrive. She was initially able to live independently, but family noted a progressive functional decline, anorexia, and depressed mood. She was started on sertraline 3 months prior to arrival. The malignancy was found 3 years ago when a CT scan showed liver and pancreatic masses. Biopsy revealed atypical cells with a salt-and-pepper chromatin pattern arranged in clusters and a low mitotic index. As she was asymptomatic, her disease was managed conservatively. Upon admission, her anti-depressant dose was increased. While hospitalized, she developed profuse diarrhea, delirium and asymptomatic hypoglycemia. Physical exam revealed a cachectic woman with a diffuse erythematous scaly rash and glossitis. Facial flushing and Raynaud’s phenomenon were evident. Initial hypoglycemia workup showed plasma glucose consistently above 80 mg/dL without evidence of endogenous hyperinsulinism, which was suggestive of artifactual hypoglycemia from acrocyanosis. Elevations in Chromogranin A (531 ng/dL), 24-hour urine 5-hydroxyindoleacetic acid (16 mg/day)
and a low tryptophan at 9 umol/L were noted. Sertraline was stopped, while Octreotide and Niacin were started. The patient was discharged home after resolution of her diarrhea and dramatic improvement of her mental status.

Discussion: Carcinoid syndrome is caused by hormonally active tumors from the digestive tract. Symptoms are derived from the vasoactive and pro-secretory actions of humoral peptides, which may include serotonin, histamine, among others. Manifestations include intractable diarrhea, flushing and tachycardia. These tumors arise from enterochromaffin cells from the mid and hindgut. The funneling of tryptophan towards serotonin production can be so extreme that it may lead to niacin deficiency. This hypovitaminosis causes widespread defects in protein synthesis, infrequently giving rise to Pellagra. Common features include psychosomatic pathology ranging from confusion to dementia, a scaly dermatitis and the previously described hormonally mediated symptoms. The unmasking and exacerbation of symptoms of carcinoid syndrome after initiation of selective serotonin reuptake inhibitors (SSRIs) has been infrequently reported. The mechanism behind this effect is unknown, but presumed to be from neuronal accumulation of serotonin in the synapse.

Conclusion: We present a case of new onset carcinoid syndrome after starting an SSRI, in a patient with a neuroendocrine tumor previously thought to be nonfunctional. Alternative antidepressants such as tricyclic agents may be preferred, particularly in patients with signs of pellagra.

Abstract #825

EFFECTS OF GROWTH HORMONE THERAPY IN CHILDHOOD CANCER SURVIVORS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Growth hormone deficiency (GHD) is common among childhood cancer survivors (CCS) with tumors/surgery in the hypothalamus-pituitary (HP) region and CCS exposed to radiation. Studies have shown that the final height of the CCS is affected and the response to GH therapy (GHT) is variable. GHD has been thought to impact CV risk factors and the quality of life. Among the various abnormalities observed in CCS, the contribution of GHD is debatable and whether GH replacement reverses these anomalies. GHT has been used in CCS to treat short stature but there have been concerns that GH replacement may increase the risk of tumor recurrence, secondary tumors and other adverse effects.

Our objective was to evaluate the effect of GHT in CCS with tumors/surgery in HP region, CCS exposed to HP radiation and CCS exposed to total body, spinal, abdominal/pelvic or chest radiation at a young age on final height, risk of diabetes mellitus, abnormal lipids, metabolic syndrome, quality of life, secondary tumors and disease recurrence as compared to CCS not treated with GHT.

Methods: We searched for cohort studies, case series, randomized clinical trials evaluating chosen outcomes in CCS receiving GH. Reviewers independently and in duplicate screened for eligible studies and collected data. Meta-analysis using random effects model was conducted in those studies which had CCS without GHT as controls. Results: We included 7 observational studies at moderate to high risk of bias in meta-analysis (512 patients, average GH dose 0.3 to 0.9 IU/kg/week). CCS who were treated with GHT had a significant gain in height as compared to CCS not treated with GHT (SDS 0.57; 95% CI 0.06 to 1.07). There was no statistically significant different in the occurrence of secondary tumors with GHT (RR 1.27; 95% CI 0.87 to 1.87).

Additional studies (n=13) of CCS on GHT that were not included meta-analysis because they did not have enough data to be used for meta-analysis for controls or used controls other than CCS without GHT showed either an improvement or no difference in the risk of diabetes, lipid profile, metabolic syndrome and improvement in quality of life in CCS as compared to controls. GHT did not appear to increase the risk of tumor recurrence in the studies.

Conclusion: CCS who are treated with GHT gain height as compared to untreated controls. GHT does not appear to have negative impact on risk of diabetes, lipids, quality of life and the risk of secondary tumors and recurrence. Studies were observational and had moderate to high risk of bias.
Abstract #826
OUTCOMES AFTER RADIATION TREATMENT FOR PATIENTS WITH PERSISTENT OR RECURRENT ACROMEGALY AFTER SURGERY

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Objective: Acromegaly is associated with increased morbidity and mortality when inadequately controlled. Although several treatment options are available for patients who have ongoing acromegaly despite surgery, radiation treatment (RT) is often considered third line therapy due to the risk of hypopituitarism and concerns regarding cerebrovascular complications.

Aim: To assess the outcomes and complications associated with RT in patients with persistent or recurrent acromegaly after pituitary surgery at a single institution.

Methods: A retrospective analysis of all patients with a new diagnosis of acromegaly treated from 1995-2015 who failed to achieve remission, defined as a normal age adjusted IGF-I level 3-6 months after surgery at our institution or who recurred after surgery and underwent RT.

Results: One hundred thirty-nine (139/248, 56%) patients [female, n=62/139 (45%)] had persistent or recurrent acromegaly following initial surgery. Among those with persistent or recurrent disease, RT was performed in 90/139 (65%) patients (Gamma knife radiosurgery, n=78, 86%; fractionated stereotactic radiotherapy, n=10, 11%; and proton beam, n=2, 2%). Patients having RT had larger tumors (2 ± 0.9 cm vs 1.4 ± 0.6 cm, P<0.001) and more often had cavernous sinus invasion (60 vs 22%, P=0.0001) compared to patients not having RT. The odds of remission was 2.1 (CI: 1.1-4.3; P=0.036) fold greater in those who had RT compared to those who did not, however the proportion of patients still requiring adjuvant medical therapy at last follow up did not differ (38/66 vs 18/28, P=0.5). Among those who had ≥6 months follow up after RT, median time to remission was 26 months (6-223). The risk of death (6 vs 2, P=0.5) or stroke (1 vs 0, P=0.45) was not increased among those who received RT. Among those with no or partial anterior pituitary dysfunction prior to RT, 28/86 (33%) developed a new anterior pituitary hormonal deficit after radiotherapy. The median time to new hormonal deficits was 24.5 months (4-161).

Conclusion: Although new hormonal deficits following RT can occur, the risk of stroke or death was not found to be increased in the extent of follow up available for the current analysis. Therefore given that more patients who received RT achieved normal IGF-1 levels, RT remains an effective and safe form of treatment for select patients with persistent or recurrent acromegaly.

Abstract #827
PANHYPOPITUITARISM DUE TO IMMUNE CHECKPOINT INHIBITORS

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Objective: To describe a case of panhypopituitarism secondary to immune checkpoint inhibitors.

Methods: Panhypopituitarism due to immune checkpoint inhibitors has been reported in multiple studies although the exact prevalence and mechanism is unknown. We report a case of panhypopituitarism in a patient who received nivolumab and ipilimumab treatment for malignant melanoma.

Case Presentation: A 77-year-old male noted a lump in his right axilla and was treated with antibiotics, without resolution. The patient underwent resection of the lump and was diagnosed with metastatic malignant melanoma. The patient was started on immune checkpoint inhibitors nivolumab and ipilimumab by oncology. The patient received the chemo treatment every three weeks and completed four doses of ipilimumab and five doses of nivolumab. During his course of chemotherapy, he experienced severe fatigue and generalized weakness. He denied excessive urination. Labs were obtained and showed low serum cortisol at 1mcg/dl, low TSH at 0.13 mIU/ml, and low free T4 at 0.46 ng/dl consistent with panhypopituitarism. The patient was started on prednisone 40 mg twice a day with a tapering dose schedule and thyroxine 50 microgram daily. Chemotherapy was stopped. A brain MRI showed an unremarkable pituitary gland. Labs for other hormones showed low ACTH at <5 pg/ml, low total testosterone at 133 ng/dl, low free testosterone at 23.4 pg/mL, low LH at 8.8 MIU/mL, inappropriately normal FSH at 14.2 mIU/mL, normal prolactin at 4 NG/ml, and low normal IGF1 at 68 ng/ml. Prednisone was subsequently changed to hydrocortisone 15 mg in the morning and 10 mg late afternoon. He is doing well on hydrocortisone and thyroxine with resolution of fatigue and weakness.

Discussion: Immune checkpoint inhibitors are monoclonal antibodies that inhibit the cytotoxic T-lymphocyte antigen-4 receptor. These agents are used for treatment of several cancers such as lung, prostate, and metastatic melanoma. Immune related adverse events, such as hypophysitis and hypopituitarism have been reported by use of these
Abstract #828

RECURRENT MASTITIS: A VERY RARE PRESENTATION OF ANTIPSYCHOTIC-INDUCED HYPERPROLACTINEMIA

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Case Presentation: Hyperprolactinemia can be secondary to physiological or pathological causes, or can be drug-induced. When caused by drugs, antipsychotics are the most common culprit. Mastitis has been reported as a rare manifestation of hyperprolactinemia, whether as idiopathic granulomatous mastitis or mammary ductal ectasia. We describe a case of a 30-year-old Hispanic woman who presented with a recurring right breast mastitis with fever and leukocytosis, one year after incision and drainage of a left mastitis. The patient had a history of schizophrenia being treated with Lurasidone and Haloperidol, and a history of chronic galactorrhea since the initiation of her anti-psychotic therapy thirteen years prior to presentation. She had no history of irregular menstruations or infertility and her last pregnancy was five years prior. She was found to have hyperprolactinemia (prolactin 139ng/mL), and an enlarged pituitary gland on MRI. Ultrasound imaging of her right breast showed a diffuse purulent process that was incised and drained and treated with antibiotics. Haloperidol was subsequently discontinued and Lurasidone switched to Aripiprazole with normalization of Prolactin level.

Discussion: Upon our review, very few cases of antipsychotic-induced hyperprolactinemia causing mastitis have been reported in the literature, mostly involving Risperidone. The case we describe is probably the first reported case of mastitis associated with the therapy of Haloperidol and/or Lurasidone. It is characterized by the recurring nature of the mastitis, the accompanying acute systemic symptoms requiring hospitalization and the coexistent enlarged pituitary.

Conclusion: Increasing awareness of mastitis as a manifestation of hyperprolactinemia among endocrinologists, breast surgeons, and psychiatrists would help provide conservative management and guide long-term preventive therapy of these patients.

Abstract #829

RHABDOMYOLISIS ASSOCIATED WITH NEPHROGENIC DIABETES INSIPIDUS

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Objective: Diabetes insipidus (DI) presents with hypernatremia and hyperosmolality in individuals with an impaired thirst mechanism or no free access to water. Hyperosmolality is associated with rhabdomyolysis which cause serum creatinine kinase (CPK) elevation and myoglobinuria. Fluid resuscitation is the mainstay of the treatment to prevent life-threatening complications including acute hyperkalemia and acute kidney injury. We present herein a first human case of nephrogenic DI who presented with rhabdomyolysis.

Case Presentation: A 74 year old man with multiple comorbidities along with an unknown type of DI was transferred to our hospital for fever and cough. Upon arrival, he was in a respiratory distress and lethargic. His vitals reported as a blood pressure of 127/49 mmHg and a heart rate of 101 beats per minute. Temperature was 104 F rectally. Respiratory rate was 29 per minute; oxygen (O2) saturation was 88 % which improved to 92 % with supplemental O2. Fluid resuscitation with normal saline and empiric antibiotics started for the treatment of severe sepsis. Patient required continuous BiPAP and was kept nothing by mouth. Urine output was noted be 10 L over first 24 h. Blood work-up revealed a blood sugar of 200 mg/dL, HbA1c of 6.1 % and creatinine of 1.1 mg/dL. Serum electrolytes indicated sodium of 129 mEq/L, potassium of 4.5 mEq/L and bicarbonate of 30 mEq/L. Urine studies showed specific gravity of 1.002 , sodium of 61 Mmol/L and potassium of 9 Mmol/L. Urine dipstick was positive for occult hematuria but RBCs were absent in urine samples. Urine drug screen was negative. In a repeat metabolic panel, serum sodium increased to 152 mEq/L along with serum osmolality of 363 uosm/kg and urine osmolality of 128 uosm/kg. Despite switching to hypotonic maintenance fluid, serum sodium rose up to 170 mEq/L and persisted around the range of 160-170 mEq/L. Serum CPK was 1927 U/L which trended up to 2240 U/L despite normal kidney function. There was no history of trauma or fall or the use of statin or other drugs which induce rhabdomyolysis. He was diagnosed with nephrogenic DI,
given sub-optimal response to desmopressin administration, started on thiazide. Later he was weaned from BiPAP and allowed to eat and drink. Serum osmolality was back to 291 uosm/kg and CPK to 90 U/L.

Discussion: Hypernatremia and hyperosmolality are significant predisposing factors for rhabdomyolysis. Nephrogenic DI should be considered in differentials of non-traumatic rhabdomyolysis along with other hyperosmolar states including severe dehydration, diabetic nonketotic hyperosmolar coma and central DI.

Conclusion: Serum CPK levels should be monitored closely to prevent complications.

Abstract #830

CLINICAL AND HORMONAL OUTCOMES OF RADIOTHERAPY IN ACROMEGALY

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Objective: The purpose of research - to study the clinical and hormonal outcomes of radiotherapy in acromegaly.

Methods: The object of the study were 50 patients with somatotropinomas who received radiotherapy traditional gammatherapy of the hypothalamic-pituitary region converged multiple method at a dose of 45 Gr to 25 fraction of a day. Duration of illness was an average of 15 years. The periods of observation after radiotherapy was an average of 10 years. Of them 36(72%) female and 14(28%) men. The age of patients ranged from 36 to 71 years. Levels of growth hormone, IGF-1, PRL, TSH, LH, FSH, fr.T4, cortisol, estradiol, testosterone; visual field and acuity tests, fundoscopy were assesed.

To assess the consequences of radiotherapy we checked all parameters before and after radiotherapy (year or more).

Results: Before radiotherapy were the following impairments: increased growth hormone (M=107) at 100%, IGF-1 (M=1138) at 100%, PRL at 16%; decreased gonadotropins in 24%, fr.T4 in 22%, cortisol in 4%; bitemporal hemianopsia was detected in 18%.

After radiation therapy showed the following results: normalized growth hormone (M=33) in 76% and IGF-1 (M=434) in 62%, hyperprolactinemy in 38%; decreased gonadotropins 42%, fr.T4 in 62%, cortisol in 28%; 90% noted a decrease in the intensity of headaches, 78% reduction of weakness, bitemporal hemianopsia decreased to 8% in different stages after radiotherapy. In 2% of patients developed post-radiation diabetes insipidus, in 26% of PTSS, in 36% of encephalopathy.

Conclusion: Thus, radiation therapy is an important additional treatment of acromegaly which allows achievements of long remission.

Abstract #831

SPONTANEOUS REMISSION OF ACTH-DEPENDENT CUSHING’S SYNDROME: A CASE REPORT.

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Objective: ACTH-dependent hypercortisolism is the most common sub-type of endogenous Cushing’s syndrome (CS). In the absence of specific treatment, features of CS usually persists, except in rare cases. We present a case of spontaneous resolution of CS in a 20 year old lady.

Case Presentation: A 20 year old lady was referred to our facility with a 3 month history of easy bruisability, weight gain, fatigue, secondary amenorrhoea and recent episodes of irrational behaviour. She also had polyuria and polydipsia and was diagnosed with diabetes mellitus and hypertension during the course of the illness. She did not have headaches or visual symptoms and had not used steroids. She had moon-like facies, acne, pedal oedema, acanthosis nigricans and proximal myopathy on examination. Admitting RBG was 350mg/dl, 24 hour urinary cortisol was elevated at 1252 (152-789) nmol/24 hr, serum ACTH was also elevated 18.4 (1.6-13.9) pmol/L, thyroid function tests and prolactin assay were normal. Patient could not afford to do brain MRI, however abdominal ultrasound scan and chest radiographs were normal.

A diagnosis of ACTH-dependent CS likely secondary to pituitary adenoma was made. She was continued on insulin therapy for diabetes, and several antihypertensives for blood pressure control, but she did not receive any specific treatment for hypercortisolism. While sourcing funds for neuroimaging, she made remarkable clinical improvement over two months necessitating gradual reduction of insulin and antihypertensives. One year later, patient's blood pressure and blood glucose remained normal requiring no medications. The patient is still being followed up.

Discussion: Spontaneous resolution of CS is thought to be due to pituitary apoplexy, causing infarction of the corticotroph adenoma and variable destruction of other parts of the pituitary gland.

The resolution of the features of CS in our patients was not preceded by symptoms suggestive of apoplexy, as is the case in most reports described in the literature. Cyclical CS may also be a consideration as cycle lengths may rarely be longer than a year.

Conclusion: Spontaneous resolution of Cushing’s syndrome as occurred in our patient is possible, though
not common. In view of possibility of recurrence, long term follow-up is advocated for such patients.

Abstract #832

METASTATIC MEDULLARY THYROID CARCINOMA PRESENTING AS ECTOPIC CUSHING SYNDROME

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Objective: Medullary thyroid carcinoma (MTC) is a rare disease accounting for 3-4% of thyroid cancers. MTC is an uncommon source of hormones like ACTH or CRH. Ectopic ACTH syndrome is seen in 0.6% of cases of MTC. Here we present a case of elderly male presenting with features of cortisol excess leading to the diagnosis of MTC.

Case Presentation: A 62 year old man presented to the neurologist with paralysis and hypertension of recent onset, gradual onset swelling of face and weight loss. On further evaluation, he was found to have cushingoid features with hypokalemic alkalosis. Basal and dynamic biochemical testing was suggestive of ACTH dependent Cushing syndrome. MRI brain showed no evidence of pituitary adenoma. Gallium(Ga)-68 DOTANOC(1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraaceticacid-1-Na3-octreotide)/ fluorodeoxyglucose (FDG)-positron emission tomography (PET)/computed tomography (CT) revealed multiple cervical nodes with diffuse uptake in thyroid and bilateral adrenal hyperplasia. Ultrasound of the neck showed oval hypoechoic thyroid nodule with small foci of calcification and multiple enlarged lymph nodes in the cervical region. Deep cervical node biopsy was diagnostic of medullary carcinoma thyroid, staining positive for cercino-embryonic antigen(CEA), calcitonin, cytokeratin(CK)-7, synaptophysin, chromogranin, thyroid transcription factor(TTF-1) and negative for CK 20, inhibin and ACTH. Serum calcitonin level was 975 pg/mL. Patient underwent thyroidectomy with lymph node dissection. Histopathology revealed widely invasive MTC. Thyroidectomy and lymph node dissection confirmed the diagnosis. After thyroidectomy, patient’s general condition gradually worsened and he succumbed after 45 days of hospitalisation.

Discussion: MTC is a rare neuroendocrine tumor, accounting for 3-4% of thyroid cancer cases. Ectopic production from medullary thyroid cancer is rare, over 50 cases have been reported overall. Our patient’s vague symptoms may have lead to a late diagnosis. Biochemical evaluation lead us to search for an ectopic source of ACTH. It was Ga68 DOTANOC/FDG PET-CT scan followed by histopathology which clinched the diagnosis. Metastatic MTC has poor prognosis, and in our patient the hypercortisolemic state added to the morbidity. Patient was given chemotherapy in the form of sorafenib. Chemotherapy could not be continued in view of worsening general condition of the patient.

Conclusion: Ectopic ACTH syndrome from medullary carcinoma is a rare but well identified entity. Treatment has been varied with different chemotherapeutic and adrenolytic agents. Prognosis even after treatment has been dismal, when associated with advanced disease.

Abstract #833

ATYPICAL CARCINOID IN MEN1 SYNDROME: A CASE REPORT

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Objective: Multiple endocrine neoplasia type 1 (MEN1) is a well-known, yet rare, autosomal dominant syndrome characterized by tumors of the parathyroid, anterior pituitary, and pancreas. Carcinoid tumors are found with increased frequency, with thymic carcinoids present in 1-5% of MEN1 patients. Thymic carcinoid in MEN1 affects men more than women, with reported M:F ratios ranging from 20:1 to 2:1. Some have also found an association between MEN1-associated thymic carcinoid and smoking. Here, we report a thymic carcinoid in a nonsmoking woman with MEN1.

Case Presentation: A 39 year old woman with a history of subcutaneous lipomas presented with abdominal pain and increased abdominal girth. Family history was not significant. She did not smoke. Imaging revealed enlarged ovaries and uterine fibroids. She underwent TAH/BSO. Pathology demonstrated bilateral granulosa cell tumors of the ovaries, Stage Ib. Imaging also showed a 4 cm anterior mediastinal mass and a 2.4 cm pancreatic head mass. On resection, the anterior mediastinal mass was consistent with thymic carcinoid and thymoma. Hypercalcemia led to a 3.5 parathyroid gland excision. During parathyroidectomy, papillary thyroid carcinoma was discovered incidentally in a paratracheal lymph node and a total thyroidectomy with central neck dissection was performed. Neuroendocrine tumor similar to the thymic carcinoid was found in one central compartment lymph
node. The pancreatic head mass proved to be a low grade neuroendocrine tumor. Genetic testing documented a rare mutation in the MEN1 gene (c.654 + 1 G>A). A pituitary microadenoma was identified on subsequent surveillance imaging. The thymic carcinoid has not recurrent.

**Conclusion:** MEN1-associated thymic carcinoid is rare and potentially aggressive with a 10-year overall survival rate of 25-36%. Most have been described in men with a history of cigarette smoking, but a study by Christakis et al reported higher than expected rates among women and nonsmokers. We report a case of MEN1-associated thymic carcinoid in a woman who has never smoked. Thymic carcinoid tumors can occur in any patient with MEN1 and their poor prognosis may warrant active surveillance.

**Abstract #834**

**CENTRAL DIABETES INSIPIDUS THROUGH GENERATIONS**

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**Objective:** To report a case of newly diagnosed central diabetes insipidus in a patient with extensive family history of polyuria and polydipsia through four generations.

**Case Presentation:** A 25-year-old woman presented for a routine physical exam with life long symptoms of polyuria and polydipsia. She reported that the oldest relative known to have the same “water” problem was her great grandfather who lived in Colombia. His daughter (patient’s grandmother) and granddaughter (patient’s mother) have also been affected. There was one fatality in the family, attributed to the same “water” disorder. None of the family members were ever tested or diagnosed with diabetes insipidus. The patient reported polyuria with nocturia and polydipsia (2 ½ gallons of water intake daily). The diagnosis of central diabetes insipidus (CDI) was later confirmed by water deprivation-desmopressin test. During water deprivation for 3 hours, patient’s urine osmolality increased slightly from 48 to 84 mOsmol/kg. After administering 20 mcg of Desmopressin, urine osmolality increased to 271 mOsmol/kg, confirming the diagnosis of CDI. Patient was started on Desmopressin 10 mcg nightly and later reported resolution of nocturia and polydipsia. Patient’s mother was subsequently tested for CDI, and had a positive water deprivation-desmopressin test, confirming the diagnosis. Given extensive family history, testing for Arginine Vasopressin (AVP) gene defect was indicated but could not be performed due to limitations of patient’s insurance coverage.

**Discussion:** CDI is the disorder presenting with polydipsia and polyuria caused by the deficiency of AVP hormone. While majority of the cases are due to underlying neoplastic, inflammatory, vascular or autoimmune processes, there are rare incidents resulting from a variety of mutations in AVP gene. These mutations result in either impaired folding of prehormone or synthesis of inactive hormone. The inheritance is either autosomal dominant or autosomal recessive and comprises about 10% of all CDI cases. Traditional method of diagnosing CDI with water deprivation test is cumbersome, potentially dangerous, and frequently requires hospital admission. Testing for AVP gene defect is a safer and more reliable option. Regrettably, at present, it can only be done in 2 genetic laboratories in the USA.

**Conclusion:** Accessibility to genetic testing for suspected CDI patient with extensive family history can hasten the diagnosis, facilitate screening of affected and unaffected family members, and potentially provide targeted therapeutic options.

**Abstract #835**

**PANCREATITIS AND DEBILITATING VERTEBRAL FRACTURES - INPATIENT WORKUP OF A UNIFYING DIAGNOSIS**

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**Case Presentation:** A 41-year-old female school teacher with prediabetes, presents with severe, necrotizing pancreatitis complicated by multiple pseudocysts. On abdominal imaging, compression fractures involving T8, T9 and L1 were discovered incidentally. After extensive workup by Gastroenterology, the etiology of her pancreatitis was determined to be idiopathic. The patient spent the majority of the next seven months hospitalized for intractable back pain attributed to her pancreatitis and was placed on Palliative Care. Subsequent imaging revealed new compression fractures in T7 through L1, L4 and L5. Endocrinology was consulted for pain control and management of osteoporosis in the setting of extensive, vertebral fractures resulting in immobilization.

On physical exam, hirsutism, alopecia, facial plethora, dorsocervical fat pad, abdominal striae, central adiposity and ecchymosis were present. Given these clinical findings, in presence of acute vertebral fractures, insulin dependent diabetes and cessation of menses, our clinical suspicion for Cushing’s syndrome was high. Biochemical diagnosis of hypercortisolism was pursued understanding
that all diagnostics had to be qualified in the context of acute illness. Workup was consistent with significant ACTH-dependent hypercortisolism. Pituitary MRI localized a 1.3 cm adenoma inferior to the pituitary gland. Inferior petrosal sinus sampling corroborated Cushing’s disease and she underwent transsphenoidal resection of the pituitary mass. Her pancreatitis resolved over the next several months. After vertebral kyphoplasty her pain improved significantly; she is now ambulatory and has returned to work. 

Conclusion: Cushing’s disease is characteristically encountered as an indolent disease diagnosed in the presence of clinical symptoms with appropriate diagnostics. Workup is typically performed as an outpatient and in the non-acute ill. Acute pancreatitis is an exceedingly rare manifestation of Cushing’s disease not typically described in humans. Pancreatitis due to exogenous glucocorticoids or ectopic ACTH production is more commonly recognized.

Osteoporosis is often overlooked as an integral part of the clinical picture in the acutely ill and management is typically relegated to the outpatient setting. Despite her dramatic serial compression fractures being the obvious etiology of her back pain, her symptoms were instead attributed to referred pain from pancreatitis. In this case, the patient’s progressive decompensation ultimately revealed the clinical symptoms necessary to obtain the unifying diagnosis of her condition.

Abstract #836

MIFEPRISTONE THERAPY SIGNIFICANTLY IMPROVED INSULIN RESISTANCE, GLYCEMIC CONTROL AND WEIGHT LOSS IN A PATIENT WITH CUSHING’S DISEASE PREVIOUSLY TREATED WITH PASIREOTIDE.

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Objective: Hypercortisolism causes insulin resistance, which negatively impacts glycemic control leading to hyperglycemia, hyperinsulinemia, and ultimately type 2 diabetes (T2DM) with increased cardiovascular morbidity and mortality. Patients with Cushing’s disease (CD) who are not surgical candidates or for whom surgery has failed may be treated with the somatostatin (SST) analog pasireotide (PASI, Signifor®, Novartis) to lower ACTH and cortisol production. However, SST analogs directly inhibit insulin secretion from pancreatic beta cells. Consequently, hyperglycemia is a major factor limiting the use of PASI in patients with CD. In contrast, treatment with mifepristone (MIFE, Korlym®, Corcept Therapeutics), a competitive glucocorticoid receptor antagonist, has been shown to reduce hyperglycemia in patients with Cushing’s syndrome with a concomitant reduction/elimination of antidiabetic medications. To our knowledge this will be the first published case report on the effects of switching a patient with CD with hyperglycemia from PASI to MIFE.

Case Presentation: A 46 yo woman with CD and a failed transsphenoidal surgery on PASI treatment (0.9 mg injection BID) for 14 months had poorly controlled T2DM (A1C 9.0%, FBG 248 mg/mL) despite treatment with several antidiabetic meds (Levemir [insulin detemir] 54 U QD, Humalog [insulin lispro] 24 U TID, Tradjenta [linagliptin] 5 mg QD and metformin 1000 mg/d). Despite a 5 lb loss of weight while on PASI, she still had a Cushingoid appearance and weighed 258 lbs when she was switched to MIFE. After 14 months of therapy with MIFE (300 mg QD titrated to 600 mg QD), glycemic control greatly improved (A1C 6.5%, FBG 136 mg/mL, fasting insulin 4.8 mU/L) while discontinuing all antidiabetic meds (including insulin) except linagliptin. Hypokalemia was managed with spironolactone 50 mg BID. The patient reported a significant change in Cushingoid appearance with a 15.5% weight loss (258-218 lbs) and is no longer depressed.

Conclusion: Switching a patient with CD with uncontrolled hyperglycemia and T2DM from pasireotide to mifepristone led to a profound decrease in hyperglycemia along with a concomitant elimination of most antidiabetic medications including exogenous insulin. Eliminating insulin injections along with a reduction of weight and improved appearance was life altering for this patient.

Abstract #837

CARCINOID SYNDROME. “ILEAL NEURO-ENDOCRINETUMOR, CLINICAL PRESENTATION AND DIAGNOSIS IN ELDERLY PATIENT”

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Objective: Neuroendocrine tumors have difficulty in diagnosis due to the nonspecific symptoms that may occur; management is also a challenge. We present our experience in diagnosis and treatment of neuroendocrine tumors of gastrointestinal tract.

Methods: Case Presentation

Case Presentation: Male patient 78 years old who 3 years ago presents moderate crampy intermittent abdominal pain in mesogastrium. In his ecography appears cholelithiasis and was scheduled for elective surgery in July 2013. Four months after surgery at Guillermo Almenara Hospital, he had diffuse abdominal pain, hyporexia and low weight of
10 kg. After two years he presented acute abdomen and programmed for exploratory laparotomy that found 20 cc serous fluid and necrotic small bowel loop length 1.5 m.in midgit (distal ileum) . Four weeks later episodes of facial flushing were added about 10-15 min duration, usually after stressful events accompanied by sweating, itching at the level of inner members, palpitations and tremor. The pathology report was ileal carcinoid neuroendocrine tumor with immunohistochemical study with positive chromogranin and Ki67 proliferation index calculated up to 3%. The dosage of 5-hydroxyindoleacetic acid in urine was found in 28.9 ug / 24 h (normal range: 0-10).

Overseas, there were secondary nodes that compromise liver segments II, VI, VII and VIII. The initial treatment was with subcutaneous octreotide and then long-acting octreotide . After six months of treatment a decrease was found in urine hydroxyindoleacetic acid 5-HIAA -5- 15.8 mg / 24 hrs. After 7 months of treatment with Octreotide recovery was gradual with weight gain and decrease in 5-HIAA.decreased to 1.6 mg / 24 hr.

Discussion: Neuroendocrine tumors are difficult to diagnose and it can be delayed for a few years. Although most of them are no functioning , symptoms may be vague or may even remain long asymptomatic. Among symptomatic patients, abdominal pain is the most common symptom, occurring in approximately 40 percent and often is non-specific, intermittent and present for many years and can be misdiagnose. Intermittent bowel obstruction occurs in 25 percent.

Conclusion: We conclude, after discovering our findings and compare them with other worldwide experiences, ileal neuroendocrine tumors should be considered in the differential diagnosis of abdominal pain syndrome in particular in elderly patients. Overseas,apart of locate the primary tumor we should take account the number and location of metastases to plan a single therapy or in combination with other adjunctive treatments. Staging by counting mitosis and Ki67 index % as a normal practice before this tumor types in the diagnostic process and depending on the therapeutic approach is necessary.

Abstract #838

AN UNUSUAL CAUSE OF PANHYPOPITUITARISM

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Objective: Intrasellar chordomas (ISC) are uncommon but can be locally aggressive. We present a patient presenting with panhypopituitarism and an unilateral 6th nerve palsy secondary to an ISC.

Case Presentation: A 29 years old man complained of lethargy, loss of weight and horizontal diplopia. Examination: No postural hypotension. Tanner Stage 5, testicular size 15ml. Left 6th nerve palsy and left temporal visual field defect noted. Investigations: Panhypopituitarism with IGF1 87 ug/L (NR: 128-336), total testosterone < 1nmol/L, FSH < 1 IU/L, LH < 1 IU/L, fT4 6 pmol/L (NR: 8-21), TSH 0.05 mIU/L (NR: 0.34-5.60), ACTH < 2 pmol/L, Cortisol 50nmol/L (0 min) to 228nmol/L (30min) after 250mcg synacthen. Prolactin 1420mIU/L (NR: 77-274) under dilution. MRI Pituitary: 3.2 x 2.8 x 3.7cm lobulated mass in the sellar-suprasellar region invading both cavernous sinuses and partially encasing the intracavernous portions of both internal carotid arteries. Bony erosion of the roof of the sphenoid sinus, extension into the pre pontine cistern and mass effect on the optic chiasm and the adjacent pons noted. He was started on hydrocortisone, thyroxine and had trans-sphenoidal surgery done with histology showing features of an invasive chordoma invading the pituitary gland and bones of the sphenoid sinus and pituitary fossa. Immunohistochemical analysis:Positivity for pan keratin AE 1/3 and S-100. Ki-67 proliferation index was 15-20%. He underwent adjuvant radiotherapy. 2 years later, he continued to require hormonal replacement therapy.

Discussion: Chordomas are rare, slow-growing malignant tumours arising from the remnants of the primitive notochord. Within the cranium, they are usually located at the clivus and account for about 0.15% of all intracranial neoplasm. Intracranial chordomas are commoner in young male patients. The elevated prolactin level is due to pituitary stalk compression and should not be mistaken as a macroprolactinoma. Clinically, patients with sellar chordomas complaining of headache, visual field defect, diplopia and ptosis, and rarely with symptoms from endocrine dysfunction. On contrasted MRI scans, chordomas usually appear hypointense on T1-weight images but show high intensity on T2-weighted images. CT images may demonstrate intra-lesional calcifications and bony erosions. These findings may help distinguish ISCs from pituitary macroadenomas or craniopharyngiomas.
**Conclusion:** Sellar chordomas are locally aggressive and can present with panhypopituitarism and an isolated unilateral 6th nerve palsy. Total surgical resection is desirable but challenging due to the infiltrative nature of the lesion. Adjuvant radiotherapy is recommended. Pre-operative suspicion of an ISC may improve outcome for patients.

**Abstract #839**

**MIFEPRISTONE REDUCED U500 INSULIN USAGE IN A PATIENT WITH CUSHING’S DISEASE AND NORMALIZED CONCOMITANT FATTY LIVER DISEASE AND RETINOPATHY**

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**Objective:** Insulin resistance and type 2 diabetes (T2DM) are hallmarks of endogenous Cushing’s disease (CD). In some cases, T2DM is so severe it requires large doses of insulin that can only be given by using concentrated insulin (Humulin R U500, Lilly). Mifepristone (MIFE, Korlym®, Corcept Therapeutics) is a competitive glucocorticoid receptor antagonist indicated for treating hyperglycemia secondary to hypercortisolism in patients with endogenous Cushing’s syndrome (CS). It has been shown to improve insulin sensitivity and reduce the need for insulin in controlling hyperglycemia. To our knowledge, this will be the first reported case of using MIFE to decrease usage of high dose (U500) insulin to control severe T2DM leading to improvements in associated complications from endogenous CS.

**Case Presentation:** A 40 yo woman with a 12 y history of CD (relapses from 2X TSS + γ-knife in 2003 & 2009 and an unsuccessful bilateral adenalecctomy in 2012 presented with uncontrolled T2DM (A1c 11.5%, FBG 150 mg/dL on U500 Insulin [110 IU/d] and metformin ER [500mg BID]), obesity (345 lbs), biopsy proven fatty liver disease with elevated liver enzymes (AST 125 U/L, ALT 133 U/L; normal range 10-40 and 7-56, respectively) and retinopathy. MIFE therapy for 30 months (escalation from 300 mg/d to a final dose of 1200mg/d) resulted in significant improvement in glycemic control (A1c 6.7%, FBG 102 mg/dL) and a reduction in insulin usage to 30 IU/d in combination with metformin ER. Also significant was a concomitant resolution of fatty liver disease (confirmed with imaging), normalization of liver enzymes (AST 20 U/L, ALT 19 U/L) and resolution of retinopathy (confirmed by eye exam).

**Conclusion:** Mifepristone treatment in this patient with CD with poorly controlled diabetes resulted in a significant decrease in the use of concentrated (U500) insulin to reestablish glycemic control and resolve accompanying fatty liver disease and retinopathy.

**Abstract #840**

**ACROMEGALY IN 40 WOMEN OF REPRODUCTIVE AGE: MENSES PROFILE**

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**Objective:** Acromegaly may be early detected due to performing imagery and endocrine tools thus issues of fertility might be involved in young patients, both females and males. We aim to introduce the parameters of gonad axes in adult acromegalic women.

**Methods:** The endocrine profile involved the assays of estradiol, FSH (Follicle Stimulating Hormone), LH (Luteinizing Hormone) in association with specific descriptive parameters of GH (Growth Hormone) function at baseline and after therapy. The study is non-interventional. The data were retrospectively collected. The inclusion criteria was women of reproductive age (between 22 and 50 years); therapy of acromegaly of different types (type 1: only surgery, type 2: only medical approach, type 3: all the three lines of therapy: surgical + medical + radiotherapy); at least two moments of evaluation: at baseline and after one year since the first diagnosis/procedure was applied.

**Results:** 40 women were enrolled with a mean age at acromegaly confirmation of 29.17+/-9.2 years. Before any therapy was introduced, 10% of them had no menstrual disturbances (average of these was of 27.5 years), 57% had oligomenorrhea (average age of 29.8 years), and 33% had secondary amenorrhea (this subgroup had an average age of 39.4 years). A pituitary macroadenoma was confirmed in 72.5% of cases and 67.5% of them had menses anomalies. High levels of prolactin was identified in 20% of patients and 62.5% of these had menses disturbances. Nadir of GH was higher in women with secondary amenorrhea (22.6 vs. 14.6 ng/mL vs. 8.85 ng/mL). Women with secondary of 4.6 mU/mL consistent with pituitary axes damage while for women with oligomenorrhea was of 7.2 mU/mL. Initially, average values (for the entire cohort) were for estradiol of 12.8 ng/L, FSH of 3.26 mU/mL, and LH of 2.86 mU/mL. Type 1 of therapy was used for 41% of patients, type 2 for 17%, and type 3 for the others. The normalization of GH and IGF1 (Insulin-like Growth Factor 1) was obtained in 17% of group 1, 13% of group 2, and 15 of group 3. The normalization of gonad axes parameters according to phases of menstrual cycle was obtained only for group 1.

**Discussion:** The effect on gonad si also related to non-GH
pituitary dysfunction not only to acromegaly itself.

**Conclusion:** Secondary amenorrhea was correlated with higher GH levels while surgical approach of pituitary tumour was superior to any other regarding gonadal axes.

**Abstract #841**

**A CASE OF ACROMEGALY PRESENTING AS TRANSIENT HYPOPITUITARISM**

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**Objective:** To report a case of partial and transient pituitary insufficiency due to compression of a GH secreting macroadenoma.

**Methods:** We report the clinical presentation, laboratory imaging studies and management of a patient with hypopituitarism and pituitary macroadenoma.

**Case Presentation:** A 33-year-old woman presented with a ten days history of headache, nausea, vomiting, dizziness and diplopia. Right sixth cranial nerve palsy and progressive tiredness also occurred. During the previous 8 months she had had oligomenorrhea and decrease libido. Cortisol 1.38 mcg/dl, ACTH 1.0 pg/mL, FSH 2.86 mIU/mL, LH 1.25 mIU/mL, estradiol 43.3 pg/mL, PRL 42.5 ng/mL, TSH 1.19 uIU/L and FT4 10.8 pmol/L. A mass measuring 2.4 x 2.2 x 2.5 cm, compressing the optic chiasm and partially infiltrates the right cavernous sinus was demonstrated. She received hydrocortisone in preparation for a transsphenoidal hypophysectomy. The biopsy showed a non-functioning pituitary adenoma (ACTH-, PRL- GH-) with partial hemorrhage. One month later, the patient got pregnant and gave birth to a normal baby by cesarean section, lactating for 4 months and reassuming menses. During pregnancy and post partum she did not have headache, or changes in the visual field and was not on medication. TSH 2.69 uIU/L, FT4 13.3 pmol/L, IGF-1 127 ng/mL, cortisol 19.2 ug/dl. A MRI demonstrated a remnant tumor on the right half of the pituitary gland of 17 x 15 x 22 mm, which invades the right cavernous sinus englobing the internal carotid artery. A year later, the patient noticed changes in shoe size number and a wider nose without visual field abnormalities; PRL 12.6 ng/mL, TSH 2.99 uIU/mL and FT4 11.7 pmol/L, and IGF-1 387 ng/mL (115-307 ng/ml). An OGTT showed a non-suppressible GH, and a 99m Tc octreoscan demonstrated hypercaptive focus in projection to the pituitary. Due to the size of the adenoma and normal visual fields the patient started octreotide 20-mg/ month.

**Discussion:** Restoration of the hypophysial-pituitary axis was achieved by decompression of the pituitary gland and the patient got pregnant, reassumed menstrual periods and did not require hormone replacement therapy. The gradual onset of clinical manifestations of GH excess, originated from the pituitary macroadenoma was evident after two years of observation associated with a rapid tumor growth, as demonstrated in the sequential image studies.

**Conclusion:** This case illustrates an unusual presentation of acromegaly, as pituitary insufficiency was the primary manifestation, but also the successful pregnancy in a patient with a previously surgically treated GH-producing adenoma.

**Abstract #842**

**CLINICAL PROFILE AND TREATMENT OUTCOME IN PATIENTS WITH CUSHING SYNDROME: A 10 YEAR EXPERIENCE AT A TERTIARY CARE HOSPITAL IN PAKISTAN**

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**Objective:** This study was the first one of its kind in Pakistan and designed primarily for the establishment of the prevalence of different etiologies of Cushing Syndrome (CS) other than iatrogenic hypercortisolism, evaluation of the clinical, biochemical and treatment profile of patients with CS.

**Methods:** It was a Descriptive cohort study. Total 44 patients with biochemical and radiological diagnosis of Hypercortisolism were included in study between October, 2005 to September, 2015. Patients with history of intake of Glucocorticoids were excluded. Patients' medical record files were reviewed & data was recorded.

**Case Presentation:** Of the 44 subjects, with mean age of 34.86±14.64 years, 29 (66%) were female while 15 (34%) were male. The mean duration of presentation was found to be 2.19± 2.05 years after onset of symptoms. Weight gain was the most common presenting complaint. Pituitary lesion was the culprit source in 33 (75%) cases, ectopic ACTH source in 7 (16%) cases and adrenal lesion in only 4 (9%) cases. Among the 33 patients with Cushing’s Disease, 32 (97%) underwent TSS and 17 (53.1%) attained remission. Among the 7 patients with Ectopic ACTH source, 6 (86%) underwent surgical excision and 3 (50%) attained remission. Out of the 4 patients with Adrenal source, 3 (75%) underwent uni/bilateral adrenalectomy and all (100%) attained remission.

**Discussion:** Cushing’s Syndrome (CS) results from chronic exposure of body to excessive production of glucocorticoids. Etiology of CS may lie in the adrenal gland, pituitary gland, exogenous glucocorticoid administration or ectopic ACTH production by certain malignancies. Our study established that pituitary lesion is the most common source of CS in Pakistan. Women
are 3-8 times more likely than men to develop Cushing’s disease and our study showed the same consistent finding. Cushing’s syndrome may present with a variety of clinical manifestations like progressive obesity, purple striae, menstrual irregularities & insulin resistance. Similar findings were also observed in our study. The same biochemical diagnostic methods were used in our patients as being done internationally. The success rate to achieve remission after Transsphenoidal surgery (TSS) in CD is variable, ranging from 53-96% in different studies. Our study reflected the presence of low remission rate in Pakistan as compared to the worldwide rates. Most of the patients had to undergo a repeat TSS.

Conclusion: Pituitary lesion is the most common source of endogenous hypercortisolism in Pakistan. Trans-sphenoid surgery is followed by a relatively low remission rate of 53.1% as compared to the developed world. This figure is expected to rise in the years to come with the improved surgical techniques and expertise.

Abstract #843

A LARGE CRANIOPHARYNGIOMA COMPROMISED BY POST-OPERATIVE TRIPHASIC RESPONSE

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Objective: While cranial diabetes insipidus (D.I.) is the most common disorder of salt and water balance post-pituitary surgery, a triphasic response is rare, occurring in only 1%. We describe a young patient with newly diagnosed craniopharyngioma and highlight her post-operative course.

Case Presentation: A 28 year-old female presented with a 1-week history of early morning headaches associated with vomiting, and secondary amenorrhea for 3 years. Urgent Magnetic Resonance Imaging of the brain revealed a 2.2 by 2.4 by 2.6 cm solid-cystic suprasellar mass complicated by obstructive hydrocephalus. There was secondary hypogonadism and low IGF-1 on the pituitary profile; there was no central hypocortisolism or hypothyroidism. She underwent emergency insertion of extraventricular drains and trans-cranial resection of the tumour. She developed polyuria within the first 24 hours of surgery whilst still intubated, and laboratories showed D.I. (serum Na 148 mmol/L, serum Osm 307 mmol/kg, urine Na 28 mmol/L, urine Osm <130 mmol/kg). Hypotonic fluids and intravenous desmopressin 1 mcg were administered for the treatment of D.I. Thereafter, the urine osmolality rose to 571 mmol/kg, indicating cranial D.I. She developed repeat episodes of polyuria from POD 1 to POD 4, and desmopressin was administered on an as-needed basis. On POD 4, more than twelve hours after the last dose of desmopressin, her urine output remained low and urine osmolality rose from 363 to 711 mmol/kg. Laboratories showed severe SIADH (serum Na 132 mmol/L, serum Osm 275mmol/kg, urine Na 121 mmol/L, urine Osm 711 mmol/kg). Hence, she was started on a high protein diet, sodium chloride tablets and fluid restriction. 3% saline was also administered to arrest the fall of sodium in order to avoid exacerbation of post-operative cerebral edema. On POD 8, polyuria recurred, and laboratories were again consistent with D.I. (serum Na 136 mmol/L, serum Osm 280 mmol/kg, urine Na 25 mmol/L, urine Osm 147 mmol/kg). Serum sodium remained normal as she was drinking to thirst. She was initiated on regular intranasal desmopressin 10 mcg daily in the evening, as D.I was expected to be permanent. Post-operatively, she developed pan-hypopituitarism, and was started on hydrocortisone and thyroxine replacement.

Conclusion: Post-operative triphasic response is a rare but challenging complication. Close monitoring of urine output and urine osmolality are essential, and serve as early indicators of the transition between the various phases. To avoid cerebral vasospasm or cerebral edema, judicious therapy must be administered to avoid hyper- and hyponatremia.

Abstract #844

PITUITARY MASS WITH ANTERIOR HYPOPITUITARISM FROM METASTATIC DIFFUSE LARGE B CELL LYMPHOMA

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Objective: Pituitary involvement in lymphoma is very uncommon and can present as a primary pituitary lymphoma or as CNS metastases from widespread disease (<1%). For the latter, diabetes insipidus or symptoms related to posterior pituitary gland deficiency remain the more common initial presentation. We describe an interesting case of metastatic diffuse large B cell lymphoma to the pituitary, presenting solely with anterior hypopituitarism, absent of any posterior pituitary features or other initial signs of systemic lymphoma.

Case Presentation: A 58 year old male presented with 1 week of headaches but absent diplopia or visual field deficits. Initial CT head showed sphenoid sinusitis and an enlarged pituitary gland. MRI confirmed an enhancing pituitary sellar mass (1.6 x 1.6 x 1.7cm) extending to the optic nerves/chiasm, hypothalamus and central sphenoid
sinus. Labs were remarkable for central hypothyroidism with low TSH 0.073(0.450-4.500 uU/ml) and fT4 0.64(0.82-1.77 ng/dL), low serum and free testosterone at 126(348-1197 ng/dl) and 1.0(7.2-24 ng/dl), low normal cortisol 5.2(2.3-19.4 ug/dL), elevated IGF-1 336(54-194 ng/ml) and prolactin 24(4.0-15.2 ng/ml), with normal ACTH, FSH, LH, GH and electrolytes. Patient denied any polyuria, polydipsia, night sweats or weight loss. Sphenoid sinus biopsy pathology returned as DLBCL. PET scan highlighted widely metastatic disease to bilateral pleural spaces, lung, pancreas, thighs and neck. Hydrocortisone and levothyroxine therapies were initiated but tapered off as hypopituitarism resolved after (RCHOP, salvage RICE) chemotherapy. Patient ultimately underwent allogenic stem cell transplant.

**Conclusion:** Metastatic DLBCL, although rare, can involve the hypothalamus-pituitary axis. Typically, metastatic DLBCL patients will first exhibit systemic lymphoma manifestations prior to any hypopituitary symptoms given the pituitary’s significant reserve. Posterior hypopituitarism remains the more common feature if there is pituitary association, which suggests metastatic predominance to the posterior pituitary lobe given its direct supply by the systemic circulation [1,2]. Our case highlights how metastatic lymphomas may first present as an enhancing or invasive pituitary lesion with hypopituitarism. With treatment of lymphoma, posterior and anterior hypopituitarism will often resolve. Interestingly, elevated IGF-1 levels, which may be associated with tumor growth, have also been noted in few cases of lymphoma with pituitary involvement. It is important to consider pituitary lymphoma (whether primary or metastatic) as part of the initial differential for any pituitary mass with corresponding symptoms, which can significantly alter further work-up and treatment.

**Abstract #845**

**TREATMENT DILEMMA AND CHALLENGES IN A PATIENT WITH HYponATREMIA AFTER SUPRASELLAR BRAIN SURGERY**

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**Objective:** Achieving appropriate water balance can be challenging in the setting of complex pathologies, such as patients after brain surgery involving the sellar and suprasellar areas. This is a case of a patient status post brain tumor surgery with difficult to control sodium concentration.

**Case Presentation:** We present a case of a 46-year-old female with history of type 2 diabetes mellitus, partial resection of a suprasellar epitheloid hemangioendothelioma 4 months prior to admission, as well as subsequent development of central diabetes insipidus requiring desmopressin therapy. She presented with an acute onset of altered mental status, and on admission was found to have hypotension and hyponatremia with serum sodium of 122. CT of the head without contrast and MRI of the brain with and without contrast showed a residual 2.5 cmX2.5 cmX2.2 cm heterogeneous suprasellar mass with peritumoral edema in the hypothalamic tissues and mass effect on the optic chiasm and optic tract. Further workup revealed secondary adrenal insufficiency and secondary hypothyroidism. Her hyponatremia was thought to be secondary to a combination of hypopituitarism and her continued desmopressin use despite decreasing sodium levels. Her sodium level started improving after initiation of steroid therapy and treatment with hypertensive saline. However, upon cessation of desmopressin therapy, the patient developed abrupt polyuria, thus desmopressin was reintroduced. Her sodium concentration control was also complicated by her lack of thirst sensation. Eventually, these syndromes were balanced out by a seemingly unusual combination of using steroids for adrenal insufficiency, sodium chloride tablets, desmopressin and structured water consumption to substitute for the lack of thirst. Eventually, these syndromes were balanced out by a seemingly unusual combination of using steroids for adrenal insufficiency, sodium chloride tablets, desmopressin and structured water consumption to substitute for the lack of thirst.

**Conclusion:** This case highlights the complex pathology of hyponatremia, which presents post brain tumor surgery and involves secondary adrenal insufficiency, secondary hypothyroidism, central diabetes insipidus and loss of thirst sensation. To achieve water balance, physicians need to recognize all concurrent physiology and take it into consideration when formulating a treatment plan.  

**Abstract #846**

**A RARE CASE OF MACROPROLACTINOMA PRESENTING WITH SIADH.**

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**Objective:** To describe a rare case of macroprolactinoma associated SIADH & intact pituitary-adrenal axis.

**Case Presentation:** A 52-year-old man was admitted to our hospital with dizziness & collapse. He had no significant past medical history apart from dyslipidemia treated with statin. On examination, he was hemodynamically stable with BP: 131/72. Cardiovascular, chest, abdomen & neurological examinations were unremarkable. Initial investigations revealed low sodium: 109mmol/L, urea: 2.80mmol/L & creatinine: 60umol/L. Random glucose was normal at 5.4mmol/L. Further investigations were consistent with SIADH (Serum Osmolality:...
243mOsm/kg, Urine Na: 59mmol/L & urine Osmolality: 191mOsm/kg). Head CT scan showed enlarged pituitary gland with sellar expansion. Pituitary hormonal profile showed high prolactin: 8305mIU/mL, low IGF-1: 78.1mcg/L & low testosterone: 3.83nmol/L with normal LH & FSH. His thyroid function was normal & he had intact pituitary-adrenal axis (Normal Short Synacthen & Normal Glucagon Stimulation tests). MRI pituitary confirmed pituitary macroadenoma with heterogeneous solid-cystic mass (2.0 x 1.9 x 1.5 cm) with deviation of pituitary stalk up & to the left. No extension to cavernous sinuses & Optic chiasm was pushed superiorly. Visual fields were normal.

He was treated with Cabergoline 0.5 mg per week & few days of fluid restriction with improvement of sodium level to 137mmol/L & prolactin to 61mIU/L after 2 weeks of treatment.

During follow up in endocrine clinic, he remained asymptomatic, had no further hyponatremia & maintained normal sodium & prolactin levels 5 months following discharge, on Cabergoline treatment. His hypogonadism has resolved and IGF-1 has normalized. Repeat pituitary MRI 4 months after discharge showed significant reduction in the macroadenoma size to 1.4 x 1.3 x 0.7 cm with concave appearing superior surface with normal configuration & pituitary stalk in midline.

Discussion: Hyponatremia is a recognized complication of pituitary macroadenomas and is mostly due to secondary adrenal insufficiency. However, the presence of SIADH with intact pituitary-adrenal axis in such cases is very rare with only 7 cases reported in the literature (6 non-functioning macroadenomas & 1 macroprolactinoma). The mechanism of AVP release in these cases is not fully understood, but is thought to be related to local mechanical stress on the AVP neurons axonal terminal and dislocation of pituitary stalk and neurohypophysis by pituitary tumor. Conclusion: We hereby report the second case of SIADH secondary to macroprolactinoma with normal pituitary-adrenal axis. Pituitary macroadenomas should be considered in the differential diagnosis of SIADH even in the context of preserved pituitary-adrenal axis.

Abstract #847

CLINICAL ACROMEGALY WITHOUT PITUITARY ADENOMA

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Westchester Medical Center

Objective: To describe a patient with clinical features of Acromegaly and elevated IGF-1 but with inconclusive pituitary imaging.

Methods: History, physical examination, laboratory results, biochemical and imaging results were analyzed.

Case Presentation: A 47-year-old male with history of hypertension was transferred to WMC secondary to acute intracranial hemorrhage due to hypertensive emergency. On physical examination, he was noted to have macroglossia with prominent macrognathia and hoarseness of voice. He stated as a child he always had a physically big jaw, he was much taller than his parents. He denied headaches, visual symptoms, or increasing shoe or ring size. Patient underwent MRI with pituitary protocol, which revealed chronic hydrocephalus in the setting of aqueductal stenosis, with resultant extension of 3rd ventricle CSF into the pituitary fossa and compression of the pituitary gland without gross evidence of a pituitary tumor. Biochemical evaluation, however, did not reveal hypopituitarism; gonadotrophins were mostly within normal limits FSH 3.18 mIU/mL (normal for males 1.4-13.6 mIU/mL), LH 2.0 mIU/mL (normal for males .6 -12.1 mIU/mL), Free Testosterone 6.60 ng/dL (normal 4.26 – 16.4 ng/dL), Total Testosterone 165 ng/dL (normal 240-950 ng/dL), TSH 2.802 mIU/L (normal .350-4.700 mIU/L), Free T4 .9 ng/dL (normal .7 – 1.9 ng/dL), and prolactin 10.2 ng/mL (normal 2.6-18.2 ng/mL). Morning cortisol was 8.2 ug/dL (normal 6.2 – 19.4 ug/dL). IGF-1 level was persistently elevated with initial result of 442 ng/mL followed by 356 ng/mL (normal 40 – 259 ng/mL); however, patient had a normal oral glucose tolerance test with one hour growth hormone level of .9 ng/mL. After prolonged hospitalization patient was discharged to follow up as outpatient with Neurosurgery and Endocrinology.

Discussion: This case demonstrates a clinical dilemma in a patient with discordant biochemical evaluation for acromegaly with elevation of IGF-1 and normal oral glucose tolerance test.

Conclusion: We conclude that given discordant biochemical results the diagnosis of Acromegaly cannot be completely ruled out. Ongoing follow up is required and specific guidelines are needed for patients with similar presentation.
Abstract #848

A RARE CASE OF PITUITARY MEDIATED HYPERCORTISOLISM (CUSHING’S DISEASE) WITH MEN-1 SYNDROME

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University at Buffalo

Objective: Multiple Endocrine Neoplasia type 1 (MEN 1) is an autosomal disorder transmitted by mutations in the MEN-1 gene located on 11q13 with a prevalence of 2 per 100,000. The most common presentation is hyperparathyroidism (almost 100%), pituitary tumors (40-50% of adult MEN 1) and enteropancreatic endocrine tumors. Most pituitary tumors are prolactinomas or growth hormone producing tumors, whereas corticotrophin (ACTH) producing tumors causing Cushing’s disease (CD) are rare (5-10%). We present a unique case of MEN-1 with hyperparathyroidism and CD from an ACTH secreting pituitary adenoma.

Case Presentation: A 19-year-old female with family history significant for MEN-1 in her father was referred to endocrine clinic for hypercalcemia and hirsutism. Lab work showed serum calcium level of 11.3 mg/dl (8.9-10.4), parathyroid hormone 112 ng/L (14-64), phosphorus 2.6 mg/dl (2.5-4.5). Neck ultrasound was suspicious for parathyroid adenoma. Sestamibi scan showed increased focal activity in the right side of the neck. A complete work up of pituitary hormones showed elevated late night salivary cortisol levels on 4 occasions, with other hormone levels within normal limits. She had high 24 urinary cortisol level of 138 mcg (4-50) and abnormal low dose overnight dexamethasone suppression test (serum cortisol 7.3 mcg/dl). A high morning serum cortisol levels with inappropriately normal ACTH level of 32 pg/ml (6-50) indicated a ACTH mediated source of Cushing’s syndrome (CS). A high dose dexamethasone suppression test showed serum cortisol level of 1.4 and ACTH suppressed to <5, indicating a pituitary source of the CS. MRI of the pituitary gland showed a 3.5 mm microadenoma. The patient fits into MEN-1 syndrome clinically with pituitary mediated hypercortisolism and primary hyperparathyroidism. She was referred for genetic testing which showed a pathological variant of C,969 C>A (p.Tyr323) in the MEN-1 gene. She was referred to neurosurgery for bilateral inferior petrosal sinus sampling localization and surgical resection of the microadenoma.

Conclusion: MEN-1 mutations are associated with pituitary adenomas which can be the first and only lesion in younger age. These pituitary tumors may harbor distinct patterns compared to sporadic tumors and their clinical presentation and the evolution, more often aggressive, invasive and resistant to treatment, can be quite different from the sporadic tumors. Cushing’s disease can cause significant morbidity and mortality, hence its detection in suspected patients is of utmost importance. Given the incidence of pancreatic islet cell adenomas as well, one should also watch out for symptoms of hypo/hyperglycemia. These patients need a careful life-long follow-up.

Abstract #849

A RARE CASE OF ECTOPIC ADRENOCORTICOTROPIN HORMONE SYNDROME FROM A PANCREATIC NEUROENDOCRINE TUMOR WITH LIVER METASTASIS

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Albert Einstein Medical Center

Objective: The estimated annual incidence of pancreatic neuroendocrine tumors (PNETs) is 2.23 per 100,000 people. Ectopic adrenocorticotropin syndrome (EAS) occurs in approximately 7% of PNETs. Patients with EAS typically present with Cushingoid features. Diagnosis depends on both laboratory evaluation and imaging. Treatment consists of a combination of surgery, medical management, and chemotherapy.

Case Presentation: A 53-year-old female with a history of type 2 diabetes mellitus, hypertension, and obesity presented with dyspnea on exertion and increasing lower extremity edema for one month. She was in hypertensive urgency but in no acute distress. She was morbidly obese with Cushingoid features and skin hyperpigmentation. Computed tomography (CT) showed a 9 cm hypervascular mass on the pancreas and multiple liver metastases. Early morning cortisol was 58.9 mcg/dL (nl 3.7-19.4) and ACTH was 463 pg/mL (nl 6-50). Cortisol remained 55.0 mcg/dL after 1mg dexamethasone. Pituitary imaging was normal. Endoscopic ultrasound-guided biopsy of her pancreatic mass revealed PNET. Tissue from a liver biopsy showed Large Cell Neuroendocrine Carcinoma, WHO G3, with Ki-67 index of about 35%. Staining for ACTH is pending. Octreotide led to significant improvement in her hyperglycemia and insulin requirements. High doses of spironolactone improved her resistant hypertension and persistent hypokalemia. Her extensive disease deemed her a nonsurgical candidate. She will likely undergo transarterial chemoembolization (TACE) with concomitant systemic chemotherapy.

Conclusion: Most PNETs are non-functional tumors, however, some secrete hormones such as insulin or gastrin. EAS is extremely rare. Patients typically present
with Cushingoid features. Cortisol and ACTH are elevated and insuppressible. Differentiation between a pituitary and ectopic source of the ACTH may require high dose dexamethasone test, pituitary imaging, or inferior petrosal sinus sampling.

Treatment goals are to reduce the tumor burden and to control the production of ACTH and cortisol. Optimal treatment of a localized malignancy is surgical resection. When metastatic lesions are involved, treatment is controversial. In the presence of high metastatic burden, TACE has been useful. Medical management may include reducing ACTH production with octreotide and decreasing cortisol production with metyrapone, ketoconazole, or even adrenalectomy. Mifepristone and spironolactone can be used to block glucocorticoid and mineralocorticoid receptors. These tumors tend to be aggressive with poor prognosis.

Abstract #850

CASE REPORTS OF BLUNTED CORTICOTROPIC AND GONADOTROPIC FUNCTION AFTER ACUTE AND CHRONIC ADMINISTRATION OF MORPHINE SULPHATE

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Salem VAMC

Objective: Being reported sporadically, opiate-induced suppression of gonadotropic and corticotropic axes are not fully recognized by most practitioners. The two cases herein reported are examples of iatrogenic disruption of adrenal and gonadal function after acute and chronic morphine administration.

Case Presentation: Case 1: 55 y/o male admitted due to cellulitis of left lower extremity and dry gangrene of 1st and 2nd digit of left foot. Therapeutic intervention included parenteral morphine administration at a dose of 2 mg q 4 hour prn. While on morphine, a morning serum cortisol of 1.78 µg/dL prompted a Cortrosyn stimulation test, with serum cortisol (µg/dL) increasing from a baseline of 1.2 to values of 9.93 and 16.7. CT scan of head reported no intracranial abnormality. Patient was started on hydrocortisone, which continued intermittently for about 2 years. The morning cortisol levels have been consistently above 10 µg/dL off glucocorticoid replacement for a year. Although not assessed during this admission, evaluation of gonadal function after acute and chronic morphine administration.

Case Presentation: Case 2: 54 y/o male was referred to Endocrine for evaluation of low serum cortisol (1.63 µg/dL) and testosterone (72 ng/dL) concentrations. Patient was on morphine sulfate at a dose of 30 mg twice a day for several years. Low total testosterone was associated with low free testosterone (17.9 pg/mL), low LH (1.3 mIU/mL), and borderline low FSH 2.9 (mIU/ML). Endocrine work-up revealed normal thyroid tests and prolactin. Baseline cortisol of 4.5 µd/dL increased to 21 and 27 µg/dL after Cortrosyn administration. Pre-Cortrosyn ACTH was 7 pg/mL. MRI of pituitary was normal.

Discussion: Low circulating cortisol and testosterone concentrations with inappropriately low ACTH and gonadotropin levels after acute and chronic use of opiates are consistent with a hypothalamic-pituitary etiology, which has not been fully explored to date. The adrenal response to exogenously administered ACTH, and more pronounced suppression of LH than FSH distinguish this entity from other causes of central hypoadrenalism/hypogonadism, and therefore warrant prospective studies to establish logical diagnostic algorithm, as well as proper approach to hormonal replacement.

Conclusion: Opiates particularly in large doses could functionally disrupt corticotropic and gonadotropic axes. This entity requires increased level of awareness among clinicians.

Abstract #851

ASSOCIATION OF CHANGES IN LIVER TRANSAMINASES WITH CHANGES IN GLUCOSE PARAMETERS AND ADIPONECTIN IN HIV-INFECTED PATIENTS TREATED WITH TESAMORELIN, A GROWTH HORMONE-RELEASING HORMONE ANALOGUE

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Objective: Tesamorelin, a stabilized analogue of human growth hormone-releasing hormone, has been shown to reduce visceral adipose tissue (VAT) in HIV+ patients with lipodystrophy. The reduction in VAT in responders (27-30%) was associated with improvements in ALT and AST in patients with baseline elevations (>30 U/L) in these enzymes. Because elevated transaminases levels are associated with impaired glucose homeostasis, the current analysis tested the hypothesis that changes in ALT and AST in responders would be associated with changes in glucose parameters and adiponectin.

Methods: Combined data from two Phase 3 studies of
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Tesamorelin in HIV+ patients with excess abdominal fat. “Responders” were defined as individuals who experienced ≥8% reduction in VAT. Changes in ALT and AST were assessed by multivariable linear regression. Spearman’s correlations were performed to evaluate the relationships between changes in liver transaminases and changes in glucose parameters and adiponectin.

Results: Among responders receiving tesamorelin for 26 weeks, change in ALT was significantly positively correlated with changes in fasting blood glucose (r=0.15, p<0.025) and HbA1c (r=0.14, p=0.036). Among responders without hepatitis B or C, change in ALT was positively correlated with change in fasting blood glucose (r=0.17, p=0.018) and trended toward association with changes in fasting insulin (r=0.14, p=0.061) and HbA1c (r=0.13, p=0.076). Among responders receiving tesamorelin for 52 weeks, change in ALT trended toward positive association with changes in fasting blood glucose (r=0.21, p=0.09), fasting insulin (r=0.21, p=0.085), and HOMA-IR (r=0.22, p=0.084), and toward negative association with change in adiponectin (-0.22, p=0.094). Among responders without hepatitis B or C, change in ALT was positively correlated with changes in fasting insulin (r=0.36, p=0.0008) and HOMA-IR (r=0.33, p=0.016) and negatively correlated with adiponectin (r=-0.29, p=0.041). Change in AST was positively correlated with changes in fasting glucose (r=0.27, p=0.048) and adiponectin (r=-0.28, p=0.049).

Discussion: Excess VAT is associated with liver fat in HIV-infected patients on antiretroviral therapy. Liver damage, as indicated by elevations in ALT and AST, is associated with insulin resistance and later development of diabetes. Strategies aimed at reducing VAT and liver fat may help preserve glucose homeostasis in HIV-infected patients.

Conclusion: Changes in liver transaminases were associated with changes in glucose parameters and adiponectin in tesamorelin responders. This finding may account for the preservation of glucose homeostasis seen in these patients.

Abstract #852

A RARE CASE OF HYPOGLYCEMIC SYNDROME SECONDARY TO PRO INSULIN PREDOMINATE SECRETING NEUROENDOCRINE TUMOR

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Objective: Insulin secreting neuroendocrine tumor is a rare cause of symptomatic fasting hypoglycemia in adults and diagnosis is often difficult to make. Patients should fulfill Whipple’s triad with lab data which shows inappropriately high levels of insulin and C-peptide at the time of the hypoglycemia. We are reporting an unusual case of fasting hypoglycemia in the presence of low insulin level secondary to pro-insulin predominate secreting neuroendocrine tumor.

Case Presentation: A 40 year old woman was referred to the endocrinology clinic for evaluation of symptomatic hypoglycemic episodes. Initially her symptoms consisted of feeling tired, lightheaded and tremulous. As her condition progressed, she developed episodes of confusion and difficulty concentrating. These episodes tended to occur after prolonged fasting and could be triggered by exercise. Her symptoms were associated with hypoglycemia with documented finger stick BGs in the 40s and would resolve about ten minutes after eating carbohydrates. Her past medical history was significant for lichen sclerosis and depression. Her only medication was Ibuprofen as needed. There were no family history of endocrine tumors/MEN associated conditions. Review of symptoms was unremarkable aside from ten pounds weight gain over the last few months. Her physical examination was within normal limits.

The patient was brought in to the office for evaluation after fasting overnight. She developed symptomatic hypoglycemia with a BG of 33 mg/dl, with an insulin level of 1.3 uIU/ML (3-25), C-peptide of 1.2 NG/ML (0.8-3.9) and high proinsulin level of 48.9 pmol/L (Nl<18.8). She had a negative sulphonylurea screen and insulin autoantibodies, normal beta hydroxybutyrate, cortisol, ACTH, TSH and IGF1 levels. CT scan of the abdomen was normal and an octreotide scan showed no uptake.

She underwent an endoscopic ultrasound which showed 8.8 x 6.6 mm hypoechoic well defined mass at the head of the pancreas. Biopsy of the mass revealed low grade well differentiated neuroendocrine tumor. She had an exploratory laparotomy with enucleation of the tumor and pathology showed functional insulin producing neuroendocrine tumor (insulinoma). She had no further episodes of hypoglycemia after her surgery.

Conclusion: We present a case of a woman with symptomatic hypoglycemia who was subsequently found to have a pro-insulin secreting neuro-endocrine tumor which is a very rare subtype of insulinoma with only a few cases being reported in the literature. Diagnosing and localizing these tumors can be challenging. Localization of smaller tumors can be enhanced with endoscopic ultrasound and trans-gastric biopsy. Surgical resection is the preferred treatment.
REPRODUCTIVE ENDOCRINOLOGY

Abstract #900

STROKE IN THE SETTING OF TESTOSTERONE ABUSE

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Case Presentation: A 28 year-old male presented with complaint of acute-onset vertigo while lifting weights. He also had associated nausea, emesis and an unsteady gait. His exam was notable for ataxia on the right during finger-to-nose testing. Imaging studies included magnetic resonance imaging of the brain which revealed small acute infarcts involving the left cerebellum and brainstem and was suggestive of an embolic pattern. He was found to have total testosterone 2626 ng/dL, calculated free testosterone 5104 pmol/L and estradiol level 22.3 pg/mL. His lipid profile revealed LDL 186 mg/dL, triglycerides 104 mg/dL, total cholesterol 225 mg/dL, and HDL 18 mg/dL. His liver function studies revealed AST 47 IU/L and ALT 51 IU/L. Extensive testing for pro-thrombotic disorders was unrevealing. A trans-thoracic echocardiogram revealed mild concentric left ventricular hypertrophy with ejection fraction of 50-55%. A trans-esophageal echocardiogram (TEE) was also performed with agitated saline which did suggest a small patent foramen ovale (PFO).

Further history revealed that the patient was otherwise healthy but had been abusing testosterone and trenbolone (an oral androgen resistant to aromatase) for at least six years. He was self-administering testosterone injections of 325mg every other day and using unspecified amounts of trenbolone. The patient denied having a family history of stroke or myocardial infarction.

Discussion: This case describes a cerebrovascular event related to exogenous testosterone use in an otherwise healthy young male. The patient may have had a deep vein thrombosis that embolized to his brain in the setting of a pre-existing PFO. Testosterone supplementation has been associated with both erythrocytosis and dyslipidemia, specifically increased LDL and reduced HDL cholesterol. Previous case reports and case series studies have also suggested a correlation between thrombophilia and exogenous testosterone use, generally in the setting of a preexisting prothrombotic disorder. These events typically manifest as deep vein thrombosis or pulmonary embolism. In 2014 the FDA also added a general warning requirement in testosterone drug labeling about the risk of venous thromboembolism.

Conclusion: The case demonstrates a serious adverse effect of exogenous testosterone use. A careful review of a patient’s risk status including prior history of thrombotic events and stroke as well as a discussion of risk and benefit is important before initiating testosterone therapy.

Abstract #901

PREGNANCY RELATED BIOCHEMICAL HYPERANDROGENISM IN A FEMALE FETUS CARRIER

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Case Presentation: A 21-year-old Hispanic female patient G1P1A0 with history of left sided Sertoli-Leydig cell ovarian tumor (SLCT) was consulted to our Endocrinology clinics due to elevated testosterone levels during pregnancy. Two years prior to evaluation, an ovarian tumor was discovered upon workup for irregular menses, suprapubic pain, and abdominal fullness sensation. At that time, the patient presented no clinical manifestations of hyperandrogenism. It was successfully removed without complications and patient remained stable for the following years until pregnancy. The patient started prenatal care at 6 weeks of gestational age. Initial total testosterone levels measured at 458 ng/dL (nl 2-45 ng/dL; nl during first trimester of pregnancy 26-211ng/dL) that progressively increased to a peak level of 1264 ng/dL (nl during third trimester of pregnancy 63-309 ng/dL) at 25 week of gestation with a sex hormone binding globin (SHBG) of 616 nmol/L (nl during third trimester of pregnancy 63-309 ng/dL) that progressively increased to a peak level of 1264 ng/dL (nl during third trimester of pregnancy 63-309 ng/dL) at 25 week of gestation with a sex hormone binding globin (SHBG) of 616 nmol/L (nl during first trimester of pregnancy 26-211ng/dL). During evaluation, the patient had no signs of virilization, acne, alopecia, or hirsutism with a Ferriman–Gallwey score of 4 (nl during first trimester of pregnancy 26-211ng/dL).

Discussion: Hyperandrogenism caused by pregnancy is an extremely rare condition. Normal pregnancy is characterized by a progressive increase in serum total testosterone concentrations secondary to an increase in SHBG concentrations, and a late increase in serum free testosterone and androstenedione concentrations. Differential diagnoses include luteomas, theca lutein cyst, progesterin and androgen use, and ovarian tumors such as SLCT. No evidence of these aforementioned causes or SLCT recurrence was found in our case. Interestingly, neither mother nor fetus showed clinical evidence of hyperandrogenism or virilization at any moment.
No medical treatment or intervention was required. Biochemical hyperandrogenism resolved after delivery with no adverse outcomes.

**Conclusion:** This illustrates a strange case of pregnancy-related hyperandrogenism without maternal or female fetal virilization and with complete resolution after an uncomplicated delivery.

**Abstract #902**

**MEGACE (MEGESTROL ACETATE) INDUCED HYPOGONADISM IN A MALE PATIENT - A CASE REPORT**

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**Case Presentation:** We present a case of a 48 year-old male with history of hyperlipidemia, HIV and latent secondary syphilis who presented for evaluation of loss of libido and erectile dysfunction for 2 months duration. On examination, the patient was hemodynamically stable and did not show any signs and symptoms of adrenal insufficiency. The only physical finding was small testicular size. On lab work, his total testosterone level was 21.47 ng/dl. The corresponding luteinizing hormone (LH), follicular stimulating hormone (FSH), thyroid-stimulating hormone and morning cortisol levels were also low. His serum electrolytes were within normal limits. Upon reviewing his medication list, we found that the patient was taking Megace 800mg daily as an appetite stimulant. About 2 months prior to starting Megace, on lab work his Total and Free Testosterone levels were normal (548 ng/dl and 83 pg/ml respectively). FSH, LH, prolactin level, prostate specific antigen and sex binding globulin) were also normal at that time. Brain MRI was done which showed no pituitary mass and only a partial empty sella. He reported some biochemical but no significant clinical response of hypogonadism on dopamine agonist therapy. Upon tapering Megace the patient immediately started showing improvement in his symptoms.

**Discussion:** Megestrol acetate (megace) is a synthetic progestin and is in use since the 1970s to treat advanced cancer, anorexia and weight loss especially in patients with HIV. It is also used as an appetite stimulant although the exact mechanism by which it stimulates appetite is still unknown. Megace has been shown to cause suppression of the pituitary-adrenal axis due to its affinity for the glucocorticoid receptor. High doses or prolonged treatment with it may cause Cushing’s syndrome, hyperglycemia and suppression of ACTH and cortisol levels. It has also been shown to cause suppression of the gonadal axis leading to symptomatic androgen deficiency. Megace also has profound effects on testosterone, reducing levels to near castration levels in elderly men and this could be a result of reduction in LH levels. Clinicians should be mindful of these side effects when prescribing Megace.

**Conclusion:** The hypothalamic-pituitary-adrenal and gonadal axis regulates thirst, mood, hunger, energy level, sexual function including libido. Physicians prescribing Megace should be aware of the possibility of suppression of the hypothalamic-pituitary-adrenal and gonadal axis by it and patients should be monitored accordingly.

**Abstract #903**

**AN ALTERNATIVE TREATMENT FOR A HYPOGONADOTROPIC HYPOGONADISM PATIENT WITH A PARADOXICAL RESPONSE TO TESTOSTERONE REPLACEMENT**

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**Objective:** The standard treatment of symptomatic central hypogonadism is testosterone replacement. We report a case of a young patient with central hypogonadism who had a paradoxical response to testosterone replacement but has better sustained clinical and biochemical response to an aromatase inhibitor.

**Case Presentation:** A 37 years-old 46XY karyotype male with intact smell was diagnosed with central hypogonadism in 2009 when he presented with fatigue and erectile dysfunction. He has two biological children. Etiology was attributed to class I obesity (BMI 30), obstructive sleep apnea, empty sella syndrome with central hypothyroidism and hyperprolactinemia. The peak prolactin level was 65 ng/dl (ref 2.6-13.1 ng/dl). The rest of his HPA axis were intact. He was treated with dopamine agonist for a few years but it was stopped as he was not tolerating to either bromocriptine or cabergoline. He reported some biochemical but no significant clinical response of hypogonadism on dopamine agonist therapy. Prolactin level remained mildly elevated at 43-63 ng/dl (ref 2.6-13.1 ng/dl). after stopping dopamine agonist. Testosterone replacement was started as an Androgel and then as testosterone cypionate. However, the testosterone level decreased further and estradiol increased further from baseline on testosterone therapy. He stopped taking his testosterone replacement due to worsening fatigue and impotence. Clomiphene was started at 50 mg once daily with improvement of symptoms and testosterone level. One year after initiation of clomiphene, his symptoms recurred and testosterone level declined to 1.7 ng/mL (ref 1.7-7.6ng/mL). Estradiol was increased at 89 pg/mL (ref <57pg/mL). Given the elevated estradiol level,
the aromatase inhibitor, Letrozole, 2.5mg po weekly was started in August 2015. The patient reported improvement of his energy, libido and erectile dysfunction. Testosterone level has improved and maintained at therapeutic range 4.6-6.1 ng/dL (ref 1.7-7.6ng/mL). Estradiol level has reduced but able to maintain at or above safety lowest level of 40 pg/ml on Letrozole therapy.

Discussion: In obese patients there is an associated increase in estradiol production as a result of aromatase dependent conversion of testosterone to estradiol in fat tissues leading to a hyperestrogenic hypogonadotropic hypogonadism.

Conclusion: In patients with central hypogonadism who do not tolerate testosterone replacement or have a paradoxical response in the setting of obesity and an elevated serum estradiol an aromatase inhibitor may be considered.

Abstract #904

MUTATION NEGATIVE ANDROGEN INSENSITIVITY SYNDROME (AIS)

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Case Presentation: We present a 51-year-old male with a history of hypertension and obsessive compulsive disorder, who presented for evaluation of elevated testosterone. He had a history of gynecomastia and poor libido since puberty at age 14. He noted a small penis and minimal hair growth as well as low libido and rare morning erections. He denied headaches, vision changes, galactorrhea, and head nor testicular trauma. He denied taking any hormones or supplements. His twin brother and older brother were reportedly normal and had fathered several children. He has no offspring. Physical exam revealed gynecomastia and normal testicular size. As part of a workup for hypogonadism, his testosterone profile was checked. Total testosterone was elevated to more than 1500ng/dL with concurrent elevated sex hormone binding globulin (208 nmol/L) and inappropriately elevated luteinizing hormone (LH) (8.86 mIU/mL). Other pituitary hormones, DHEA-s and estradiol levels were within normal range. MRI brain was without pituitary abnormality. The patient subsequently had genetic evaluation for AIS. Gene sequencing with deletion and duplication analysis of the androgen receptor (AR) gene did not reveal any mutations. Given clinical signs and symptoms, partial androgen insensitivity remains a possible diagnosis. The patient was offered weekly testosterone injections as treatment.

Discussion: AIS is an X-linked inherited genetic disorder affecting the androgen receptor. It represents a spectrum of defects in androgen action and can be subdivided into complete, partial, and mild AIS. The most common phenotype includes feminization of external genitalia, abnormal secondary sexual development, and infertility. Diagnosis of AIS is based on clinical findings of poorly androgenized genitalia, impaired spermatogenesis, and normal or increased levels of testosterone and LH. The AR gene is the only gene that is known to cause AIS. However, there may be individuals with normal AR but decreased or defective androgen binding activity due to mutations undetected by current tests. Somatic mosaicism and abnormal post-genomic events can also result in the AIS phenotype. Thus, the diagnosis of AIS is often based on clinical signs and symptoms.

Conclusion: AIS represents a spectrum of clinical presentations and genetic analysis alone may miss some patients with defects in androgen receptor activity. Thus, physicians need to be aware of AIS as a clinical diagnosis with appropriate testing.

Abstract #905

REVERSAL OF LONG-ACTING OPIOID-INDUCED HYPOGONADOTROPIC HYPOGONADISM BY CLOMIPHENE

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Objective: Narcotics have been used and abused since 3400 B.C. The opioid prescribing epidemic in the United States has been affecting the American population at an increasing rate. Long acting opioids in particularly are associated with addiction, tolerance and systemic side effects. Hypogonadotropic hypogonadism has been associated more prominent with long-acting opioids.

Case Presentation: A 69-year-old man with a past medical history of hypertension, COPD, obesity class 1, degenerative disk disease and spinal stenosis was referred to the Endocrinology Clinic after his primary care provider noted his complaints of hypogonadism. His biochemical profile revealed a total testosterone (tT) 56ng/dL (normal range 250-1100), free testosterone (fT) 8.1pg/mL (35-155), sex hormone binding globulin (SHBG) 26nmol/L (17-54), luteinizing hormone (LH) 2.3mIU/mL (1.5-9.3), follicle-stimulating hormone (FSH) 7.3IU/L (1.6-8), estradiol (E) 7pg/mL (<29) and a prolactin (P) 8.4ng/mL (2-18). The patient was diagnosed with degenerative disk disease and spinal stenosis ten years before and was suffering from chronic back pain that failed treatment with physical therapy, surgery and non-steroidal anti-inflammatory. He was treated with hydrocodone that was titrated up and later transitioned to Methadone when his hypogonadal symptoms became prominent. After discussing the risks and benefits, the patient was started on Androgel, but he
stopped a few months later due “angry outbursts”. The patient was switched to a selective estrogen receptor modulator (SERM) Clomiphene 25mg daily followed by resolution of his clinical symptoms. The six-month follow up biochemical profile showed improvement with tT 547, fT 47, LH 17, FSH 20.5, P 6.6, E 35.

**Conclusion:** Opioid-induced androgen deficiency is a known consequence of long-term opiate use but has been under recognized in the primary care setting. Hypogonadism can lead to decreased libido, erectile dysfunction, oligomenorrhea, bone loss, and infertility, and monitoring of gonadal function prior to initiation of narcotic regimen is not the standard of care currently. In male hypogonadotropic hypogonadism testosterone therapy has been the main stay of treatment. Clomiphene has been shown to be a good alternative when testosterone therapy is not tolerated or when the hypogonadal patient is interested in maintaining fertility. We report in our patient that following prolong methadone use for more than ten years resulted in disruption of the hypothalamic-pituitary-gonadal axis and the use of clomiphene restored his testosterone production.

**Abstract #906**

**TESTOSTERONE REPLACEMENT THERAPY FOR SECONDARY HYPOGONADISM AND RISK OF MYOCARDIAL INFARCTION, STROKE OR ALL-CAUSE MORTALITY**

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Cleveland Clinic Foundation

**Objective:** To evaluate the effect of testosterone replacement therapy (TRT) on the risk of myocardial infarction (MI), stroke (CVA) or all-cause mortality, in men with secondary hypogonadism.

**Methods:** We conducted a retrospective cohort study using the electronic health record in a large, integrated healthcare system. Men ≥ 40 years of age, with at least two testosterone levels < 220 ng/dL, with one level obtained between 7am and 10am, were identified. Men with primary hypogonadism, secondary hypogonadism related to overt hypothalamic pituitary pathology, Human Immunodeficiency Virus infection, metastatic cancer, history of prostate cancer, prostate specific antigen > 4ng/mL, elevated hematocrit, or history of previous thromboembolic disease were excluded. Men exposed to TRT were matched 1:1 with replacement to controls that were not exposed on the following variables: duration of low testosterone, age, income, diabetes diagnosis, smoking status, LDL cholesterol, hypertension diagnosis, statin use, body mass index, and history of established cardiovascular or cerebrovascular disease. A survival analysis was performed on the composite outcome of MI, CVA, or all-cause mortality.

**Results:** 418 patients exposed to TRT were matched with 283 controls. The median (IQR) age (years), and the prevalence of established CVD (%), in the TRT exposed group vs. the control group were 53.8 (47.3, 60.1) vs. 54.9 (49.9, 61.4), P=0.04 and 9.8% vs. 12.7%, P=0.23, respectively. The median duration of follow-up (years) for the TRT exposed group was 3.8 vs. 3.4 in the control group (P=0.02). The event rate (composite outcome) of the TRT exposed group was 3.3% vs. 6.4% in the control group (P=0.06). Exposure to TRT reduced the odds of the combined cardiovascular endpoint (Hazard Ratio: 0.49; 95% CI: 0.24 to 0.99; p=0.046).

**Discussion:** TRT in hypogonadal men has become a controversial topic over the past decade. There has been continued concern regarding whether or not TRT increases the risk of adverse cardiovascular outcomes or mortality. The available data has been conflicting. The effect of TRT may vary considerably depending on the etiology of low testosterone, the patient’s age, and whether or not they have established CV disease. Our study adds to the growing body of evidence which has suggested TRT may afford a protective effect in certain populations of hypogonadal men. **Conclusion:** In a population of hypogonadal men with a rather low prevalence of established CVD, TRT may conferr a protective effect on the risk of MI, CVA or mortality. These results would support future prospective studies evaluating the effect of TRT in men with secondary hypogonadism.

**Abstract #907**

**BENIGN LEIOMYOMA METASTASIZING TO MULTIPLE ORGANS CASE REPORT AND LITERATURE REVIEW**

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**Case Presentation:** 35y/o G0, presented to the ER complaining of left upper quadrant pain 9/10 on pain scale. Patient denies vaginal bleeding or discharge. The last time the patient visited an Obstetrics and Gynecology specialist was one and a half years ago. The patient had one abdominal myomectomy 2 years prior. On admission the patient has a transvaginal Ultrasound (US) and an abdominal and pelvic Cath scan (CT). The impression on the CT is of a large heterogenous lobular uterus measuring...
19x14x19cm that occupies the entire pelvic (figure 2). In addition, there is a separate mass measuring 4x3.6cm which is adjacent to the uterus. This could represent a pedunculated fibroid on a stalk or enlarged lymph nodes on the iliac chain. Furthermore, the US detects vertebral body sclerotic lesions on L1,2,3,5,T6,10,11,12. No gross reduction or expansion is seen. The radiologist reports that the radiologic structure is not typical for endometrial carcinoma but Leiomyosarcoma should be excluded. The US indicated that there is a huge heterogenous lobular uterus with a structure typical for fibroid uterus. The adnexa and ovaries are not visualized. Tumor markers were drawn as well. HCG, CA 19-9, Alpha-fetoprotein, testosterone total, free, bioavailable and SHBG were all within normal limits. In addition, serum albumin, CA 125 and CEA were all normal. The only nonspecific marker which was found to be elevated was LDH. It was found to be 1592 IU/L. 2 days into admission it was decided to perform a chest CT with no contrast. The impression was of sternal lesions, focal area of pleural thickening at the costophrenic angle, 3 nodules in the right and 8 in the left lung, lytic lesions in the distal end of the left clavicle, mixed lytic and sclerotic lesions in the right fourth rib, sclerotic and destructive changes seen in the anterior aspect of the vertebral body with associated soft tissue mass in the superior mediastinum anterior to the vertebral body. The soft tissue mass measured 4.2 cm. CT guided biopsy was performed, 2 days into the admission from one of the pleural lesions (figure 3). The final histologic report including all specific dyes were of smooth muscle cells with 0 mitotic figures, consistent of benign Leiomyoma. Hormonal treatment was recommended by the oncologist. This was recommended for fertility reasons.

Conclusion: This report is very unusual, rare and creates an ethical challenge due to the fact that the patient has multiple lesions in various organs and was not pregnant yet. More consideration should be given to disease pathogenesis and pathophysiology. A better understanding of the disease will shine light on new and better treatment options.

Abstract #908

AT LONG LAST: SUCCESSFUL PREGNANCY ON GLUTEN-FREE DIET IN A WOMAN WITH SEVEN MISCARRIAGES AND NON-CELIAC GLUTEN SENSITIVITY

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Objective: To describe a case in which a gluten-free diet led to a successful full term delivery in a woman with recurrent miscarriages and non-celiac gluten sensitivity (NCGS).

Methods: Fewer spontaneous abortions have been reported in patients with Celiac disease who adhere to a gluten-free diet, but little is known about improvement in reproductive issues in women with NCGS. We present a case of a woman with recurrent miscarriages and NCGS who successfully carried a pregnancy to term after adopting a gluten-free diet.

Case Presentation: A 33-year-old Caucasian woman presented to the Endocrinology clinic in March 2013 for evaluation of elevated adrenocorticotropic hormone (ACTH) and hypothyroidism. She had a history of recurrent first trimester fetal loss and was on aspirin. Prior workup by her obstetrician showed ACTH level of 64.07pg/mL and cortisol level of 21.6mcg/dL. She reported fatigue for the past 5 years, with improvement on levothyroxine. On exam, body mass index was 24.9, and she did not appear Cushingoid. Thyroid exam was normal. Recheck of ACTH was 16pg/mL, and dexamethasone suppression test showed normal cortisol level (1mcg/dL). Thyroid function tests were within normal limits. Thyroid peroxidase antibody was negative. Over the next year, she had three miscarriages, for a total of seven. The possibility of undiagnosed Celiac disease was considered, as the patient had two cousins with Celiac disease and a sister with gluten sensitivity. Antigliadin IgG antibody was detected, while antigliadin IgA, tissue transglutaminase IgA, and anti-endomysial IgA were negative. Esophagogastroduodenoscopy and biopsy showed normal mucosa. These findings were consistent with a diagnosis of NCGS. The patient was advised to adhere to a gluten-free diet. She became pregnant again, and was able to carry the baby to full term with delivery in June 2016.

Discussion: Lack of Celiac disease-specific serology, positive antigliadin IgG antibodies, and normal biopsy are consistent with NCGS. Gliadin peptides from gluten that resist degradation can trigger an inflammatory response. A possible mechanism for recurrent fetal loss includes immunologic changes in placental function. Gliadin is abundant in extravillous trophoblast that attaches the placenta to the mother. Reduction in antigliadin IgG antibodies after adopting a gluten-free diet has been
reported in a NCGS population. 

**Conclusion:** We present a case in which adherence to a gluten-free diet resulted in a successful full-term pregnancy in a woman with recurrent fetal loss and NCGS. Celiac disease and NCGS are considerations for women with unexplained infertility. Appropriate screening and implementation of a gluten-free diet may help improve pregnancy outcomes.

Abstract #909

**PRIMARY AMENORRHEA AND DIABETES MELLITUS: A CASE REPORT**

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**Case Presentation:** Miss A.O. presented on account of a 3-week history of elevated fasting blood glucose of 332mg/dl and random blood glucose of 389mg/dl on routine employment screening. No history of polyuria, polydipsia and weight loss. History of inability to initiate menstruation since adolescent. Her growth was comparable with other children. Physical examination revealed a phenotypic female with eunuchoid habitus and scoliosis. She had a wide carrying angle and a positive prayer sign with hammer deformity on both fifth finger. Her height was 152cm with a body mass index of 23.6kg/m². She had a longer arm span of 168cm compared to crown to heel measurement. Breast examination was thelarche stage 4, adrenarche was Tanner stage 3 and the vagina was patent.

Random blood glucose at presentation was 204mg/dl. Initial assessment of new onset diabetes mellitus with primary ovarian failure keep in view chromosomal abnormality was made. Hormonal profile showed low levels of estradiol 12.6pg/ml (43-214pg/ml), progesterone 0.4ng/ml (1.5-20ng/ml) and elevated levels of luteinizing hormone 13.6m IU/ml (0.2-6.5m IU/ml), and Follicle Stimulating Hormone (FSH) 57.5mIU/ml (1.5-7.0 mIU/ml). Serum prolactin and serum testosterone were normal. Thyroid hormonal profile was essentially normal with elevated glycated hemoglobin of 12.2%.

Abdominopelvic ultrasound scan and MRI showed hypoplastic uterus with no ovaries seen. DEXA scan of her distal radius gave a T-score of -3.8 (<-2.5) diagnostic of osteoporosis. Her electrocardiogram, echocardiography, and kidney function test were essentially normal, however serum lipid profile showed hypercholesterolemia of 307mg/dl, low density lipoprotein of 216mg/dl and triglycerides 185mg/dl. Chromosomal analysis showed an abnormal female mosaic complement with 17/30 analyzed cell having 45X complement and 13/30 cells showed a pseudo isodicentric X chromosome. A definitive diagnosis of Turner Syndrome, mosaic type was made. She was also counselled on the clinical condition and fertility. She was commenced on subcutaneous novomix (50/50) 10 units twice daily with meals, oral metformin 1g 12 hourly, rosuvastatin 10mg daily, alendronate 10mg daily and thereafter 70mg weekly. She was also commenced on combined oral contraceptive pills to initiate withdrawal bleed after counselling.

She is presently 31 years old and currently engaged. She has been counselled on available fertility options and on follow up at the out-patient clinic.

**Conclusion:** This illustrates a rare case of gonadal dysgenesis with co-existing asymptomatic diabetes mellitus. High index of clinical suspicion is required to avoid a misdiagnosis of secondary causes of diabetes.

Abstract #910

**AMPHETAMINES MAY IMPROVE CHRONIC FATIGUE SYNDROME AND STIFFNESS IN PARKINSON’S DISEASE**

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**Objective:** When a cause of chronic fatigue syndrome cannot be found by the internal medicine specialist, rheumatologist and infectious disease specialists, referral to an endocrinologist to look for an endocrinopathy, e.g., thyroid or adrenal disease may occur. If, however, the endocrinologist rules out an endocrinopathy, it is this specialty that is most familiar with the increased cellular permeability syndrome. There are anecdotal reports of improving chronic fatigue following treatment with amphetamines. The objective of this study was to determine if the fatigue from a man diagnosed with Parkinson’s disease could be relieved with amphetamines.

**Methods:** A 42 year old male with recently diagnosed Parkinson’s disease based on clinical symptoms of
weakness of left arm with stiffness so that it was not swinging with walking. He also dragged his right foot. Clinical signs suggested Parkinson’s and an MRI ruled out other pathological conditions. A tremor was also found in the left arm. He also complained of pain in the mid and upper back. He was started on 15mg amphetamine extended release capsules.

**Case Presentation:** In one month he noticed significant improvement in his fatigue and muscle stiffness. His pain in neck and upper back were also abrogated. He failed to note any improvement in the tremor. He was now able to pick up his newborn baby when he was unable to do so before. His dosage was increased and it will be determined if there is any further improvement.

**Discussion:** Amphetamines cause the release of dopamine from endogenous neurons as well as blockage of dopamine re-uptake. However, in Parkinson’s disease neural stores of dopamine are known to be depleted. Perhaps, at least in early cases, the dopamine stores are not completely depleted and some symptoms may be improved by adding amphetamines. Perhaps amphetamines added to L-DOPA could provide better relief of symptoms of Parkinson’s disease than L-DOPA alone.

**Conclusion:** Though a large randomized controlled study 40 years ago evaluating only 15mg of dextroamphetamine sulfate was not overly impressive in improving symptoms of Parkinson’s disease, there may be some cases where certain aspects of this disorder could be helped by taking amphetamines. For early cases the side effects of dextroamphetamine sulfate are much less severe than L-DOPA.

**Abstract #911**

**INCREASED CELLULAR PERMEABILITY SYNDROME CAUSING MULTI-ORGAN SYSTEM ABNORMALITIES AND RESPONSE TO TREATMENT WITH SYMPATHOMIMETIC AMINES**

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**Objective:** The objective of the study was to determine if a treatment with the sympathomimetic amine dextroamphetamine sulfate could improve a large variety of symptoms from multiple organ systems. Her multiple diagnoses provided by a variety of specialists included neurological/muscular system dysautonomia including 1) orthostatic light headedness, 2) severe muscle spasticity (varying between chronic and sporadic throughout different muscles), 3) pelvic floor dysfunction, 4) bladder sphincter dyssynergia. In addition she had, 5) interstitial cystitis, 6) history of transient ischemia attacks, 7) chronic migraine headaches, 8) low frequency hearing loss, 9) chronic fatigue syndrome, 10) fibromyalgia, 11) cardiovascular/respiratory postural orthostatic tachycardia syndrome (POTS), 12) vasovagal syndrome, 13) labile blood pressure, 14) pulmonic valve stenosis, 15) asthma, 16) chronic hyperventilation syndrome related to functional abnormality of diaphragm, 17) severe constipation, 18) gastroesophageal reflux disorder (GERD), 19) non-functional pituitary adenoma, 20) polycystic ovarian syndrome, 21) pelvic pain (endometriosis).

**Methods:** The patient was treated with dextroamphetamine sulfate in the form of amphetamine salts. She was started on 15mg extended release capsules which was increased to 30mg extended release capsules a.m. and 30mg twice daily amphetamine salts immediate release tablet. As part of her diagnostic tests, she had a muscle biopsy and evaluation of mitochondria.

**Case Presentation:** She had marked improvement in almost all of her symptoms except the polycystic ovarian syndrome. She has had relief of most of her bladder symptoms, bladder pain, pelvic pain, fibromyalgia and constipation and significant improvement in her chronic fatigue, postural hypotension, migraines, and muscle spasticity. There was no improvement in her mild asthma. Her low frequency hearing loss was not retested. She had previously failed to demonstrate any significant improvement despite a potpourri of previous treatments. She has been treated for 2 ½ years. The biopsy was consistent with the mitochondrial disorder known as the mitochondrial encephalopathy lactic acidosis stroke-like syndrome (MELAS).

**Discussion:** This is the second case of MELAS syndrome treated by amphetamines. The first case was wheelchair ridden for 25 years and now walks with no problems and feels completely better.

**Conclusion:** Even when pelvic pain is only a minor part of a constellation of symptoms the reproductive endocrinologist should consider treatment with dextroamphetamine sulfate first to see how many other symptoms before referring to a potpourri of different specialists.
Abstract #912

MARKED EFFICACY OF SYMPATHOMIMETIC AMINE TREATMENT FOR CHRONIC RECURRING PREMENSTRUAL URTICARIA

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Objective: Progesterone (P) is hypothesized to inhibit dopamine secretion. There is evidence that one function of dopamine is to inhibit cellular permeability allowing unwanted irritants to infiltrate the uterus causing a purposeful inflammation of the endometrium for the first 6 days after ovulation to allow uterine remodeling of the implantation site. Thus other conditions related to permeability defects may be exacerbated premenstrually because of P secretion. Leakage of histamines from its vesicles could possibly occur only during the premenstrual time related to this increased cellular permeability thus causing urticaria occurring only premenstrually. The objective of this study was to determine if treatment with the sympathomimetic amine dextroamphetamine sulfate, which is known to improve many chronic disorders related to increased cellular permeability, could abrogate premenstrual hives in a young woman.

Methods: Dextroamphetamine sulfate in the form of amphetamine salts was prescribed for a 17 year old female with a 2 year history of severe premenstrual urticaria beginning 5 days before expected menses. She also suffered with severe dysmenorrhea which also had a premenstrual component.

Case Presentation: The urticaria and dysmenorrhea were both markedly improved with a daily dosage of 55mg amphetamine salts extended release capsules daily with an extra 15mg beginning 7 days before menses. Benefits of this treatment has persisted for 3 years now.

Discussion: It is not surprising that amphetamines helped the pelvic pain and urticaria since this therapy has been shown to provide marked improvement for women with pelvic pain of all types and patients (male or female) with chronic refractory urticaria. This case is discussed to provide support for the concept that progesterone suppresses dopamine which leads to a generalized increase in cellular permeability. Tissues that are more permeable may allow entry of otherwise precluded elements that can cause inflammation and possibly subsequent pain. Increased permeability can cause irritants, e.g., histamines to leak out of vesicles, and lead to urticaria especially if a pre-existing vesicle membrane weakness exists.

Conclusion: Premenstrual urticaria can be added to the long list of symptoms that can occur premenstrually including anxiety disorders, headaches, dysmenorrhea, backaches, fatigue, and other unusual symptoms restricted to this time. The concept of progesterone causing increased cellularity, can explain the symptomatology of the increased cellular permeability syndrome occurring only premenstrually.

Abstract #913

THE INCREASED CELLULAR PERMEABILITY SYNDROME AS THE ETIOLOGIC FACTOR IN EXERCISE INDUCED PRURITUS AND DERMATOGRAPHIA AND RESPIRATORY DISTRESS

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Objective: Sympathomimetic amine therapy has been found to improve chronic urticaria, cold induced urticaria, and premenstrual urticaria. The objective of this study was to determine if this treatment will improve a rare case of exercise induced urticaria.

Methods: A 25 year old athlete who trains for the triathlon noticed that with severe exercise she would suddenly develop severe generalized pruritus and shortness of breath associated with wheezing. She had other symptoms not associated with exercise including severe dysmenorrhea, back, joint, and rib pain, and hyperesthesia. She had a cardiopulmonary exercise test performed which was perfectly normal and the conclusions were that she has no exercise limitation. She was treated with albuterol but only had a 25% reduction in shortness of breath and wheezing but no improvement in the severe pruritus. She was referred by a physician aware of the increased cellular permeability syndrome to not only treat the dysmenorrhea with dextroamphetamine, but possibly also help her urticaria and respiratory distress.

Case Presentation: The dosage of amphetamine salts extended release capsules was gradually increased to 30mg/day. With that dosage she has complete relief of her pelvic pain, the fibromyalgia and the exercise induced asthmatic reactions. The pruritus was 90% improved. She is successfully training for the triathlon.

Discussion: The reproductive endocrinologist frequently is asked to treat dysmenorrhea which is generally considered by most reproductive endocrinologists and gynecologists to be related to endometriosis. Because surgery is generally not effective, with recurring pain likely to return, most reproductive endocrinologists not familiar with the increased cellular permeability may elect
to treat with gonadotropin releasing hormone agonists, e.g., leuprolide acetate, or estrogen/progestin combination or impeded androgens. If these hormonal therapies were used, the dysmenorrhea may have improved but not any of the other symptomatology related to the increased cellular permeability syndrome.

**Conclusion:** Extreme exercise anaphylactic type reaction can be added to the long list of conditions that respond to sympathomimetic amine therapy. When a woman complains of dysmenorrhea but also other medical conditions, if the gynecologist or reproductive endocrinologist is going to treat the dysmenorrhea with amphetamines, that physician should want to see what other medical conditions improve before referring the patient to other specialists.

Abstract #914

**MARKED IMPROVEMENT OF SEVERE PREMENSTRUAL KNEE SWELLING AND PAIN AND PREMENSTRUAL DYSMENORRHEA FOLLOWING TREATMENT WITH LOW DOSAGE DEXTROAMPHETAMINE SULFATE**

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**Objective:** To determine if treatment with dextroamphetamine sulfate can ameliorate severe premenstrual knee swelling and pain.

**Methods:** At the age of 16 a young lady developed swelling in both knees that would only occur beginning one week before expected menses. The swelling was so great that she needed to wear wider pants premenstrually. She rated the pain as a 7 on a 0-10 scale. Her knee pain became chronic at a level of 4 but the severe swelling only occurred during the premenstrual time when the pain exacerbated to a 9 of 10. The pain and swelling peaked at age 25 and she did not respond at all to plaquenil. She also failed to respond to two arthroscopic surgeries. She was started on 15mg amphetamine salts extended release capsules. Eventually she added a second capsule at noon just the week before menses.

**Case Presentation:** Even with just 15mg of amphetamine salts daily in the morning she noticed a marked improvement in the premenstrual swelling and pain, with just mild swelling premenstrually. With the additional increase in dosage of 15mg at noon, the swelling and pain completely dissipated. The improvement has persisted for 1 year.

**Discussion:** Symptoms that start just during the luteal phase in the past had been considered to be related to inadequate progesterone secretion. However, most times there is disappointment with progesterone therapy related to failure to improve symptomatology including emotional disturbances (premenstrual syndrome). Recent concepts consider the fact one of the roles of progesterone is to suppress dopamine, causing increased cellular permeability and thus allowing infiltration of the endometrium by irritating elements that causes a purposeful inflammatory response in the endometrium. This allows the conversion of thick walled uterine arteries into thin walled spinal arterioles which allow nutrient exchange from mother to fetus. The increased cellular permeability may also allow infiltration of irritating elements into other tissues, e.g., the knees, causing pain and swelling.

**Conclusion:** Even when the organ system seems out of the normal domain for the reproductive endocrinologist, all conditions restricted to the premenstrual time should be considered possibly related to the effect of progesterone in causing increased tissue permeability by suppressing dopamine. Thus treatment with sympathomimetic amines should be considered as the first treatment rendered. Unfortunately, specialists outside of the endocrinology field are not familiar with the increased cellular permeability syndrome so treatment with amphetamines is prescribed by the endocrinologist rather than rheumatologist or orthopedist.

Abstract #915

**THE CONFOUNDING EFFECT OF PREGNANCY ON HEADACHES FROM INTRACRANIAL HYPERTENSION (PSEUDOTUMOR CEREBRI) THAT WAS TREATED WITH DEXTROAMPHETAMINE SULFATE DURING THE FIRST TRIMESTER**

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**Objective:** To determine if headaches would resume during the second and/or third trimester in a woman with intracranial hypertension who responded well before and after conception with amphetamines but stopped the drug after the first trimester at the wishes of her obstetrician.

**Methods:** A 34-year-old woman with a two-year history of severe migraine headaches and papilledema was diagnosed with intracranial hypertension one a brain tumor or aneurysm was excluded by magnetic resonance imaging. She was treated with acetazolamide but only gained partial relief. She also did not like the side effects of acetazolamide which included a prolonged bad taste in her mouth and paresthesias of her fingers. She was switched to amphetamine salts 15mg
extended relief capsule especially because acetazolamide was not considered safe in pregnancy whereas amphetamines have a higher safety profile.

**Case Presentation:** The woman was helped to conceive initially with triplets which self reduced to twins. Her headaches were completely abrogated both before she conceived and during the first trimester. The amphetamines were dropped at 14 weeks based on the wishes of her obstetrician. The headaches did not resume throughout the pregnancy or post-partum until 7 months later when both the papilledema and headaches resumed.

**Discussion:** The opinion of the doctors in our practice was that the high levels of estrogen during the pregnancy and the fluid retention that frequently occurs would probably cause her headaches to resume. She agreed to restart the amphetamines if they did re-occur. Surprisingly they did not and not until 7 months’ post-partum. The headaches quickly disappeared as did the papilledema once the amphetamines were restarted.

**Conclusion:** It is not clear why pregnancy would have an ameliorative effect on intracranial hypertension but it did.

**Abstract #916**

COMPLETE RESOLUTION OF THE BURNING MOUTH SYNDROME IN A NORMAL ESTROGENIC WOMAN FOLLOWING TREATMENT WITH AMPHETAMINES

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**Objective:** The burning mouth syndrome, though rare, is frequently seen in menopausal women with estrogen deficiency when it occurs. It may improve with estrogen therapy. The purpose of this study was to determine if treatment of a normal estrogenic woman with the burning mouth syndrome may improve following treatment with the sympathomimetic amine dextroamphetamine sulfate.

**Methods:** Dextroamphetamine sulfate, in the form of amphetamine salts 15mg extended release capsules, was started on a woman with a 4 year history of the burning mouth syndrome. The dosage would be increased until adequate relief was noted or 60mg was reached without improvement.

**Case Presentation:** When a dosage of 45mg was reached the burning mouth syndrome was almost completely eradicated. She continued with the amphetamine salts during her pregnancy (this drug was also prescribed to help solve her infertility program). She continued it throughout the pregnancy, but stopped during nursing. The burning mouth symptoms returned after stopping the drug. She stopped nursing after 12 months and restarted the amphetamines. The pain disappeared again and has remained markedly improved now for 6 months.

**Discussion:** This patient demonstrated no mouth lesions, just pain. Dextroamphetamine sulfate has also been shown to cause dramatic improvement of another painful mouth condition known as recurrent aphthous stomatitis. Evidence supports the concept that these disorders are related to increased cellular permeability defect in the mouth tissues. The dextroamphetamine sulfate is thought to exert its beneficial effect by causing the release of dopamine from sympathetic nerve fibers, and this diminishes cellular permeability. The amphetamines were continued during pregnancy because of data suggesting that treatment with amphetamines may help prevent miscarriage by inhibiting excessive absorption of irritants into the uterus creating a greater number of cellular immune cells that could lead to damage to the fetal semi-allograft.

**Conclusion:** The burning mouth syndrome may be added to the long list of chronic pain disorders refractory to standard therapy that responds very well to sympathomimetic amines. Though just one case report, this case clearly fulfills the criteria of Koch’s postulates.

**Abstract #917**

EFFECT OF INTRANASAL INSULIN ON LH CONCENTRATIONS IN MAN

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**Objective:** One-third of men with type 2 diabetes have hypogonadotropic hypogonadism. Animal studies and in vitro data have shown that insulin action and insulin responsiveness in the brain are necessary for the maintenance of the functional integrity of the hypothalamo-hypophyseal-gonadal axis. Intranasal administration of regular insulin in men is known to increase insulin concentrations in cerebrospinal fluid by 80%. We hypothesized that intranasal insulin administration to men will increase LH concentrations.

**Methods:** We conducted a randomized, placebo, controlled trial to evaluate the effect of one dose of intranasal insulin or saline on LH concentrations in 14 men (8 with type 2 diabetes and 6 healthy lean men). 40 IU of regular insulin (Humulin R) or 0.4 ml of saline were administrated intranasally with vianase device on two different occasions, at least one week apart. Blood samples to measure LH
concentrations were collected every 15 minutes for 5 hours. Study drug was administered intranasally after a 2 hour baseline sampling period. Patients remained fasting throughout the procedure. The primary endpoint of the study was to compare the change in LH concentrations after intranasal insulin as compared to saline. Change was defined as the difference between baseline LH concentrations (average of the 9 samples collected in the two hours prior to drug administration) and average LH concentrations following drug administration (average of the 12 samples collected in the 3 hours).

Results: The mean age, BMI and baseline LH concentrations of men with type 2 diabetes (62±6 years, 34±5 kg/m2 and 7.8±3.5IU/L) were higher than those for lean men (29±7 years, 23±1 kg/m2and 3.6±0.9 IU/L, p<0.01 for all). There was no change in LH concentrations following insulin (0.4±0.7, p=0.17) or saline administration (0.1±1.8, p=0.86) in men with diabetes (mean difference as compared to saline [95% C.I.]: 0.3 [-1.2, 1.7], p=0.70). There was also no change in LH concentrations following insulin (0.1±0.6, p=0.76) or saline administration (0.2±0.8, p=0.58) in lean men (mean difference as compared to saline: -0.1 [-1.1, 0.9], p=0.83). Glucose concentration was measured by fingerstick before drug administration and 30min, 60min and 180min later. The glucose concentrations after insulin administration (average of measurements at 30, 60 and 120 minutes) did not change as compared to baseline in lean men(mean difference as compared to saline: 1 [-8, 9] mg/ dl, p=0.91) or in those with diabetes (mean difference as compared to saline: 2 [-10, 13], p=0.75).

Conclusion: One dose of 40IU of regular insulin administered intranasally does not change LH concentrations acutely in men.

Abstract #918

MORE INSIGHT INTO THE ETIOLOGY OF THE USUAL SUBSEQUENT FETAL DEMIS FOLLOWING A SLOW RISING SERUM HUMAN CHORIONIC GONADOTROPIN LEVEL EVEN WHEN VIABILITY IS SEEN DURING THE FIRST TRIMESTER

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Objective: To perform an autopsy and chromosome analysis on a fetus with a second trimester miscarriage where there was demonstrated inadequate rate of rise of sera beta human chorionic gonadotropin (b-hCG) levels during the first trimester.

Methods: Though finding a pregnancy with slower than normal rising serial b-hCG levels demonstrating fetal viability after the first trimester is rare, the hope was to find such a case that had a second trimester miscarriage so that an autopsy and chromosome analysis could be performed to shed more light on the cause of miscarriage. Physicians and nurses were alerted and frequently reminded to be on the lookout for such a case.

Case Presentation: One case was found that had a second trimester miscarriage with fetal demise at 22 weeks detected by ultrasound. The last time viability had been determined was 16 weeks. By the size of the fetus, death seemed to occur shortly before 22 weeks. The failure of levels of hCG to rise properly began when her level of 2375 mlU/mL only increased to 4084 mlU/mL 3 days later (a level ~ 6000 mlU/mL may have been expected). Subsequently the 4084 mlU/mL level only increased to 6071 mlU/mL (expected 10,000 mlU/mL). There were no abnormal autopsy results. All organs appeared normal. Chromosome analysis showed a normal male.

Discussion: During this 10 year period there were 4 cases that had viability past the first trimester despite the demonstration of a slow rising b-hCG level. The large majority of women showing viability at 8 weeks but slow rising b-hCG levels had a miscarriage before 12 weeks. However, 3 of the 4 cases with viability by ultrasound at 12 weeks delivered live healthy babies. The large majority of women with a slow rising b-hCG level in the first trimester will have a miscarriage in the first trimester even if viability is seen at 8 weeks. Possible causes of miscarriage could be an organ abnormality that allows fetal life to a certain point before death occurs. Organ abnormalities could be related to a trisomy. If so, it would be interesting to see which trisomy may be more consistent with later rather than earlier miscarriages. However, the cause of death in this case was unexplained. HCG is made by placental cells. Since this patient was supported with extra progesterone (P) supplementation, a deficiency of P by inadequate hCG stimulation of the corpus luteum is not a likely cause of the second trimester loss.

Conclusion: These data are most consistent with a slow rising hCG level not as the cause of miscarriage but a marker for a placental disorder which leads to subsequent pregnancy loss in most cases.
Abstract #919

NORMAL SPERMATOGENESIS 32 YEARS LATER DESPITE CHEMOTHERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA AND TOTAL BODY IRRADIATION FOR BONE MARROW TRANSPLANT

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Objective: To present a second case of normal spermatogenesis 3 decades later following intense chemotherapy for childhood leukemia and bone marrow transplant and the first where total body irradiation was used for bone marrow conditioning.

Methods: A 37-year-old male and his 32-year-old wife presented with infertility. He gave a history of intense chemotherapy for acute lymphoblastic leukemia at age 3. This was followed by total body irradiation and more intense chemotherapy at age 5. As part of the infertility work-up a semen analysis was performed.

Case Presentation: The semen analysis showed a volume of 3.2 mL, sperm concentration of 32 million/mL, 54% motility, with a motile density of 17.3 million/mL, and strict morphology showing 7% normal morphology and a hypo-osmotic swelling test of 87% (semen considered perfectly normal).

Discussion: A review of the literature only found one other case report of a normal semen analysis following bone marrow conditioning for acute leukemia. In that case the bone marrow suppression was performed by chemotherapy rather than total body irradiation. The clinical bone marrow suppression by chemotherapy as opposed to total body irradiation was thought to be less toxic to subsequent spermatogenesis. Also, the semen analysis was performed only 5 years after the bone marrow transplant in the previous published case rather than 32 years in the patient described herein. The previous case report also involved acute myelogenous leukemia. Also, the treatment was started as a young adult in the former case not as a child in the present case.

Conclusion: This case shows that normal spermatogenesis is possible even 30 years later despite bone marrow conditioning even using total body irradiation and intense chemotherapy. It is not clear why a rare case can be resistant to damage to spermatogenesis despite intense radiation and chemotherapy. Perhaps this case could generate a hypothesis by some other scientist or clinician who is made aware of this case to propose a method to prospectively protect other children who need a bone marrow transplant and intensive chemotherapy for childhood leukemia or other cancers.

Abstract #920

A CASE OF POLYCYSTIC OVARIAN SYNDROME WITH SUBSEQUENT DEVELOPMENT OF LUTEINIZING HORMONE (LH) DEFICIENCY HELPS TO DEFINE THE ROLE OF THE LH/ FOLLICLE STIMULATING HORMONE (FSH) RATIO SERUM TESTOSTERONE (T) AND ANTIMULLERIAN HORMONE (AMH) IN THE DEVELOPMENT OF THE OVARIAN HYPERSTIMULATION SYNDROME (OHSS) FOLLOWING CONTROLLED OVARIAN HYPERSTIMULATION (COH)

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Objective: To determine what role does the endogenous high LH serum levels, high LH/FSH ratio and increased serum T levels play on the development of ovarian hyperstimulation syndrome in women with polycystic ovarian syndrome (PCOS) treated with COH.

Methods: Sera levels of LH, FSH, T, AMH, thyroid stimulating hormone (TSH), free thyroxine (T4) along with ultrasound evaluation of ovaries were obtained at different times of change of menstrual status from oligomenorrhea in a hyperestrous environment to estrogen deficiency environment related to severe LH deficiency. The study would then determine the type of ovarian response to COH in a woman with PCOS with now superimposed LH deficiency.

Case Presentation: Her menstrual status at age 16, 25, 27, and 28 were oligomenorrhea with normal estrogen at age 26, and amenorrhea with estrogen deficient for 25, 27, and 28. The sera LH (mIU/mL) at these ages were 18.4, 3.9, 2.0, and <1. The FSH (mIU/mL) levels were: 4.4, 9.2, 5.9, AND 4.0. The T (ng/mL) levels were 55.0, 20.0, 12.9 and not measured. A serum AMH (ng/mL) was only measured at age 28 and was 12.4 ng/mL. Thyroid levels were normal at all ages. Ultrasound appearance suggested PCOS at all ages. Her serum prolactin was 4.3 ng/mL at age 27. IVF was required because there were only 2 vials of frozen sperm obtained prior to orchiectomy and chemotherapy for testicular cancer. She conceived with twins following the transfer of 2 embryos on day 3. She was given a relatively low dose gonadotropin stimulation regimen which included LH.

Discussion: These results are consistent with the hypothesis that she developed a pituitary microgonadotropinoma secreting FSH only that damaged her normal gonadotropin secreting cells to explain the initial increase in FSH from low normal to top normal and its detection in low normal ranges despite LH not measurable when in vitro
fertilization (IVF) was started. Unfortunately, no pituitary MRI was performed. Her response to gonadotropin and ultrasound appearance eliminated the possibility of ovarian tumor secreting AMH.

**Conclusion:** These results show that high level of endogenous LH is not a prerequisite for developing OHSS in women with PCOS. Her exuberant response confirms that only a small amount of LH is needed to allow for development to dominant follicles. These results show that POCs is an intrinsic disease possibly caused by an increased basal AMH level preventing androgen dominant follicles from progressing to estrogen dominant follicles by the inhibiting effect of AMH on FSH induced aromatase activity.

**Abstract #921**

**TESTOSTERONE INDUCES AMP KINASE-α EXPRESSION**

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**Objective:** AMP kinase-α induces phosphorylation of AKT kinase, thus activating it. This, in turn, results in the transport of GLUT4 to the membrane to increase glucose transport. This mechanism, though independent of insulin action, can amplify insulin signal transduction since insulin action also involves AKT kinase and GLUT4. AMP kinase is important in mediating the action of exercise and in enhancing glucose transport. This pathway also mediates the action of adrenergic stimulation and metformin treatment. Following our recent observation that type 2 diabetes (T2DM) with hypogonadotropic hypogonadism (HH) is associated with increased insulin resistance by 36% when compared with eugonadal T2DM and that this reverses with testosterone replacement, and that there is a concomitant fall in fasting blood glucose concentrations, we hypothesized that this phenomenon may be associated with an increase in cellular AMP kinase.

**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. 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 after HEC procedure on each occasion.

**Results:** The expression of AMP kinaseα was significantly lower by 37% and 29%, in adipose tissue and muscle, respectively, from HH patients compared to eugonadal patients and did not respond to hyperinsulinemia (clamp) in either tissue in HH patients at baseline.

**Discussion:** Following testosterone replacement, the expression of AMP kinase-α did not alter in the fasting state but increased markedly by 41±9% and 46±11% in adipose tissue and muscle, respectively, after the infusion of insulin and glucose during the clamp procedure.

**Conclusion:** We conclude that testosterone modulates insulin and glucose induced expression of AMP kinaseα. This may contribute to the improved insulin sensitivity and glucose homeostasis after testosterone replacement.

**Abstract #922**

**AGE DISTRIBUTION OF MYOCARDIAL INFARCTION PATIENTS ON TESTOSTERONE: THE LOW T EXPERIENCE**

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Low T Institute

**Objective:** There are ongoing concerns for safety with testosterone therapy. Our goal was to assess if MI occur at an earlier age in patients with testosterone therapy among our Low T Center patients. These 48 community based centers across the United States have strict protocols requiring regular 1-2 week monitoring in the office for efficacy and safety.

**Methods:** Following IRB application and GCP training, we conducted a retrospective analysis of patients that had MI post testosterone therapy. Data was extracted from our electronic health record (Advance MD) of the multi-site Low T Centers. Prior to extraction of data; ICD-9 were updated to ICD-10, with attention to MI. We also did case findings on patients that had MI and reviewed risk factors.

**Results:** A total of 96,065 charts of patients seen between years 2009-2016 were reviewed. Using ICD definition of MI (ICD 9: 412 & ICD-10: I21.29), there were 174 identified cases of MI, giving an overall prevalence of 1.8 cases per 1000 male adults. The rate of MI by age is reported below: <40=0.03%, 40-60=0.2%, 61-80=0.62%, >80=0. The rate of MI was compared to the NHANES data set which was <40=0.3%, 40-60=3.3%, 61-80=11.3%, >80=17.3% respectively. Comparative statistics were applied for the 2 groups and the rate ratio (RR) for MI in the Low T group versus the NHANES group was 0.1, 0.06, 0.05, 0 (p=0.0001) respectively. The rate of increase of MI with age in both data set was compared for those <40 to 80 years (R2=0.99, C.I. 14-74-22.7)

**Discussion:** Patients who get MIs may or may not be receiving testosterone concurrently. The rate of MI appears
to be a function of age. We find that our rate of MI increases with age, akin to other population data sets, except after 80. We postulate that we have few patients (147) in that age group and hence did not detect MI. Testosterone treated patients in our cohort have consistently lower rates of MI than community based models at every age group. **Conclusion:** This study further supports a non-associative role of testosterone with MI, and even suggesting a protective effect of testosterone against MI, considering finding lower rates of MI in all age groups with patients on testosterone as compared to a general community sample. Our study shows that there is no evidence to suggest that testosterone leads to the development of MI at an earlier age. MI rates rises with age in testosterone treated patients like in community models. There are limitations to this observational study and causal links cannot be established.  

**Abstract #923**

**WHERE IS IT? THE HUNT FOR AN ECTOPIC ACTH DEPENDENT CANCER**

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WVU

**Case Presentation:** Female cervical neuroendocrine carcinomas are incredibly rare (less than 1-2% of all cervical cancers) and of these, presentations as Cushing’s with ACTH/cortisol producing tumors are even more uncommon. Survival is very poor among these patients and there is not a clear cut treatment. Treatment options include surgery and chemoradiation but the disease is well known to be aggressive and the earlier the diagnosis, the better the prognosis. Patient A.S. was a 35 year old female with generalized worsening fatigue and weakness with a previous diagnosis 5 months ago of untreated Cushing’s disease. She had elevated glucose, creatinine, CEA, CA125, CA 19-9, with low potassium, pancytopenia, and hypertensive emergency. Exam demonstrated a Cushingoid appearance including the classic buffalo hump, hirsutism, purple striae along her thighs and abdomen, lower extremity edema, central weakness, and supraclavicular fat pads. She failed a dexamethasone stimulation test both high and low dose and was diagnosed with ACTH dependent Cushing’s syndrome. Imaging of the brain and abdomen was not helpful in finding a source of the cancer in the most likely locations: the pituitary, lung, and the adrenals. Two weeks after her initial admission a PET scan and Pap smear revealed her diagnosis: High grade metastatic neuroendocrine carcinoma of the cervix. The unusual nature and location of her disease made for a prolonged diagnosis and likely further spread of her disease. The patient underwent one round of chemotherapy. After, she developed fever and altered mental status. She was eventually intubated due to AMS and was never able to be extubated successfully. It was believed that her disease had spread to her brain with hemorrhagic metastasis. The patient passed away only 6 weeks after her initial admission. **Conclusion:** The importance of this case lies in its rarity. Very few cases are reported in literature about neuroendocrine tumors of the cervix and most of those are small cell carcinomas. There is one case report of diagnosis after presenting with Cushing’s syndrome. We hope to add to the literature so that diagnosis of these tumors can be expedited with faster treatment.  

**Abstract #924**

**DIAGNOSING 5-ALPHA REDUCTASE DEFICIENCY IN TWO ADULT BROTHERS**

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Wright State University

**Case Presentation:** A 25-year-old male presented for microphallus and cryptorchidism. He recently underwent hypospadias repair, and reports that his younger brother recently had the same procedure as well. Physical exam revealed a male with normal outward virilization but with microphallus and cryptorchidism. The rest of the physical exam and vital signs were normal. Labs indicated normal total (839 pg/ml) and free testosterone (144 pg/ml) with low (15 NG/dL) DHT. Ultrason sound showed small undescended, but otherwise normal-appearing testicles. Treatment with 2.5% DHT cream applied locally to the scrotum and penis led to increase in the length and girth of penile shaft and development of the scrotum. Serum DHT levels increased to 226. Genetic testing confirmed homozygous mutation of the SRD5A2 gene for 5-alpha reductase with mutation at c.623C>T, a variant of uncertain significance. His 21-year-old brother had microphallus and cryptorchidism. His lab studies were similar, with elevated total (632 pg/ml) and free testosterone (166 pg/ml) and undetectable levels of DHT. Genetic testing is currently pending. **Conclusion:** Five-alpha reductase is an intracellular enzyme responsible for converting testosterone to DHT. DHT is responsible for development of the male external genitalia, urethra, and prostate.1 Deficiency of DHT production is due to inherited mutation of the SRDA2 gene. More than 850 single nucleotide polymorphisms have been reported, though only a few of these
polymorphisms affect enzyme activity.2 Our patient has a single nucleotide mutation at c.623, which has not been previously recognized to cause this disorder. Treatment for 5-alpha reductase deficiency is through DHT replacement. DHT cream has shown benefit in the pediatric population1 as well as for the adult patient in this case. Five-alpha reductase deficiency is rare and the majority of cases are diagnosed in childhood or early pubertal years. Our case of discovery in two adult males emphasizes the importance of considering congenital causes for disorders in the adult patient.

Abstract #925

TOPICAL TESTOSTERONE THERAPY ADHERENCE AMONG MALES WITH PRIMARY OR SECONDARY HYPOGONADISM

Michael Grabner, PhD1, Zsolt Hepp, PharmD2, Amit Raval, PhD1, Mohit Khera, MD3


Objective: Low medication adherence is often associated with suboptimal clinical outcomes. This study used a real-world commercially insured population of males with primary or secondary hypogonadism (HG) to estimate adherence to topical testosterone therapy (TTh), and to compare baseline characteristics and follow-up outcomes between adherent and non-adherent patients.

Methods: A retrospective cohort of male patients aged 18+ years, who were diagnosed with primary or secondary HG and initiated topical TTh between January 1, 2006, and September 30, 2015, was identified in the HealthCore Integrated Research Database, which contains administrative claims associated with a large commercial U.S. health plan. All patients were required to have at least 12 months of health plan enrollment prior to (baseline) and after (follow-up) their initial topical TTh prescription fill. Comorbidities were assessed using ICD-9-CM codes. Adherence to the initial topical TTh was defined as PDC (Proportion of Days Covered) ≥80% during 12 months of follow-up. Total testosterone results were available for a subset of patients.

Results: We identified 3,184 topical TTh initiators, of whom 17% (n=538) were adherent and 83% (n=2,646) were non-adherent. Mean age was 49 years. Mean (SD) number of topical TTh fills over 12 months was 6 (3.8), with a mean (SD) of 49 (45.3) days between fills. Compared to non-adherent patients, adherent patients had a higher share of initial topical TTh fills over 12 months was 6 (3.8), with a mean (SD) of 49 (45.3) days between fills. Compared to non-adherent patients, adherent patients had a higher share of initial topical TTh prescription fills from endocrinologists (38% vs. 31%), a lower share from primary care physicians (35% vs. 44%), and a lower baseline comorbidity burden, including coronary heart disease (9% vs. 13%), depression (24% vs. 29%), hypertension (40% vs. 49%), insomnia (20% vs. 24%), and obesity (9% vs. 15%; all p-values <0.05). Among the subset of patients with available lab results (n=210 adherent, n=839 non-adherent), approximately 65% had low testosterone levels (<250 ng/dL) at baseline. At follow-up, the increase in testosterone was larger among adherent patients (change of 239 ng/dL vs. 165 ng/dL, p<0.01).

Discussion: Study findings provide further evidence for suboptimal topical TTh adherence among men treated for HG. Presence of comorbidities may adversely affect adherence. While all patients experienced an improvement in their testosterone levels between topical TTh initiation and end of follow-up, the increase was more pronounced among adherent patients.

Conclusion: Suboptimal topical TTh adherence suggests unmet need and scope for improved health outcomes in this population of men with HG.

Abstract #926

LOW FGF2 IN MALES WITH HYPOGONADOTROPIC HYPOGONADISM IN DIABETES: INCREASE AFTER TESTOSTERONE REPLACEMENT

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Objective: Basic Fibroblast growth factor (FGF2) is an important stimulatory modulator of satellite cells in the skeletal muscle which have a cardinal role in muscle growth and repair. We hypothesized that the plasma FGF-2 levels and skeletal muscle expression of FGF2 and FGF receptor-2 (FGFR2) in patients with hypogonadotropic hypogonadism (HH) and type 2 diabetes (T2DM) are reduced and that testosterone replacement results in the restoration of levels of FGF2.

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 while the other 10 were injected with saline. Fasting blood was collected before and at 15 and 25 weeks following treatment. Quadriceps muscle biopsies were obtained before and after euglycemic hyperinsulinemic clamps (EHC) prior to and after treatment with testosterone.

Results: The expression of FGF2 and FGFR2 in skeletal muscle of HH patients were significantly lower than that in eugonadal patients by 57% and 39%, respectively (p<0.05). Following 24 weeks of testosterone replacement
to achieve mid normal testosterone levels in plasma, the expression of FGF2, but not FGFR2, increased significantly by 134±45% and was comparable to those in eugonadal patients. While the infusion of insulin during EHC in HH patients raised the expression of FGF2 significantly (by 142±37%) to levels comparable to those in eugonadal patients, there was no significant increase of FGF2 expression in eugonadal patients after EHC. Insulin infusion during EHC increased FGFR2 expression by 53±19% in eugonadal and by 86±26% in HH patients with no effect of testosterone treatment. Plasma FGF2 concentrations were similar in both groups at baseline but increased significantly (by 37±15%) following testosterone treatment.

**Discussion:** These data show for the first time that testosterone is a major modulator of FGF2 expression and that insulin also has an acute potent stimulatory effect on FGF2 and FGFR2 expression. Testosterone also induced an increase in plasma concentration of FGF2. Our previous work has shown that testosterone is an insulin sensitizer and thus it would appear that the two hormones work in concert to ensure appropriate growth and repair of the skeletal muscle.

**Conclusion:** These observations on HH and testosterone replacement are of clinical relevance to patients with hypogonadism, those with muscle injury and body builders.

**Abstract #927**

**AZOOSPERMIA IN A 32 YEAR OLD NIGERIA MALE WHO PRESENTED WITH GYNAECOMASIA - A CASE REPORT AND REVIEW OF LITERATURE**

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**Objective:** A case report of Nigeria male who presented on account of bilateral gynaecomastia and was found to be azoospermic on investigation with a view to draw attention of clinicians to underling endocrine problems associated with gynaecomasia.

**Methods:** A case report of a 32 year old Nigeria male who presented with progressive bilateral breast enlargement was reviewed.

**Case Presentation:** A 32 year old Nigeria male with bilateral breast enlargement since 2013 presented to the endocrine clinic on account of the progressive increase in size of the breast which was protruding from his cloth. There was positive history of occasional pain from the breast. No history suggestive of kidney, thyroid nor liver diseases. No history of use of recreational drugs nor any other drugs. Does not smoke but occasionally takes alcohol. No history of erectile dysfunction or previous surgery to the pelvic region. Had similar problem at age of 18years for which he was given some drugs by a nurse. On examination, the breasts were enlarged 3.5cm bilaterally and there were testicular atrophy (5ml with orchidometer). Other physical examinations were normal. Investigations showed elevated LH ( 82miu/ml), FSH (53.94miu/ml) and prolactin (878.90uIU/ml) with normal testosterone, estradiol, bHCG, liver function test and electrolyte and creatinine. Testicular ultrasound shows bilateral testicular atrophy with varicocele and semen analysis was azoospermic. Brain MRI. Shows pituitary microadenoma

Patient was commenced on carbegoline and refers to the urologist for surgery. Had varicocelectomy done. Follow up at 2months post surgery shows reduction in breast size to 1.2cm bilaterally and increase in testicular size to 15ml bilaterally using orchidometer. He was to continue with drugs and come back for hormonal assays and seminal analysis.

**Discussion:** Gynecomastia is enlargement of the male breast palpable >2cm and results from an imbalance in the hormonal environment in the body, with a relative excess of estrogens (female hormones) when compared to androgens (male hormones). Gynecomastia can result as a side effect of numerous medications and drugs of abuse. Gynecomastia is associated with certain medical conditions including hyperthyroidism, chronic kidney failure, cirrhosis of the liver, hypogonadism which could be primary or secondary. Rarely, hyperprolactinemia may lead to gynecomastia through its effects on the hypothalamus to cause central hypogonadism.

**Conclusion:** Early referral of patients with gynaecomasia to endocrine clinic is necessary for adequate clinical and biochemical assessment to determine the cause and prompt treatment to prevent irreversible complications.

**Abstract #928**

**THYROTOXIC PERIODIC PARALYSIS**

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**Objective:** Thyrotoxic periodic paralysis (TTP) is a rare condition that occurs usually in men of Asian and Hispanic heritage with high thyroid hormone levels. The incidence in 2% in thyrotoxicosis patients. The lower extremities are most often affected. Hypokalemia results in TTP due to intracellular shift in potassium induced by thyroid hormone sensitization of Na-K-ATPase rather
The purpose of this study is to report a case of TTP in an untreated Grave’s disease patient and to point out the importance of recognizing this condition in order to correctly treat it.

Case Presentation: 24 year old male with long-standing history of hyperthyroidism due to Grave’s disease came to the hospital complaining of severe weakness of both lower extremities to the point that he could not get out of bed due to severe muscle weakness. In the ER, the patient was found to have a potassium of 1.6 and therefore admitted. The patient had a history of medical non-compliance and was lost to follow up. He was offered RAI ablation multiple times but refused and was noncompliant with taking methimazole. He had a TSH that was very suppressed at <0.015 and an elevated free T4 of 5, free T3 of 6.12 and total T4 of 22.4. During the hospitalization course the patient was treated with IV steroids, potassium and beta blockers. His potassium improved to 4.6. Upon discharge, he was given tapazole 10mg Q8, inderal 20mg BID, and potassium 25 mEq PO and his paralysis had resolved.

Discussion: Thyrotoxic periodic paralysis is treated with IV steroids, beta blockers and potassium in order to prevent intracellular shift of potassium. Lack of correct recognition of this condition can lead to rebound hyperkalemia if only high doses of potassium are given. Once euthyroid state is achieved, thyrotoxic periodic paralysis is resolved.

Conclusion: The recognition of Thyrotoxic Periodic Paralysis as a condition resulting from excess thyroid hormone is key to correctly treating it and preventing it.

Abstract #929

HASHIMOTO ENCEPHALITIS

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Objective: To report a rare case of Hashimoto disease manifesting as encephalitis

Methods: Patient was examined and interviewed at hospital, and her medical records were reviewed.

Case Presentation: A high-functioning 75 year old female with hypothyroidism presented with agitation, psychosis with hallucinations, memory loss, and frequent falls for 3-4 days. On exam, repetitive coughing and sneezing, lingual and buccal dyskinesias, and slowing of rapid movements were observed.

TSH level was elevated at 5.269 mcIU/mL on admission, but increased to 8.875 mcIU/mL during her stay, and anti-thyroid peroxidase (TPO) antibody titer was elevated at >1000 IU/mL (normal <35 IU/mL). Erythrocyte sedimentation rate and intact PTH were increased at 30 mm/hr (normal <16 mm/hr) and 79.7 pg/mL (normal <72 pg/mL, respectively). Lab tests such as CBC, CMP, proteinase 3 antibody, myleperoxidase antibody, HIV, thyroglobulin antibody, Scl 70, dsDNA, SSaRo and SSbLa, RPR, quantiferon, CSF studies (other than elevated protein at 53.1 mg/dL), AFB, VDRL, West Nile, cryptococcal antigen, fungal culture, Lyme, CMV, CSF H. influenza, strep pneumonia, Group B strep, N. meningitides, and enterovirus were negative. MRI revealed periventricular white matter hyperintensities. With high dose glucocorticoids, the patient’s mental status improved; however, she remained unable to care for herself and sustained significant memory loss and cognitive deficits at least 3 years after discharge.

Discussion: Hashimoto thyroiditis is the most common form of hypothyroidism, with auto-immune injury that impairs glandular function. Antibodies against glandular antigens that cause lymphocytic infiltrate and glandular enlargement can impair response to TSH. Most Hashimoto patients will be euthyroid, with a subsection experiencing transient hyperthyroidism due to premature release of hormone. Treatment is levothyroxine (0.05 to 0.2 mg daily). Anti-TPO antibodies form immune complex depositions, resulting in autoimmune vasculitis and disrupting the cerebral microvasculature, leading to encephalopathy, responsive to steroids or immunomodulation (intravenous immune-globulin and plasma exchange).

Conclusion: In a Hashimoto thyroiditis or hypothyroidism patient, encephalitis with exclusion of other encephalopathy causes and positive anti-TPO antibody titers are consistent with Hashimoto Encephalitis.
Abstract #1000

WHEN TSH IS NOT ENOUGH: A CASE OF PERSISTENT TACHYCARDIA

Aaron Nelson, David Lieb, Jagdeesh Ullal

Objective: Resistance to thyroid hormone (RTH) is most commonly the result of a mutation in the thyroid hormone receptor β gene. This condition has a highly variable clinical presentation but is often associated with goiter and a mixture of hypothyroid and hyperthyroid symptoms. We present a case of RTH associated with tachycardia and discuss methods for treatment.

Case Presentation: A 31 year old male with deafness, asthma and hypertension was evaluated for multinodular goiter and abnormal thyroid function tests. He had longstanding, constant tachycardia of unknown etiology despite high doses of calcium channel blockers. Beta blockers were not tolerated due to asthma. TSH was within normal limits on several instances between 2008 and 2016. He had no symptoms or signs of thyrotoxicosis aside from tachycardia. Deafness was present from birth without severe illness or delayed growth during childhood. He communicates through sign language and reported a 70 lb weight gain over the past 10 years. No history of hearing impairment but a grandmother and a cousin underwent thyroidectomies for unknown reasons. His heart rate ranged from 120-130 beats per minute despite high dose verapamil. Exam showed an obese male with mildly enlarged thyroid without palpable nodules, and was otherwise normal. EKG demonstrated sinus tachycardia, and echocardiogram demonstrated normal left ventricular function and no congenital heart disease.

Thyroid ultrasound demonstrated multinodular goiter without increased vascularity. The two largest nodules were biopsied with benign results. Thyroid antibodies were negative and I-123 uptake scan showed no focal or diffusely increased uptake. Laboratory testing was consistent with resistance to thyroid hormone with TSH 0.36 mcU/ml, free T4 1.9 ng/dl, free T3 4.9 pg/ml, sex hormone binding globulin 14.7nmol/L and alpha subunit 0.4ng/ml. He was started on methimazole 5 mg daily to control his tachycardia. Heart rate improved to 107 bpm with a decrease in free T4 to 1.6 ng/dl and a decrease in free T3 to 4.5 pg/ml. TSH remained stable at 0.33 mcU/ml. He had no increase in weight or development of symptoms of hypothyroidism. Energy level improved subjectively.

Conclusion: Resistance to thyroid hormone is uncommon, but it is important for clinicians to consider this diagnosis during workup of thyroid dysfunction. TSH alone may be misleading and an incorrect diagnosis may lead to unnecessary surgical procedures and/or radioiodine therapy. Treatment of RTH depends on the clinical presentation and methimazole is an option in those patients with tachycardia uncontrolled by rate-lowering medications.

Abstract #1002

SEVERE HYPOTHYROIDISM PRESENTING AS SYMPTOMATIC BRADYCARDIA

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SIU School of Medicine

Case Presentation: A 29 year old woman was brought to the emergency room after a brief episode of syncope while seated at her work desk. She spontaneously recovered before arriving at the hospital. Heart rate was 45-60 bpm, and systolic blood pressure was 80-100 mm Hg. The patient was alert and oriented, though there was significantly delayed recovery phase of deep tendon reflexes. ECG revealed sinus bradycardia with low precordial QRS voltages and absent or attenuated T waves, but QT interval was unremarkable. No pericardial effusion was visible on transthoracic echocardiogram, left ventricular (LV) filling pressure was normal, and LV ejection fraction was estimated at 65-70%. Eight years prior to admission, the patient had received I-131 for treatment of Graves’ thyrotoxicosis. Though she reported good compliance with levothyroxine, serum TSH was > 200 mIU/L (0.34-5.60), and free T4 was 0.1 ng/dL (0.5-1.3). An ACTH stimulation test was unremarkable. The patient was treated with parenteral thyroxine 0.1 mg daily for 72 hr, with improvement of heart rate simultaneous with a four-fold increase in free T4 and recovery of a detectable triiodothyronine (T3) level (30 ng/dL, 87-178). She was discharged home on oral thyroxine 0.125 mg daily (1.6 mcg/kg/d). TSH repeated after approximately 10 weeks of treatment was 1.66 mIU/L, and bradycardia had resolved.

Discussion: Cardiovascular manifestations of hypothyroidism include reduced left ventricular contractility, bradycardia, and increased systemic vascular resistance, resulting in diminished cardiac output. T3 influences sinoatrial node function through both genomic (e.g. expression of hyperpolarization activated cyclic nucleotide-gated channels 2 and 4) and non-genomic (e.g. β-adrenergic receptor pathway activity) mechanisms. Hypothyroidism may also increase QT interval and predispose to ventricular arrhythmias, including the “torsade de pointes” variant of ventricular tachycardia. It is difficult to find an estimate of the prevalence of bradycardia in hypothyroidism, though sinus bradycardia, flattened T waves, and low QRS voltages as observed in this case are well known. LV filling pressure and ejection fraction were surprisingly well preserved given the degree of hypothyroidism, making bradycardia the most likely cause of the patient’s transient loss of consciousness and marginal blood pressure.
**Conclusion:** Thyroid function should be promptly evaluated when patients present with syncope and bradycardia. Screening for primary adrenal insufficiency should be considered before starting thyroid hormone. Treatment with levothyroxine reverses the adverse effects of hypothyroidism on heart rate and LV function.

**Abstract #1001**

**EXTREMELY AGGRESSIVE PAPILLARY THYROID CANCER (PTC) WITH WIDESPREAD METASTASES INCLUDING SPLEEN AND CLEAR CELL RENAL CELL CARCINOMA (RCC) IN ONE PATIENT: AN UNKNOWN SYNDROMIC ENTITY OR MANIFESTATION OF FAMILIAL PTC?**

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**Objective:** Recognize the possibility of inherited thyroid cancer syndromes with PTC and RCC as featured components. The exact genetic etiologies for familial nonmedullary thyroid carcinoma syndromes are not clear. Currently described inherited PTC cancer syndromes, some of which include RCC, are: PTC with Papillary RCC (1q21), PTC-oxphilia (19p13.2), familial clear cell RCC with PTC (t3;8)(p14.2;q24.1), multinodular goiter (14q31) and a few cases of Birt-Hogg-Dubé (BHD) syndrome, an autosomal dominant disorder with cutaneous lesions, lung cysts, spontaneous pneumothorax and both RCC and PTC as key syndromic components.

**Case Presentation:** We present a 69 year-old male with no family history of PTC was diagnosed with stage-IV PTC (pT3, N1b, Mx) in 11/2010, treated with total thyroidectomy and left modified radical neck dissection, and followed by radioactive iodine ablation(RAIA) with 150mCi of 131-I. He was ATA high-risk category with an incomplete response to treatment as the thyroglobulin levels remained consistently high. TSH was at goal of <0.1 uIU/mL. His disease course from 7/2011 to 4/2013 included sternotomy and mediastinal dissection of multiple metastatic PTC mediastinal lymph nodes, re-treatment with 172mCi of 131-I for right orbital and left paranasal uptake on WBS, central neck dissection that removed 2 PTC-positive lymph nodes, and re-treatment with 240mCi of 131-I with increased post-scan uptake in the mediastinum and right lower abdomen. From 7/2013 to 5/2015 he had a PET scan that showed a hypermetabolic retrosternal mass and bilateral internal mammary lymph nodes suspicious for malignancy, a hemisternotomy to resect these metastatic lesions, and bilateral thyroid bed recurrent PTC masses. A renal mass found on surveillance CT imaging was clear-cell RCC on biopsy. He started Pazopanib for RCC and PTC in 1/2014, and had surgical resection of the RCC in 5/2015. In 8/2016, a splenic mass was documented to be metastatic PTC. He was changed to Levatinib. In 11/2016, CT imaging showed progression of disease in the mediastinum and spleen. Levatinib was changed to Sorafenib.

**Discussion:** Our patient fits the constellation of familial clear cell RCC with PTC, and the unusually aggressive behavior of the PTC. Specialized genetic testing of this patient is not generally available, but it may reveal that he belongs to one of the above-mentioned familial PTC-RCC syndromes, or that he may have a novel genomic or sporadic mutation.

**Conclusion:** Familial PTC case reports are rare or unreported. Our presentation of this patient with PTC-RCC adds to the pool of case reports for investigation of a potential inherited or sporadic PTC-RCC syndrome.

**Abstract #1003**

**THYROID CANCER PRESENTING AS SKELETAL METASTASIS: CLINICAL AND PATHOLOGICAL CORRELATES IN 7 PATIENTS**

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**Objective:** To review the clinical, histological and mutation characteristics of thyroid cancer (TC) manifesting as skeletal metastasis.

**Methods:** TC presenting with pathological bone fracture or as spinal cord compression is rare. We retrospectively analyzed the clinical and pathological findings in 7 patients (pts). Archived specimens were retrieved to perform mutation analysis.

**Case Presentation:** Seven pts, 4 men and 3 women presented with bony metastasis from unknown primary cancer. 3 of them manifested acute pathological fracture of long bones. Their age ranged 57 – 77 yrs. Tumor size ranged from 0.6 to 7.5 cm. 3 of the pts had pelvic, 2 had spinal, 1 had humeral and 1 had clavicular sternal metastasis. Pre ablation TG levels ranged 25 to > 4000. TTF-1 was performed on 5 pts and all of them were positive. Pathology revealed TC- Follicular variant in 5, Tall cell variant in 1 and TC with anaplastic features in 1 pt. All pts underwent high dose RAI therapy while 2 had EBRT following RAI. BRAF Mutation testing was negative in two of the tested pts. All of the specimens are being analyzed for detailed mutation testing.

**Discussion:** Bone metastasis from TC occur in 2–13% of pts. They are more frequent in follicular subtypes (7–28%)
than with papillary types (1.4–7%). Skeletal metastasis portends poor prognosis, with reduced 10 years survival ranging 13 to 21%.

Multiple hypothesis have been proposed for bony metastasis of TC including mutations of RET, RAS and BRAF genes. TCs with BRAF mutations also have higher recurrence rate with diminished radio-iodine avidity. Earlier study has shown that both TTF-1 and TG are demonstrable by immunohistochemistry in majority of TCs. Compared with TG, an antibody to TTF-1 has similar sensitivity as a marker for thyroid tumors. However TTF-1 has been shown to be more sensitive marker for poorly differentiated carcinomas and metastasis. Similarly all of our pts having TC with bony metastasis demonstrated TTF-1 positivity.

Whole body MRI or PET scans are used for risk assessment and treatment planning in PTC bone metastasis. Post therapy whole body I 131 scan identified skeletal metastasis in each of the pts. In addition, other unknown sites of metastasis was identified in 2 of pts. All pts had reduction in their TG levels and remained stable. Tumor mutation testing is being conducted in these subjects.

Conclusion: In this small series, there is no female preponderance for skeletal metastasis. Also, the average age is 64. Malignancies with certain characteristics may have a predisposition to develop skeletal metastasis. TTF-1 positivity has shown to be found in 100% of our pts that led to the evaluation of TC. 2 of the tumors were negative for BRAF, detailed mutation profiling is underway.

Abstract #1004

A NEW PARADIGM IN LOW RISK PAPILLARY MICROCARCINOMA: ACTIVE SURVEILLANCE

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Objective: Classical Papillary Thyroid Microcarcinoma [PTMC] is a variant of Papillary Thyroid Carcinoma [PTC] known to have an excellent prognosis. Recent American Thyroid Association [ATA] guidelines recommend a conservative approach in the treatment of this type of tumors as emerging new evidence favors active surveillance over the more aggressive surgical treatment. Active surveillance consists of regular follow up. Research has shown that the complications that may arise after surgery carry far more morbidity than regular monitoring. This case serves as an excellent example of how first line surgical treatment may result more harmful than the actual disease.

Case Presentation: This is the case of a 37-year-old woman without medical history of systemic illness. The patient was evaluated at our endocrinology clinics due to a thyroid nodule of 2 years duration. Upon evaluation, she was asymptomatic. Thyroid function tests were normal. Thyroid ultrasound [US] showed a solid hypoechoic nodule on the right lobe measuring 0.7 x 0.5 x 0.8 cm and a left lobe solid hypoechoic nodule measuring 0.4 x 0.2 x 0.2 cm. A fine needle aspiration biopsy (FNAB) was performed and resulted positive for PTC in the right nodule and suspicious for malignancy in the left nodule. A total thyroidectomy was performed. Surgical pathology reported a well demarcated, 1.0 cm x 0.8 cm x 0.5 cm and 0.4 x 0.4 x 0.2 cm classical PTC, without angiolymphatic, perineural invasion or extrathyroidal extension. Immediate post operative course was complicated due to hypocalcemia that prolonged patient hospital stay. Up to this moment, there has been no evidence of disease recurrence. Nonetheless, her quality of life has been greatly affected by metabolic effects of severe hypocalcemia requiring multiple hospital admissions due to nonadherence to treatment.

Discussion: PTMC is considered an indolent thyroid neoplasm with a mortality of less than 0.3% even with the presence of distant metastasis. The last ATA guidelines recommends that this type of tumor, with low risk of recurrence could be treated with lobectomy rather than total thyroidectomy, although it states that active surveillance can be considered. However, the Korean Thyroid Association (KTA) now adopts this less invasive approach for low risk variant. Since aggressiveness of this papillary variant is low and studies show similar outcome between both approaches, active surveillance should be strongly considered as initial approach.

Conclusion: More studies are needed for stratification of PTMC behavior to determine if conservative management is adequate for all patients with this specific disease variant.

Abstract #1005

ORAL IODINE FOR TREATMENT OF DECOMPENSATED HYPERTHYROIDISM IN METHIMAZOLE INDUCED CHOLESTATIC LIVER INJURY

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Case Presentation: A 41 year old woman recently diagnosed with Graves’ disease presented with yellowing of sclera, dark urine, diarrhea, abdominal pain and pruritus 1 month after starting methimazole(MMI) 30mg. She was clinically thyrotoxic. She had no prior medical
history, illicit drug or alcohol use nor recent travel. Labs prior to and 2 weeks after starting MMI showed normal liver function test and complete blood count. MMI was held and testing revealed elevated total bilirubin (TBILI) of 16.7(0.2-1.2mg/dL), direct bilirubin (DBILI) 9.8(0.0-0.6mg/dL), alkaline phosphatase (ALP) of 575 (33-115U/L), aspartate aminotransferase (AST) 57(10-30U/L), alanine aminotransferase (ALT) of 110 (6-29U/L), INR 0.9, with TSH 0.01 (0.4-4.20IU/ml), triiodothyronine (T3) 402.8 (76-181ng/dL) and free thyroxine (FT4) 4.5 (0.8-1.8ng/dl). Biliary tree calculus, viral and autoimmune hepatitis were excluded. Liver biopsy showed drug induced cholestatic injury with preserved architecture. Hyperbilirubinemia and hyperthyroidism worsened in spite of cholestyramine, ursodiol and metoprolol. Therapy was altered to prednisone and propranolol but TBILI and FT4 rose to 39mg/dl and 5.4ng/dl respectively. At this point Lugol’s iodine was begun. In 1 week, TBILI fell to 6.6mg/dl, DBILI 3.1mg/dl, ALP 77U/L, AST 32U/L, ALT 75U/L, FT4 0.8mg/dl and T3 80ng/dl. Thyroidectomy was performed on day 12 of iodine therapy and her liver function continued to improve.

Discussion: Cholestatic liver injury is a rare but potentially fatal complication of MMI. Drug induced liver injury was suspected based on absence of risk factors, mechanical obstruction, or concomitant liver diseases, plus a temporal relationship of MMI use and onset of cholestasis. Hyperthyroidism and liver injury are interrelated as thyroxine can cause liver hypoxia, while its metabolism is reduced in liver dysfunction. There are case reports of use of ursodiol, magnesium isoglycyrrhizin, glutathione, or steroids for treatment of drug induced cholestatic hepatitis. Our patient did not improve with such agents. Iodine was tried to treat the hyperthyroidism worsening the hepatitis. This resulted in prompt clinical and biochemical improvement. As soon as she was safe from a liver viewpoint, urgent thyroidectomy was performed to avoid escape from Wolff-Chaikoff effect. The therapeutic effect of prednisone in this case cannot be neglected. Successful treatment with iodine of uncontrolled hyperthyroidism in the setting of drug induced liver injury, has rarely been reported.

Conclusion: Combination iodine-steroid therapy should be considered along with other modalities in the treatment of uncontrolled hyperthyroidism in the setting of severe drug induced cholestatic liver injury.

Abstract #1006

MISDIAGNOSIS OF HYPOTHYROIDISM DUE TO FALSE ELEVATION OF TSH FROM HUMAN ANTI-MOUSE ANITOBODY INTERFEERENCE

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Objective: Commercially available Thyroid stimulating hormone (TSH) tests utilize two-site immunoassay-based assays. The presence of interfering substances such as heterophile antibodies, anti-TSH antibodies, rheumatoid factor and biotin can lead to aberrant results. We discuss a case of falsely elevated TSH levels from Human anti-mouse antibodies (HAMA) assay interference that led to inappropriate diagnosis of hypothyroidism.

Case Presentation: 27 year old female was evaluated for fatigue, mood changes and mental fogginess. She had an elevated TSH of 82.7 (0.27-4.2 uIU/ml) and a normal free thyroxine (FT4) level of 1.29 (0.93 – 1.7 ng/dl). She was started on levothyroxine 100 mcg daily with some improvement in her symptoms but her fatigue persisted. She had a small goiter and appeared clinically euthyroid. Repeat testing revealed persistently elevated TSH of 74.67 (0.4 – 5.5 uIU/ml) by Roche Diagnostics Cobas electrochemiluminiscence assay and an elevated FT4 of 2.3 (0.7 – 1.8 ng/dl). This led to the suspicion of erroneous TSH values due to TSH assay interference. She was not taking biotin. Her thyroglobulin antibodies and serum protein electrophoresis were normal. Her TSH value after HAMA precipitation treatment was suppressed at 0.03 (0.40 – 4.50 uIU/L) by ADVIA Siemens Centaur TSH 3 Ultra immunochemiluminometric assay. Follow up thyroid tests 8 weeks after stopping levothyroxine showed persistent TSH elevation at 74.47 uIU/mL, while she had normal TSH with HAMA treatment (0.54 mIU/L), FT4 (1.2 ng/dl) and Free T3 (3.3 (1.8 – 3.6 pg/ml). She was advised that she does not have hypothyroidism and does not require levothyroxine treatment, though she will require special testing if she needs future thyroid evaluation.

Discussion: HAMA are the most common type of heterophile antibodies and can affect immunoassays utilizing mouse immunoglobulins. HAMA can lead to falsely high or low TSH values due to the binding of capture and detection antibodies and immunoglobulin aggregation. The prevalence of these antibodies varies between <1 and 80% and is under-recognized. Heterophile antibodies are more common in patients with autoimmune diseases and can be induced through exposure to animal antigens via environmental contact, vaccines containing
murine immunoglobulins, and use of mouse monoclonal antibodies. TSH values can be accurately assessed utilizing alternate methods such as HAMA precipitation, HAMA/ heterophile antibody blocking reagents, and use of non-immune mouse sera.

Conclusion: It is important for medical providers to be aware of factitious elevation of TSH due to HAMA induced assay interference and should be considered if there is a discrepancy between clinical and laboratory findings.

Abstract #1007

NIVOLUMAB INDUCED THYROIDITIS IN A PATIENT WITH HISTORY OF GRAVE’S DISEASE.

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Objective: Immune checkpoint inhibitors (ICI) such as programmed death-1 (PD-1) inhibitors are new anticancer drugs based on specific monoclonal antibodies. These agents can lead to a spectrum of endocrine toxicities, possibly thought to be due to the breaking of immune self-tolerance. Here we report a case of asymptomatic hyperthyroidism associated with PD-1 inhibitor, Nivolumab use.

Case Presentation: A 60 year old female who was diagnosed with stage IV adenocarcinoma of lung approximately five months ago initially showed no improvement with chemotherapy. She was later started on ICI therapy with Nivolumab and has received 5 cycles so far. Her medical history was significant for Grave’s disease in remission, treated with Methimazole 20 years ago. She has been following with Oncology and was closely monitored for neutropenia, transaminitis and thyroid dysfunction. Her thyroid function tests (TFTs) were within normal range prior to the initiation of the therapy and after 3-4 cycles of therapy. Repeat labs done at 3 months of Nivolumab therapy showed abnormal TFTs with suppressed TSH (<0.030, normal-0.27-4.2 u/mL) and elevated FT4 (4.02, normal-0.9-1.7 ng/dL) and T3 (345.30, normal 80-200ng/dL), which were confirmed on repeat labs. Her labs showed normal TSI and thyroglobulin antibody. Anti TPO antibody was mildly elevated (42.1 IU/mL). Other anterior pituitary hormones were within limits with normal MRI brain with pituitary protocol. Patient was completely asymptomatic and she remained clinically euthyroid. She was closely followed up while continued on Nivolumab therapy. Follow up TFTs in 4 weeks showed a TSH of 33 u/mL and 2 weeks later TSH was 74 u/mL. She was subsequently started on low dose Levothyroxine replacement with close monitoring.

Discussion: Nivolumab is a PD-1 inhibitor indicated for the treatment of advanced melanoma, metastatic non-small cell lung cancer, renal cell carcinoma and Hodgkin Lymphoma. Treatment with Nivolumab has been associated with various immune related adverse events (IRAE), thyroid dysfunction being most commonly associated with PD-1 inhibitor therapy, incidence of 1.8-9% of patients in larger trials. Median time to onset is 2.8 months. The mechanism of thyroid dysfunction may be related to breaking of immune self-tolerance but it is unclear at this point.

Conclusion: Careful monitoring of TFTs and other hormone levels are essential for the early recognition and management of the endocrine toxicities. The thyroid dysfunction associated with PD-1 inhibitors rarely requires drug discontinuation, unless associated with severe symptoms or life threatening consequences. Thyroid replacement or suppression therapy is indicated in symptomatic patients.

Abstract #1008

A CASE OF PAPILLARY THYROID CANCER IN A PATIENT WITH TOXIC MULTINODULAR GOITER

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Objective: We describe a case of a woman which atypical approach to Hyperthyroidism lead to the diagnosis of Papillary Thyroid Cancer.

Case Presentation: 28 year old woman with PMH of HTN presented to her PCP complaining of palpitations, anxiety, heat intolerance and tremors. She denied any hoarseness, dysphagia or neck pain. Lab work revealed TSH <0.02 uIU/mL (0.35 -4.94) and FT4 3.47 ng/dL (0.7-1.48). A Thyroid ultrasound showed a Multinodular Goiter with 3 nodules in the left lobe, the largest being 12 mm in size, with normal blood flow on Doppler. She underwent FNA of the dominant nodule, cytology was consistent with Papillary Carcinoma of the Thyroid. She was started on Methimazole and Propanolol and referred for surgery. She underwent a Total Thyroidectomy with Right and Left central neck dissection and left lateral neck dissection. Final Pathology report showed Papillary Thyroid Cancer, classic variant with tall cell features with minimal extra thyroidal extension and positive lymph nodes. 2 months after the surgery she received RAI ablation with 123.2 mCi I-131, stimulated Tg <1 ng/mL (<55) Tg Ab <20 IU/mL (<40), TSH 37.4 uIU/mL (0.35-4). Pre and post ablation scans did not show any evidence of distant metastasis. The patient was put on Levothyroxine 125 mcg daily.

Discussion: Hyperthyroidism have previously been regarded as low risk for Thyroid cancer. A review of
the literature shows an increase number of case reports showing this association. The cause of high level of TH in thyroid malignancy is thought to be secondary to an active mutation of the gene of TH receptor. Thyroid Cancer coexisting with Hyperthyroidism can be aggressive and might present without any signs or symptoms suggestive of malignancy, as seen in this patient. A detailed physical exam must be part of our complete evaluation and imaging studies should always be considered.

Conclusion: Although the coexistence is rare, we should keep Thyroid Cancer in the differential diagnosis of a Hyperthyroid Goiter and do a thorough evaluation in order not to miss this important association.

Abstract #1009

RECURRENT INFECTIONS OF A THYROGLOSSAL DUCT CYST IN AN ADULT: TIME TO REMOVE IT

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Objective: Thyroglossal duct cysts (TGDC) are the most common congenital cysts in the neck which usually present as an asymptomatic neck mass in the pediatric population. In adults, the most common presentation of TGDCs is underlying infection of the cysts. We describe a case of recurrent infection of a TGDC in an adult patient, which was surgically resected using the Sistrunk procedure.

Methods: Case Presentation

Case Presentation: A 37-year old female was referred for recurrent infection of a TGDC. An infected TGDC was initially diagnosed at age 7, when she presented with a painful midline neck swelling. At that time, the patient was scheduled for surgery but she decided to put it off since the symptoms improved with antibiotics. Interestingly, the infection did not recur, until age 33, when she experienced 4 more episodes of infection, each requiring antibiotics course, for 4-6 weeks each. The latest episode occurred 3 months prior to this presentation. A subsequent thyroid ultrasound revealed a thick walled structure of the isthmus in the hyoid bone region with internal cystic appearing component measuring 1.48 x 0.66 x 1.0 cm, consistent with infected TGDC. The thyroid gland was normal. At presentation, the patient was asymptomatic, and the thyroid and neck exam was unremarkable. Thyroid labs were normal. She underwent a Sistrunk procedure and surgical pathology confirmed the diagnosis of TGDC with no malignancy.

Discussion: Located midline in the neck, TGDCs can occur anywhere along the path followed by the primordial thyroid gland during descent from the base of the tongue. They present as asymptomatic neck masses in the pediatric population but in adults, the most common presentation is infection of the cyst. Physical exam findings typically reveal a midline mobile neck mass that moves with swallowing or protrusion of the tongue. Differential diagnosis includes dermoid cysts, branchial cleft cysts and lipomas. Imaging is prudent, to make the diagnosis and to identify the presence of normal thyroid gland. Recurrent infection is the most common complication of TGDCs (Staphylococcus epidermis, Haemophilus influenza, and Staphylococcus aureus), requiring antibiotics. Another, less common complication of TGDCs is thyroid cancer, originating from the thyroid component of TGDCs. It is recommended to remove TGDCs by the Sistrunk procedure. However, surgery is not recommended during the acute phase of infection.

Conclusion: TGDC can be complicated by recurrent infection and thyroid cancer. Surgical resection with the Sistrunk procedure is the best treatment of choice.

Abstract #1010

A DIAGNOSTIC DILEMMA: SUBACUTE THYROIDITIS OVERLAPPED WITH HASHIMOTO’S THYROIDITIS

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Case Presentation: Hashimoto’s thyroiditis (HT) is an autoimmune thyroid disorder that usually presents as a diffuse, non-tender goiter, whereas subacute thyroiditis (SAT) is characterized by tender goiter, transient thyrotoxicosis, and an elevated ESR. Rarely, patients with HT can also present with a tender goiter and mimic SAT. Coexistence of HT with SAT is a rare entity and very few cases have been reported so far, particularly in last 2 decades. We describe a case of SAT that overlaps HT. A 69-year-old white male with a known history of hypothyroidism, who was well controlled with levothyroxine 25 mcg daily, presents with a 2 month history of worsening anterior neck pain radiating to ear, palpitations, diaphoresis, weight loss, tremors, dyspnea on exertion and chest pain. He was prescribed analgesics and antibiotics by other physicians initially, which did not help. On examination, his thyroid gland was exquisitely tender along with tender cervical and axillary lymph nodes. Initial thyroid function tests (TFTs) were as following, TSH: <0.02 mIU/L (0.5 - 4.7), Free T4: 4.19 ng/dL (0.78 - 2.2), Free T3: 9.35 pg/dL (2.77 - 5.27). Patient was started on propranolol and methimazole. His ESR was 38 mm/hr (0 - 20), TSH Receptor Ab: < 0.9 IU/L (<1.75), Thyroid Stimulating Ig: 90% (<=122%) and TPO Ab: 850.9 WHO
Units (0 - 100). On ultrasound (US), thyroid gland was diffusely heterogeneous with increased vascularity. He showed no improvement on ibuprofen in the initial hyperthyroid phase. He was continued on propranolol and methimazole for one month until his symptoms improved. His TFTs reached a hypothyroid phase after 3 months of symptom onset.

**Discussion:** Coexistence of Graves’ disease (GD) with SAT is not uncommon but an overlap of SAT with HT is rare. Our patient’s clinical picture was inconsistent with GD. The TPO Ab were strikingly high along with heterogeneous inflammation of thyroid gland on US, which were consistent with HT. However, his clinical picture got complicated with an elevated ESR, lymphadenopathy and thyroid tenderness, which is seen in SAT. Such systemic inflammation is absent in “Hashitoxicosis”. Steroids were not used in treatment because of a history of steroid induced pancreatitis. Also NSAIDs could not be used for a long time because of development of erosive gastritis.

**Conclusion:** It is important to distinguish between SAT and HT as prognosis of both entities are different. SAT is self-limited while transient thyrotoxicosis from HT may recur until entire thyroid gland is destroyed by disease process. Sometimes the diagnosis and management can be challenging in a patient scenario as ours and in such cases, focus should be made on clinical improvement with regular follow up.

**Abstract #1011**

**CAN DIETARY SUPPLEMENTS PROVOKE THYROID DISEASE?**

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**Case Presentation:** Dietary supplements have gained popularity by claiming to improve strength, metabolic activity, and weight loss. A 39-year-old male presented for evaluation of an intentional 10-lb weight loss over two months while taking a supplement whose name he could not recall. The supplement was taken as a fad in his office to promote increased energy and weight loss. He had no significant medical or family history. At presentation, physical exam was unremarkable with a heart rate of 90 bpm, blood pressure 138/89 mmHg, BMI of 24kg/m2. There was no exophthalmos, thyromegaly, thyroid nodules, tremor, or hyperreflexia. Laboratory testing showed an undetectable TSH, elevated FT4 of 2.88 ng/dl (0.9-1.8), and elevated TT3 of 470 ng/dl (80-200). TSH receptor and thyroglobulin antibodies were negative, however thyroperoxidase antibody titer was positive at 56 IU/ml (0.0-34.0). Radioactive iodine uptake study was recommended, but was declined. Thyroid US revealed a homogenous non-enlarged thyroid gland with normal vascularity and a 1.3 x 0.8 x 0.9 cm nodule in the right lobe with solid and cystic components and high internal vascularity. FNA of the nodule revealed nodular goiter. The supplement was later identified as “Survival Shield X2.” It was discontinued and the patient’s thyroid function tests normalized two months later. Thyroperoxidase antibody titers decreased gradually and were in the normal range at six months and at one year follow up.

**Discussion:** Iodine excess has been implicated in the development of hyperthyroidism and hypothyroidism, especially in patients with underlying thyroid disease. Thyrotoxicosis may occur in patients with underlying Graves’ disease who were previously iodine deficient, or in patients with autonomous nodules. Hypothyroidism may be immune-mediated in the presence of excess iodine, which promotes the development of auto-antibodies. Supplements with iodine are often contraindicated in patients with thyroid disease. “Survival Shield X2” is an unregulated supplement containing 1950 mcg of potassium iodide per daily serving (3 drops). The FDA recommended daily value of iodine is 150 mcg for non-pregnant healthy adults, which is easily found in a typical American diet. Makers of various iodine containing supplements (to be discussed) claim that increased iodine consumption can boost brain function, energy level, weight loss, immune and thyroid functions, and serve as a natural detoxifier. Iodine content of supplements ranges from 150 mcg to 4000 mcg. Our investigation revealed many generic multivitamins containing at least 100% of the daily value of iodine

**Conclusion:** Many supplements exempt from FDA approval contain iodine and may have unknown risks to consumers.

**Abstract #1012**

**A CASE OF LEVOTHYROXINE TOXICITY**

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**Objective:** We describe a case of intentional levothyroxine overdose associated with myalgia and elevated creatine kinase (CK). Massive administration of levothyroxine could occur either accidentally in children or intentionally in adults with suicidal intent.

**Case Presentation:** 30-year-old black man with epilepsy, post-surgical hypothyroidism after total thyroidectomy for multinodular goiter presented to the ED one hour after intentional overdose of levothyroxine, approximately
30 tablets of 125 mcg each (total dose 3750 mcg). On presentation, vital signs were stable and he denied chest pain, tremor, palpitation or diaphoresis. He had brisk deep tendon reflexes bilaterally and moist palms. The initial tests revealed TSH 10.5 mcIU/ml [0.35-5.50], free T3 4.7 pg/ml [2.3-4.2] and free T4 7.72 ng/dl [0.62-1.57]. He was admitted to psychiatry unit for suicidal ideation. Two days later, free T3 peaked at 10.7 pg/ml, with free T4 4.42 ng/dl and TSH 0.189 mcIU/ml. He was started on propranolol and cholestyramine. Subsequently, he developed chest pain. The EKG showed marked sinus arrhythmia without acute ST or T wave changes. Troponin was mildly elevated at 0.040 ng/ml [0.000-0.039] with normal CK 188 units/L [35-250]. He was started on propylthiouracil (PTU) and hydrocortisone to further inhibit peripheral conversion of free T4 to free T3. Serial T3 was monitored as the free T3 is anticipated to peak between day 3-10 days. Free T4 peaked on day 1 and Free T3 peaked on day 2 and both declined by half in 4 days. Patient complained of myalgia and CK peaked on day 6 at 4579 units/L. PTU was discontinued on day 6 and propranolol, hydrocortisone and cholestyramine were gradually weaned. On day 8 levothyroxine was resumed as free T3 was 4.1 pg/ml and free T4 was 1.74 ng/dl. The CK and thyroid function tests were normal at 4 weeks.

Discussion: Levothyroxine overdose could have wide range of presentation extending from minimally symptomatic with tremors, anxiety, tachycardia to dysrhythmias, convulsions, acute psychosis, MI, hyperthermia and coma. The onset of symptoms may be delayed so medical observation for at least 3 to 4 days should be considered. It is difficult to predict which patients will later be symptomatic. Serious toxicity is rare. As with thyroid storm, the clinical symptoms of overdose do not correlate with the T4 and T3 levels. The use of beta blockers, activated charcoal, PTU, glucocorticoids and cholestyramine have been reported. The indications and efficacy of these treatment options remain unclear.

Conclusion: There are no established guidelines for the treatment of T4 overdose. The signs and symptoms are best indicator for level of intervention required.

Abstract #1013

AN INTERESTING APPROACH TO PERSISTENT HYPOTHYROIDISM

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Objective: Levothyroxine is the preferred therapy for Hypothyroidism. The usual recommended dose is 1.6 to 1.8 mcg/kg ideal body weight. Occasionally, patients may not become euthyroid despite a very high dose of levothyroxine. The two most common reasons are malabsorption and medication nonadherence. A similar case scenario is presented here.

Case Presentation: A 55-year-old female was followed for post-surgical hypothyroidism secondary to thyroid cancer 20 years ago. She was morbidly obese (weight 350 lbs; BMI 65 kg/m2) with a history of cirrhosis. She reported taking levothyroxine daily in a fasting state without other medications or supplements. For the past 3 years, her Thyroid Stimulating Hormone (TSH) level remained high, highest level being 141 mIU/L (normal 0.45 - 4.5) with low free thyroxine levels, 0.37 to 0.57 ng/dl (normal 0.82-1.77). Levothyroxine dose had been gradually increased from 200 mcg to 750 mcg daily. As patient had persistent elevated TSH, a thyroxine absorption test was performed to evaluate for adherence and to exclude impaired bioavailability secondary to malabsorption of levothyroxine. She was administered oral Levothyroxine 1000 mcg under supervision to ensure complete ingestion. Total T4 levels were drawn at baseline and at 1, 2, 4 and 6 hour post ingestion. T4 level in mcg/dl were 2.7 at baseline, 6.2 (1 hr), 6.8 (2 hr), 7.1 (4 hr) and 7.7 (6 hr). Based on these results, her incremental rise in T4 in mcg/dl was 3.5 (1 hour), 4.1 (2 hour), 4.4 (4 hour) and 5.0 (6 hour). As normal T4 Volume of distribution (Vd) is 10-14% of body weight, our patient’s Vd was 16-22 liters (L). Calculated amount of absorbed T4 = Incremental rise of total T4 concentration x distribution volume (Vd). Using 16 L of Vd, her thyroxine absorption was 560 mcg (1 hr), 656 mcg (2 hr), 704 mcg (4 hr) and 800 mcg (6 hr). Patient had 80% levothyroxine absorption by 6 hours indicating no evidence of thyroxine malabsorption.

She was given 1500mcg Levothyroxine on a single day weekly for eight weeks. Her TSH improved to 15 mIU/L. Her weekly dose was gradually adjusted to a current dose of 2100 mcg/week with a TSH of 0.8 mIU/L and FT4 1.25 ng/dL. She has been followed for 2 years without any adverse events.

Discussion: About 80% of Levothyroxine dose is absorbed in the fasting state with peak serum levels at 2 hours. Doses greater than 300 mcg/day are rarely required and should prompt consideration of alternate reasons. Thyroxine absorption test can help distinguish non-adherence from malabsorption.

Conclusion: For patients having difficulty with sustained adherence to daily levothyroxine, weekly thyroxine replacement with total weekly dose given once per week is a safe alternative treatment option.
Abstract #1057

CLINICAL SUSPICION AND FINE NEEDLE ASPIRATION OF THE THYROID IN THE SUCCESSFUL TREATMENT OF ACUTE THYROIDITIS.

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Objective: Although acute suppurative thyroiditis is a rare condition, it is important that endocrinologists be prepared to promptly recognize it to avoid treatment delays. We present a challenging patient who presented with overlapping features of acute and subacute thyroiditis, in the setting of previously undiagnosed Grave’s disease and a necrotizing papillary thyroid cancer.

Case Presentation: A 50-year-old male presented to the emergency room with acute right sided neck swelling associated with pain, chills, and intermittent fever for 2 days. He had symptoms suggestive of an upper respiratory infection a week prior. He denied weight loss, diarrhea, palpitations or anxiety. On presentation he was in mild distress, tachycardic and febrile with a temperature of 100.8 F. Laboratory testing was pertinent for a TSH of < 0.02 mIU/L, Free T4 of 2.22 ng/dL and a white count of 12.6 k/uL. A contrast-enhanced CT scan of the neck performed in the emergency room revealed a large right thyroid cystic lesion measuring 4.4 cm with tracheal mass effect and lymphadenopathy. Broad spectrum antibiotics and steroids were initiated. He underwent aspiration of the thyroid lesion which under ultrasound guidance, now appeared solid with no cystic component. Within 48 hours of treatment, the fever had resolved and there was significant improvement in the neck swelling. The patient was discharged in improved condition on oral antibiotics and methimazole. Cytopathology identified atypical cells with necrosis in the thyroid sample and papillary thyroid cancer in the lymph node. TSH receptor antibodies came back positive at 10.34 IU/L.

Discussion: Because of its high vascularity, lymphatic drainage, high iodine content and encapsulated nature, the thyroid gland is very resistant to infection, making acute suppurative thyroiditis rare, particularly in adults. A preceding respiratory infection and findings of fever, pain and a neck mass should immediately raise suspicion. Antibiotic therapy needs to be promptly initiated, particularly when there is an impending threat to the airway. Necrotic papillary thyroid cancer may predispose to the development of infection.

Conclusion: Mortality risk in acute thyroiditis is high and its treatment should not be delayed even if its presentation is confounded by features suggestive of subacute thyroiditis or Graves disease. Fine needle aspiration is key in establishing a definitive diagnosis and should not be deferred due to concomitant thyrotropin suppression.

Abstract #1014

NIVOLUMAB INDUCED THYROID DYSFUNCTION

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Objective: To describe a case with nivolumab induced hypothyroidism.

Methods: Case report and review of literature.

Case Presentation: A 55 year old male with past medical history of metastatic non small cell lung cancer (NSCLC) underwent treatment with radiotherapy, adjuvant chemotherapy with carboplatin and paclitaxel followed by nivolumab. About 4 weeks after treatment with nivolumab, patient noticed swelling in the anterior neck associated with cold intolerance, fatigue, mood swings, constipation, and dry skin. On examination, thyroid gland was grossly enlarged, non-tender, and no nodularity was noted. Thyroid function test revealed elevated TSH at 48.7 uIU/ml (0.5-5.0), low free T4 < 0.40 ng/dl (0.70-1.48), positive thyroid peroxidase (TPO) antibody > 20000 IU/ml (0-5.61). Since his baseline TSH prior to starting nivolumab was within normal limits, treatment with levothyroxine was started. However, nivolumab therapy for management of NSCLC was continued along with titrated dose of levothyroxine for management of hypothyroidism.

Discussion: Nivolumab is an IgG4 monoclonal antibody against programmed cell death-1 (PD-1) receptor used for treatment of metastatic NSCLC, melanoma and renal cell cancer. PD-1 is an immune checkpoint receptor expressed on cancer cells and other immune cells. Immune related adverse events (irAEs) occur as a consequence of impaired self-tolerance from loss of T cell inhibition on a normal tissue leading to dermatologic, gastrointestinal, hepatic, endocrine and other inflammatory events. The reported incidence of thyroid dysfunction with is about 2-3%. The thyroid dysfunction can manifest as primary hypothyroidism due to destructive thyroiditis or as hyperthyroidism associated with Graves disease.

Conclusion: As Nivolumab immunotherapy is becoming more common; the incidence of thyroid dysfunctions associated with it is also increasing. It is important to be aware of irAEs in patients being treated with immune checkpoint inhibitors. If the patient develops primary hypothyroidism, it can be managed with levothyroxine...
replacement without discontinuing immunotherapy in most cases. For hyperthyroidism, after symptomatic treatment with beta-blocker, either steroids or anti-thyroid medication is used depending upon the underlying mechanism.

**Abstract #1015**

A RARE CASE OF THYROTOXIC PERIODIC PARALYSIS (TPP) PRESENTING IN A YOUNG AFRICAN AMERICAN MALE PATIENT

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**Objective:** Thyrotoxic Periodic Paralysis (TPP) is a rare disorder characterized by a triad of acute hypokalemia without total body potassium deficit, episodic muscle paralysis, and thyrotoxicosis. It is most commonly inherited as an autosomal dominant mutation in the skeletal muscle L-type calcium or sodium channel genes in the East Asian population. Though many cases are reported in overt hyperthyroidism, hypokalaemic paralysis in the African American population is very rare. We present a case of acquired TPP in a young otherwise healthy African American male patient with no Asian ancestry.

**Case Presentation:** A 24-year-old African American male presented to the emergency room with sudden onset of weakness in his arms and legs. He was unable to get out of bed due to profound lower extremity weakness. He denied any significant medical or surgical history. He was not taking any prescription or over-the-counter medications and denied smoking, drinking alcohol or using any illicit drugs. Upon exam, his vitals were within normal limits; he had zero out of five strength in his hips and knees and two out of five strength in his elbows and shoulders. He also had diffuse tendon hyporeflexia. The initial EKG showed sinus tachycardia. The CT scan of his head was unremarkable. Initial labs revealed a potassium level of 2.3 mmol/L. Further workup revealed a TSH level of <0.01 mcIU/ml, free T4 of 6.82 ng/dl and a free T3 level of 2.5 mg daily; prednisone was discontinued after 2 months.

**Discussion:** Thyrotoxic periodic paralysis is most commonly inherited in an autosomal dominant form in East Asia and rarely presents in the African American population. It affects males more than females and age of presentation is usually 20-40 years. TPP is thought to be due to an enhanced adrenergic response and excessive thyroid hormone that increases the activity of the Na-K ATPase pump, causing an intracellular potassium shift and hypokalemia. Episodes are often precipitated by a high carbohydrate meal, stress and exercise.

**Conclusion:** Neuromuscular weakness in the context of hypokalemia should prompt the clinician to check thyroid function tests to rule out this debilitating disease that has a simple management. TPP is rapidly reversed with potassium replacement and treating the hyperthyroidism.

**Abstract #1016**

PANCYTOPENIA IN A PATIENT WITH GRAVES DISEASE

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**Objective:** Pancytopenia is a rare but severe complication of Graves’ disease (GD). Given that leucopenia is a known side effect of antithyroid drugs, it is pertinent that this rare presentation is sought for before commencement of treatment. We here report a case of pancytopenia associated with GD.

**Case Presentation:** A 43 year-old female with history of GD, atrial fibrillation, CHF and cirrhosis presented with fatigue, palpitation, shortness of breath and pedal edema. She was diagnosed with Graves disease 4 years before presentation but had not adhered to therapy with antithyroid medication. She was treated with radioactive iodine 3 days before presentation following which she developed worsening palpitation, dyspnea, fatigue, heat intolerance and sweating. Examination was pertinent for irregular heart rate and tachycardia of 150-180 beats/minute and diffuse thymomegaly. Thyroid function tests confirmed thyrotoxicosis with free thyroxine of 5.15 (0.76-1.46 ng/dl) and TSH <0.001 (0.358-3.740 µIU/ml), full blood count revealed pancytopenia with total white cell count of 0.8 × 109/L (4.2-10.2) , hematocrit of 25.8 (36-48%), and platelet count of 24× 109/L (150-400). Investigation for pancytopenia including folate,B 12 , iron, coombs test, hepatitis panel, HIV test, ANA , flow cytometry and bone marrow biopsy were normal. Pt was treated with oral metoprolol 25 mg every 12 hours, propylthiouracil 100 mg every 8 hours and prednisone 40 mg daily; prednisone was discontinued after 2 months.

On follow up 6 months after discharge, thyroid function tests had normalized and pancytopenia had improved with WBC of 3.4 × 109/L, hematocrit of 37.9 % and platelet count of 86.9× 109/L.

**Discussion:** Pancytopenia is rare but a serious complication of thyrotoxicosis. Single lineage abnormalities are more
common than pancytopenia. Although the pathogenesis of pancytopenia in GD remains unclear, putative mechanisms include ineffective hematopoiesis caused by excess thyroid hormones, reduction in blood cell life span due to hypersplenism and immunological mechanisms such as antineutrophil antibodies, antiplatelet antibodies and toxicity of thyroid hormone to bone marrow stem cells. **Conclusion:** Although pancytopenia is rare in GD, hematological assessment is warranted before commencement of antithyroid drugs. Antithyroid drugs could be used in patients with GD and pancytopenia but close monitoring is. It would be worthwhile to include thyroid function tests in the evaluation of patients with pancytopenia.

**Abstract #1017**

**METHIMAZOLE-INDUCED SEVERE HEPATO-TOXICITY**

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**Objective:** To report a case of methimazole-induced severe hepatotoxicity in a patient with Graves’ disease

**Methods:** Case-based review of thionamide-induced hepatotoxicity

**Case Presentation:** A 57-year-old African American woman presented with symptoms of progressive painless jaundice, poor appetite, unintentional weight loss, and worsening generalized pruritis. A few days prior to admission she noticed a decrease in energy level, hyperdefecations, and dark urine. Six weeks before presentation she was started on methimazole (MMI) 20 mg three times a day for presumed Graves’ disease. Lab results at diagnosis showed TSH <0.02, FT4 7.7, TSI 604. AST, ALT, ALP, and total bilirubin were normal. Vital signs were normal. Physical exam revealed icteric sclera, dry skin, brittle nails, and delayed relaxation phase of bicep reflexes. The thyroid was mildly enlarged at 30 g with a bosselated surface. TSH was <0.005, FT4 2.17, total bilirubin 16, direct bilirubin 10.7, AST 128, ALT 117, ALP 1933. Acute hepatitis panel was nonreactive, autoimmune panel was negative, TPO antibody was normal. CT of the abdomen demonstrated the liver was unremarkable in appearance. Liver biopsy showed intercellular swelling and microscopic cholestasis consistent with drug-induced hepatitis. Our patient underwent total thyroidectomy. Pathology investigation showed benign toxic multinodular goiter. She was started on levothyroxine 75mcg replacement therapy. Currently she is lost to follow-up.

**Discussion:** Severe hepatotoxicity is a rare complication of antithyroid drugs. This case is unique in having elevation of total bilirubin to 16 with liver biopsy pathology confirming drug-induced toxicity. The case underscores the importance of remaining vigilant for adverse effects of antithyroid drugs. Signs of cholestasis have been reported to occur as early as 12 days and as late as 90 days after initiation of the medication. Our patient presented to the ED approximately 2 weeks after initiation of MMI. The other antithyroid drug, propylthiouracil (PTU), has been associated with severe liver injury and acute liver failure, including fatal cases. Re-challenging with PTU has resulted in reappearance of cholestasis; hence it is not recommended.

**Conclusion:** At the time of MMI initiation, patients should be educated about the symptoms associated with medication side-effects and advised to stop taking MMI and immediately contact their physician if they experience such symptoms.

**Abstract #1018**

**TOO MUCH IODINE CAN DRIVE THE THYROID CRAZY**

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Michigan State University

**Objective:** In individuals with impaired auto regulation, exposure to supra physiological levels of iodine may lead to iodine-induced hyperthyroidism. Pre-existing thyroid disorders plays an important role in the pathogenesis of this condition.

**Methods:** Case Presentation

**Case Presentation:** 61 year-old female presented to the clinic for an abnormal Thyroid function test. She had increased anxiety, palpitations, heat intolerance, sweating and 10 lb weight loss unintentionally. She was seen by her primary care physician who ordered a Thyroid function test which was consistent with hyperthyroidism. She was started on propranolol with improvement in the palpitations. Patient reported that she has been taking iodine supplements for two years to improve her energy level and to induce weight loss. She denied personal or family history of thyroid disorders or cancer. No history of acute illnesses. No goiter or nodules were appreciated on physical examination.

Repeated Thyroid labs showed persistent hyperthyroidism, Random urine iodine was 1511 which is higher than the normal range. Patient was started on methimazole with improvement in her symptoms. Thyroid ultrasound was ordered to assess vascularity and nodularity of the Thyroid gland.

**Discussion:** Iodine-induced hyperthyroidism is self-limiting (lasting 1 to 18 months) if the source of iodine...
is discontinued. The appropriate therapy for patients with iodine-induced hyperthyroidism is discontinuation of iodine, avoidance of further exposure, and the administration of a beta-adrenergic antagonist drug to minimize the manifestations of hyperthyroidism. For patients with nodular thyroid disease who have severe or prolonged (>1 month) hyperthyroid symptoms and in older patients with underlying heart disease, it is recommended to start a thionamide (methimazole) to achieve euthyroidism quickly. However, in older patients at high risk for iodine-induced hyperthyroidism, it is recommended to measure thyroid function tests (TSH, free T4, and T3) three to four weeks after exposure to radiographic contrast agents to assess for iodine-induced hyperthyroidism. In older patients at high risk for iodine-induced hyperthyroidism, it is recommended to measure thyroid function tests (TSH, free T4, and T3) three to four weeks after exposure to radiographic contrast agents to assess for iodine-induced hyperthyroidism.

Conclusion: Iodine-Induced Hyperthyroidism is a rare clinical disorder and usually associated with underlying thyroid disorders, and it is usually self-limiting but treatment might be indicated with persistent symptoms mainly with beta-blockers and thionamides, especially in older patients. Screening for thyroid nodular disease is also important in the evaluation.

Abstract #1019

ECTOPIC THYROID GLAND: THE CONCERN FOR MALIGNANCY POTENTIAL

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Objective: Ectopic thyroid gland is an uncommon disease entity which results from abnormal thyroid descent during embryological development, defined as thyroid tissue not located in the antero-lateral position between the second and fourth tracheal cartilages. Standardized management guideline are lacking due to low prevalence. Data from small case series and single centered studies generally inferring no greater malignant potential compared to normal public. We present a case of ectopic lingual thyroid with large nodule managed conservatively.

Case Presentation: A 28-year-old female with psoriasis on topical steroid was seen for hypothyroidism and tongue base mass since childhood. Initially hypothyroidism was diagnosed during hospital visit for infectious mononucleosis in 2006, which she had abnormal thyroid function and was symptomatic requiring levothyroxine. Her thyroid-peroxidase antibody was 19.8 WHO units, TSH 1.84 U/mL, free T4 1.53 ng/dL. On exam, she was euthyroid with psoriatic skin changes on elbows. A 2 x 2 cm, immobile, soft, globulated mass was seen at tongue base, with no normal palpable thyroid. Ultrasound confirmed absence of normal thyroid, but an ectopic lingual mass 4.8 x 3.7 x 4.6 cm with a solid, hypoechoic, 2.0 x 1.8 cm region suspicious for nodule. Technetium pertechnetate scan confirmed lingual thyroid tissue with homogenous uptake. Due to concern of malignancy potential and conflicting results, a contrasted CT neck soft tissue better characterized lesion to be 2.0 x1.9 x1.7 cm with appropriate iodine uptake in tissue. Patient was asymptomatic and continued on thyroid hormone replacement therapy. Routine follow up ultrasound showed stable thyroid tissue without nodular lesion.

Discussion: Ectopic thyroid gland is the most frequent form of thyroid dysgenesis with lingual presentation comprising ~90% of all forms. Primary carcinoma arising from ectopic thyroid tissue is uncommon with malignancy potential no greater than general public. Mostly, symptoms are related to mass effect and locations of tissue, with many patients diagnosed incidentally. Most authors agree on surgical resection if symptomatic or ectopic tissues are causing complications, i.e. mass effect or malignant transformations. If no symptoms, medical management with routine monitoring should be considered first.

Conclusion: Ectopic thyroid gland is an uncommon disease entity which results from abnormal thyroid tissue descent during embryological development. Although malignancy potential is a concern, the risk is not greater than general public. Patients can be managed medically if asymptomatic, with surgical resections in patients with symptoms and complications associated with ectopy of thyroid tissues.

Abstract #1020

ZERO NEUTROPHILS DUE TO METHIMAZOLE

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Objective: Antithyroid drugs (ATDs) are prescribed as the initial therapy for the majority of patients with Graves’ disease (GD). Agranulocytosis is one of the most serious side effects of ATDs. However complete depletion of neutrophils (zero) is extremely rare with few case reports published. We present a case of methimazole induced agranulocytosis with zero neutrophils with mild symptoms.

Methods: Case Presentation
Case Presentation: A 55 year old female who presented to her family physician with low grade fevers/chills, fatigue, mouth sores. Labs showed WBC 3.2 with 0 PMN’s. She was then directly admitted to the hospital for further work-up and treatment. She was afebrile and was started on Neupogen. Six weeks prior to that she was diagnosed with GD with mild hyperthyroidism for which she was started on Methimazole and Atenolol with improvement of symptoms. She remained afebrile during her hospitalization and her neutrophil count gradually improved on Neupogen and she was discharged with normal CBC. Methimazole was stopped and she was subsequently treated with radioactive iodine therapy.

Discussion: Thionamides have been used for decades to treat hyperthyroidism. Agranulocytosis is a rare, potentially life-threatening adverse effect of the thionamide, Methimazole (MMI). The drug dose, treatment duration, and patient characteristics that predispose to agranulocytosis is not completely understood. Idiosyncratic adverse reactions and immune-mediated mechanisms are postulated to play a role. Agranulocytosis has been reported in 0.17 to 0.36% of patients using antithyroid drugs (ATDs). The usual interval between starting an ATD and agranulocytosis ranges from 2 weeks to 1 year across several studies. One rare case developed delayed agranulocytosis 6 years after the initiation of MMI, which was preceded by the use of propylthiouracil (PTU) for 11 years. The occurrence is usually sudden with fever and sore throat being the earliest symptoms, and even very close routine weekly screening with white cell counts was not able to predict its occurrence in 1 study. Recovery after MMI discontinuation occurs anywhere from 5 to 31 days; however, mortality has also been reported in association with agranulocytosis. Agranulocytosis with complete depletion of neutrophils is extremely rare, with only few case reports published with complete recovery after stopping the medication.

Conclusion: Agranulocytosis is not a common side effect of thionamides but can be severe and life threatening. Periodic screening and monitoring of CBC while on treatment is crucial to monitor development of neutropenia which can be totally asymptomatic.
of LT4. The cause of LT4 malabsorption remains unclear in our patient. But in such cases, after verifying their compliance and ruling out common causes for malabsorption, selective malabsorption of oral LT4 can be considered. Such patients can be successfully treated with parenteral doses of LT4.

Abstract #1022

GRAVES DISEASE WITH CONCURRENT CRIBRIFORM MORULAR VARIANT PAPILLARY THYROID CANCER

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Case Presentation: Graves’ disease is associated with an increased risk of papillary thyroid cancer. A 44-year-old female presented for management of previously diagnosed hyperthyroidism. She reported palpitations and weight loss but was otherwise asymptomatic. Family history was notable for maternal hypothyroidism. She was taking propranolol 10mg once daily. Her exam was significant for tachycardia with heart rate of 121bpm, hypertension with blood pressure of 153/92 mmHg, and obesity with BMI of 32kg/m2. Thyroid palpation was unremarkable. Blood work revealed an undetectable TSH, elevated FT4 of 4.5ng/dl (0.9-1.8), elevated FT3 of 15.61pg/ml (2.3-4.2), and positive titer of TSH receptor antibody. Thyroid US showed an enlarged, heterogeneous, hypoechoic thyroid gland and multinodular goiter. Three nodules appeared suspicious by sonographic features, and subsequent FNA revealed atypia of uncertain significance in two of the three nodules sampled. Gene classifier expression analysis (Afirma) classified the nodules as suspicious for papillary thyroid cancer. The patient was referred for total thyroidectomy. Cytopathological analysis of the excised gland revealed the cribriform morular variant of papillary thyroid cancer. Genetic testing was positive for mutations in the DNA mismatch repair pathway gene PMS2, and SMAD4, a gene involved in cell signaling in the TGF-β pathway. Mutations in APC were not found. The patient was referred for colonoscopy. Repeat US performed 9 months postoperatively revealed no evidence of disease recurrence.

Discussion: The cribriform morular variant of papillary thyroid cancer (CMV-PTC) accounts for less than 1% of all papillary carcinomas. It is associated with familial adenomatous polyposis (FAP) but more often occurs sporadically typically affecting women in the 3rd and 4th decade. CMV-PTC is the presenting sign in 25% of patients with FAP and is often bilateral and multinodular. Conversely, sporadic CMV-PTC often presents with a large unilateral solitary nodule. Patients with FAP associated CMV-PTC typically harbor germline mutations in the APC gene as well as somatic mutations in APC, CTNNB1, and RET/PTC rearrangements. These mutations are rarely found in sporadic CMV-PTC. Both forms are generally BRAF negative. These tumors are typically indolent, with extremely rare reports of lymphatic invasion and distant metastases. Curative treatment typically consists of total thyroidectomy followed by remnant ablation with radioactive iodine. Patients diagnosed with CMV-PTC should undergo genetic testing and colonoscopy for FAP screening.

Conclusion: Patients with sporadic CMV-PTC are rarely found to have somatic mutations which predispose to nonpolyposis rectal cancer.

Abstract #1023

ENDOCRINOPATHIES RELATED TO IMMUNE CHECKPOINT BLOCKERS

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Case Presentation: We present a case of a 56-year-old male with endocrinopathies following treatment for metastatic melanoma with Ipilimumab. Following two cycles of Ipilimumab, patient reports unintentional weight loss, fatigue and difficulty sleeping despite being on ambient. He also reports worsening of his essential tremors. He denied palpitations and bowel changes. Denies recent contrast exposure or upper respiratory track infection. Significant physical exam is notable for heart rate of 94, blood pressure 110/66, positive for tremors, negative for graves ophthalmopathy. Thyroid gland is non-tender without thyromegaly or nodules. Laboratory data is significant for suppressed TSH with an elevated Free T4 of 5.88ng/dl. Review of previous thyroid function test is noted to be in the normal range prior to starting Ipilimumab. Ultrasound of the thyroid gland revealed heterogeneous hypoechoic thyroid gland. Patient also has positive thyroid peroxidase antibody and negative thyroid-stimulating antibody. Radioactive iodine thyroid uptake scan showed uptake at 6 hours of 1 percent and uptake at 24 hours of 0 percent. Due to concern for adrenal insufficiency in the setting of Ipilimumab, a random cortisol was obtained and was noted to be low at 2.3ug/dl. Patient was started on beta blocker for symptomatic treatment along with prednisone 40 mg daily. Repeat labs in one month, were notable for Free T4 of 1.9 ng/dl with improvement in symptoms.

Conclusion: Ipilimumab is an anti CTLA 4 antibody, also known as immune checkpoint blocker. Adverse
events related to immune checkpoint inhibitors present a unique set of endocrinopathies for clinicians. Adrenal insufficiency is the most critical endocrinopathy that may develop and requires prompt treatment with steroids. Other adverse events include autoimmune thyroid disease, which may result in either hypothyroidism or hyperthyroidism, and hypophysitis.

Abstract #1024

GYNECOMASTIA AS THE ONLY PRESENTATION OF GRAVES’ DISEASE IN AN ADOLESCENT MALE

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Objective: Gynecomastia is a relatively common manifestation of hyperthyroidism. Reported frequency varied from 2 to 42% of patients with hyperthyroidism. Gynecomastia as an initial presenting symptom is very rare and may pose a diagnostic challenge to the clinician. It has been described only in eight case reports to the best of our knowledge in English language literature review. All cases reported were in adults. Our case is the first case to happen in an adolescent male.

Case Presentation: A 17 year old Caucasian male with no significant past medical history was referred for bilateral gynecomastia for over one year. He had normal pubertal changes and growth spurt was at 15 years of age. He denied use of illicit drugs and cosmetics containing lavender oil or tea tree oil. He denied symptoms of thyrotoxicosis. No family history of gynecomastia. His only medication was loratadine as needed for allergies. Vitals were normal with regular pulse of 75 beats per minute and body mass index of 18.6 kg/m2. Physical examination was unremarkable except for bilateral gynecomastia; tender on palpation with no galactorrhea. He did not meet the criteria for physiologic pubertal gynecomastia, so we initiated the workup of pathologic causes. Initial workup including complete metabolic panel, LH, FSH, prolactin, total testosterone, estradiol, DHEA-sulfate, HCG and alpha fetoprotein were normal except for TSH of less than 0.01 mIU/ml (0.27-4.2). Further work up showed free T4 of 3.3 ng/dl (0.9-1.7) and total T3 294 ng/dl (80-213). Thyroid receptor antibodies 11.7 IU/l (0.0-1.75) and thyroid stimulating immunoglobulin 244% (0-139) were positive. Breast ultrasound showed heterogeneous tissue in the retroareolar area approximately 3.8 x 3.3 x 0.9 cm on the right with slightly smaller area on the left breast. Radioactive iodine uptake scan showed normal uptake of 7.8 % and 22.5 % at 2 and 23 hours respectively in a normal sized gland. He was started on methimazole.

Discussion: Gynecomastia typically results from imbalance between the level or action of estrogen and androgen. Most common cause in adolescent male is pubertal gynecomastia. Hyperthyroidism is associated with increase in total testosterone due to increase in SHBG and decrease or normal free testosterone; Increase in plasma estradiol level is due to increased glandular production, increase conversion from precursors, decrease metabolism or combination of these factors. Treatment of hyperthyroidism leads to improvement in gynecomastia.

Conclusion: Recognition of this unusual presentation of hyperthyroidism will help to avoid and reduce unnecessary investigations or surgical procedure as the condition is completely reversible with antithyroid treatment.

Abstract #1025

A CASE OF POSTPARTUM THYROIDITIS IN A PATIENT WITH GRAVES’ DISEASE

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Objective: To recognize postpartum thyroiditis in a patient with history of Graves’ disease

Case Presentation: A 28-year-old woman with history of Graves’ disease and cold thyroid nodule presented with insomnia and palpitations 3 months postpartum. She has a history of subclinical hyperthyroidism due to Graves’ disease and a cold 1.4 centimeter (cm) isthmus nodule diagnosed at the age of 20. She progressed to overt hyperthyroidism 5 years after diagnosis and was referred to our clinic for further management. At her initial visit with our clinic in 2013, she reported palpitations, tremor, and heat intolerance. She did not have diarrhea, insomnia, menstrual irregularities, ophthalmopathy, or compressive symptoms including dysphagia, dyspnea, and hoarseness. Physical exam was significant for a fine tremor and 1.5 cm palpable nodule in the isthmus, which was benign on FNA biopsy. TSH was 0.02 IU/ML (0.45-4.5), free T4 1.39 NG/DL (0.60-1.30), and total T3 177 NG/DL (79-149). After discussion with patient, which included treatment options and preconception counseling, she was started on methimazole 10mg daily and metoprolol succinate 50 mg daily with improvement in symptoms. Methimazole was gradually tapered off over the course of 2 years. She became pregnant shortly after methimazole was discontinued and remained in remission with normal TSH levels throughout her pregnancy. 3 months following delivery, the patient reported onset of palpitations and insomnia. She had resumed oral contraception and was having regular menstrual periods. She was not breastfeeding. TSH was found to be 0.05 IU/ML (0.45-4.5), free T4 2.47 NG/DL (0.60-1.3) and free T3 4.8 pg/mL (2.0-4.4). She was
started on metoprolol succinate 50mg daily. Uptake scan showed low uptake of 1.3% at 24 hours consistent with postpartum thyroiditis. She continues metoprolol for symptomatic relief with plan for repeat thyroid function tests in 2 months.

**Conclusion:** Graves’ disease is an autoimmune thyroid disorder with peak incidence in women of child bearing age. It has a tendency to improve during pregnancy and exacerbate following delivery such that recurrent Graves’ in the postpartum period, particularly in the 4-12 months following delivery, is not uncommon. It may be challenging to differentiate between recurrent Graves’ disease from postpartum thyroiditis, which is a destructive thyroiditis with subsequent release of thyroid hormone that is typically self-limiting. It is important to distinguish recurrent Graves’ disease from the hyperthyroid phase of postpartum thyroiditis which typically resolves on its own, without antithyroid medication. I 131 uptake scan may be helpful to distinguish between the two in non breastfeeding individuals.

**Abstract #1026**

**INSTITUTIONAL EXPERIENCE USING AFIRMA GEC AND THYROSEQ V2 ON INDETERMINATE THYROID FINE NEEDLE ASPIRATION BIOPSIES**

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**Objective:** Fine needle aspiration (FNA) biopsy allows definitive diagnosis of benign or malignant neoplasms in 60-80% of thyroid nodules. However, indeterminate cytologic results present significant diagnostic and management challenges. Atypia of undetermined significance/ follicular lesion of undetermined significance (AUS/FLUS) carries a 5-15% risk of malignancy. Molecular diagnostic testing is increasingly used in the management of indeterminate nodules. We report our institution’s experience with thyroid molecular testing to determine if it offers additional benefits and assists in obtaining definitive diagnosis in AUS/FLUS nodules.

**Methods:** Thyroid FNA adequacy and AUS/FLUS rates from FY16 were analyzed to confirm our indeterminate diagnoses were within acceptable range according to the benchmark of the medical literature. We then correlated all Afirma (14) and ThyroSeqV2 (44) test results from April 2014 to June 2016 with the follow up surgical results when available.

**Results:** Of the 340 thyroid aspirates in FY16, overall inadequacy rate was 14% with a 26% (n=87) AUS/FLUS rate, well within the 2-21% inadequacy range and close to the 10-25% AUS/FLUS rate as reported in the medical literature. Of 14 cases tested with Afirma, 42% (n=6) were suspicious, 50% (n=7) were benign, and 8% (n=1) were inadequate results. Surgical follow up of suspicious cases showed 33% (n=2) were papillary carcinoma, 16% (n=1) were follicular carcinoma, 33% (n=2) were false suspicious and 16% (n=1) had no follow up. All benign Afirma results have no surgical follow up to date.

44 cases were tested with ThyroSeq. 18% (n=8) were positive for high risk mutations, 4% (n=2) were suspicious for low risk mutation and 77% (n=34) were negative for mutations. Surgical follow up is available on 3 negative ThyroSeq cases and revealed 1 true negative and 2 false negative results (both were invasive encapsulated follicular variant of papillary carcinoma). Of 8 cases with high risk mutations, only 2 cases underwent surgery and revealed classical papillary carcinoma (n=1) and noninvasive follicular thyroid neoplasm with papillary-like nuclear features NIFTP (n=1) on follow up.

**Conclusion:** The presence of false positive and false negative molecular test results even in this relatively small sample size raise questions regarding the cost to benefit ratio and appropriate utilization of ancillary thyroid molecular testing in clinical practice. Clinicians still need to rely very much on light microscopy and clinical judgement to do what is best for their patients.

**Abstract #1027**

**ACUTE SUPPURATIVE AND NECROTIZING THYROIDITIS DUE TO EXTENDED SPECTRUM BETA LACTAMASE INHIBITOR(ESBL) ESCHERICHIA COLI (E COLI)**

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**Objective:** Thyroid gland is very resistant to infections. However, very rarely it can be infected by gas-forming organisms which can lead to significant complications. Early diagnosis and management can decrease the morbidity and mortality.

**Case Presentation:** A 79 years old female patient with uncontrolled diabetes noted to have anterior neck swelling for 4-5 days. She was started on amoxicillin. However, patient had worsening swelling, fever, altered mental status and was admitted. Her initial vitals, Temperature-100 degrees F, Heart rate- 100 beats/min, RR-38 /min. On examination anterior neck had erythema, 8 x 10 cm swelling with an undefined border ,firm in consistency and was tender on palpation. Initial Labs - PH 7.29,PaCo2-39 mmHg,Pao2-52 mmhg, Blood glucose of 792 mg/dl, Bicarbonate -19 meq/l, Creatinine 1.5 mg/dl, WBC 21,000/
ul. TSH-0.16 uIU/ml, fT4-1.9 ng/dl,T3-81ng/dl. Urine analysis was positive for WBC and leukocyte esterase. Chest x-ray was negative for any infiltrate. CT of the neck showed-numerous pockets of gas with surrounding fat tissue stranding on the left side of the thyroid extending in to the right side, isthmus and extension of the gas in to the right piriform sinus . Patient was started on fluids, insulin drip ,vancomycin, meropenem and consulted with ENT. Patient didn’t have any recent interventions, injury to throat or dental infection. 

Patient was taken for neck exploration and was found to have necrotizing infection of thyroid and soft tissue. Pathology was consistent with marked inflammation, abscess and necrosis of the soft tissue, skeletal muscle and thyroid. Cultures from blood were negative, urine was positive for E coli and tissue culture grew ESBL E coli. After multiple debridement’s, antibiotics and being on ventilator patient was successfully extubated. Patient postoperatively had TSH-39.42 uIU/ml; fT4-0.8 ng/dl .She was started on levothyroxine and discharged home.

Discussion: Thyroid gland due to its rich blood supply, lymphatic drainage, high iodine concentration, encapsulation is not commonly subject to infections. Thyroid infections are rare and can develop following neck infections, patent thyroglossal fistula, perforation of the gland, post needle biopsy and infections else where in the body like pyelonephritis, upper respiratory tract infections. Left lobe is more commonly affected in females and gram-positive infections tend to be more common. Excision, drainage and often-meticulous debridement’s are needed if the infection involves the surrounding tissues.

Conclusion: Suppurative and necrotic thyroid infections are not common. However in patients presenting with clinical signs of sepsis and thyroid swelling a high clinical suspicion should be maintained.

Abstract #1028

SHAM GRAVES’ DISEASE AND TREATMENT DUE TO EXCESS BIOTIN

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Objective: Caution clinicians on laboratory test interpretation

Methods: Case presentation and a cautionary tale

Case Presentation: A 36-year-old female presents with fatigue, dry skin, “internal jitteriness”, sweating and palpitations. Her thyroid function tests (TFT) indicate Graves’ Disease with markedly elevated free T4 (>7.77 ng/dL), free T3 (8.4 mg/dL) and mildly suppressed TSH (0.25 uIU/mL). She also has positive autoantibodies, TSI, TRab and TPO. A confirmatory thyroid uptake and scan shows mildly elevated homogeneous uptake. Her past medical history includes recurrent transverse myelitis, migraines and anaphylaxis. Her family history is significant for hypothyroidism. Her medications include ibuprofen, levocetizine, diazepam, pregabalin, diclofenac, atenolol, levocartinine, omega-3 fatty acids and biotin. On physical exam her pulse is 55, blood pressure is 87/53, BMI of 23.9 kg/m2 and an otherwise normal exam. With this symptomatology and evaluation she was treated with methimazole. Over a 12 week period the dose was increased without improvement in her symptoms or TFTs. During this time, the possibility of radioiodine ablation was introduced. Despite ongoing symptoms and a thyroid uptake and scan consistent with Graves’ disease, a possile assay interference due to biotin was pursued and her labs were redrawn after 24 hours off biotin. The resulting TFTs were dramatically different and consistent with subclinical hypothyroidism. Accordingly, methimazole was stopped and biotin therapy resumed. Her TFTs once again demonstrated marked hyperthyroidism (TSH 0.037 uIU/mL, free T4 >7.77 ng/dL and free T3 7.5 mg/dL). A last set of labs off biotin confirmed that she was in fact euthyroid.

Discussion: High dose biotin is used to treat mitochondrial disorders and has also been used in multiple sclerosis, a demyelinating disease. In this case, biotin was used to manage symptoms from transverse myelitis, but unfortunately led to erroneous diagnosis and management of Graves’ disease. The immunoassays use biotin-streptavidin affinity to provide accurate serum thyroid hormone levels. In the presence of excess biotin the assay is inaccurate. After discontinuing biotin treatment, the assay interference can disappear within 8 hours. Thus, a minimal interruption in biotin therapy can lead to safe and accurate assessment of thyroid function and prevent misadventures.

Conclusion: This case clearly demonstrates biotin interference with thyroid function test and the risks of misinterpretation leading to inappropriate treatment. Careful review of medications and supplements should be ascertained prior to diagnosing thyroid disease as biotin can interfere with thyroid function assays and lead to incorrect diagnosis and management.
Abstract #1029

WEIGHT CHANGE AFTER THYROID SURGERY IN PATIENTS WITH BENIGN THYROID NODULES AND THYROID CANCER: A POPULATION-BASED STUDY, SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: A key concern among the increasing number of patients who undergo thyroid surgeries every year is postoperative weight gain. Yet, the impact on weight of thyroid surgery for benign thyroid nodules or thyroid cancer is unclear. Our aim was to estimate weight change after thyroid surgery.

Methods: We used the population-based Rochester Epidemiology Project to examine weight and body mass index (BMI) changes at 1, 2, and 3 years of follow-up in patients with (1) thyroid cancer and benign thyroid nodules after thyroid surgery, and (2) thyroid nodules who did not have surgery. To place these estimates in the context of the body of evidence, we also conducted a comprehensive systematic review of the published literature from inception to February 2016. We pooled the results of the 11 studies (mostly case series with incomplete follow-up) reporting estimates using a random effects model.

Results: We identified 449 patients, 181 with thyroid cancer (diagnosed between 2000 and 2012) and 31 with benign thyroid nodules who underwent surgery, and 237 with benign thyroid nodules who did not have surgery (patients with benign thyroid nodules diagnosed between 2003 and 2006). At 1 year, thyroid surgery was not associated with significant changes in mean weight: 0.73 kg (95% CI -0.99, 2.47) vs. 0.53 kg (95% CI -0.21, 1.26) in patients with thyroid cancer treated with surgery and thyroid nodules who did not have surgery, respectively, with no change in their TFTs and symptoms. Eleven studies were included in the meta-analysis. After thyroid cancer surgery, patients gained 0.94 kg (95% CI 0.58-1.33) at 1-2 years and 0.78 kg (95% CI 0.11-1.45) at the longest follow-up; 1-2 years after thyroid nodule surgery, patients gained 1.1 kg (0.3-1.92). Patients with benign thyroid nodules who did not have surgery gained 1.33 kg (95% CI 0.41-2.25) at the longest follow-up.

Conclusion: While weight gain is common in patients with thyroid pathology, observational studies suggest no significant impact of thyroid surgery for benign or malignant nodules on weight and BMI. Clinicians and patients should review this information to discuss post-operative expectations.

Abstract #1030

CASE OF PITUITARY RESISTANCE TO THYROID HORMONE REQUIRING THYROIDECTOMY

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Case Presentation: 50 year old man was referred to Endocrinology for abnormal TSH 29.5 mU/L, FT4 2.3 ng/dL and Total T3 236 ng/dL with symptoms of anxiety, insomnia, palpitations, diarrhea and heat intolerance. Denied tobacco, alcohol or illicit drug abuse. Had a family history of coronary artery disease, type 2 diabetes, and poorly defined thyroid disorders in his mother and sisters. Physical exam revealed warm, moist skin, mild hyperreflexia and a symmetrical goiter approximately twice the normal size. Ultrasound of thyroid showed a hyper vascular multinodular goiter. MRI of the pituitary gland was normal without adenoma. He was put on Methimazole 40 mg daily and Atenolol. His symptoms improved but did not alleviate. Repeat labs revealed a TSH 144 mU/L, and Free T4 0.7 ng/dL. When Methimazole dose was reduced to less than 40 mg daily his symptoms worsened. Based on his response to changing Methimazole doses on multiple occasions, and the fact that he was least symptomatic with a TSH >100 mU/L and FT4 in the normal range a provisional diagnosis of pituitary resistance to thyroid hormone was made. Clinically a near euthyroid state was maintained for about 3 years but his goiter enlarged causing local compression symptoms with dysphagia and unable to button his shirt collar. I123 thyroid uptake and scan after holding Methimazole for 10 days revealed RAI uptake of 71.4% at 2 hours and 84.4% at 24 hours, dominant cold nodule in the right thyroid lobe and a few small cold nodules in both lobes. Subsequent CT of the thyroid gland confirmed the ultrasound findings with no adenopathy. Ultrasound guided FNA of dominant thyroid nodule showed a benign adenomatoid nodule. Radioactive iodine ablation of the gland was attempted twice with 15.9 mCi and 38.3 mCi I131 respectively, with no change in his TFTs and symptoms. Due to his compressive symptoms, a total thyroidectomy was done with no complications. Surgical pathology revealed multiple adenomatous nodules negative for malignancy. Post operatively, he gained weight and levothyroxine dose was titrated to 200 mcg daily. Latest labs showed TSH 96.6, FT4 1.9, FT3 3.0. Repeat MRI of his pituitary is scheduled to monitor for thyrotroph hyperplasia.
Conclusion: Resistance to thyroid hormone is a rare autosomal dominant entity caused by mutations in the thyroid hormone receptor β gene. Serum TSH and free thyroid hormone levels are elevated due to reduced sensitivity to the negative feedback effects of thyroid hormone. Maintaining a clinical euthyroid state may require persistently high TSH levels which can lead to clinically significant goiter requiring thyroidectomy and/ or radioactive iodine ablation. Thyrotoph hyperplasia is a risk as well.

Abstract #1031
AN INTRATHYROIDAL PARAGANGLIOMA
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Objective: To present a rare thyroid pathologic finding and discuss the clinical course

Case Presentation: A 73 y/o female truck driver was referred for a 3 month history of a painless neck mass. She had no personal history of thyroid disease, diabetes, or hypertension. Family history was non-contributory including thyroid cancer. Neck ultrasound revealed multiple right-sided thyroid nodules, the largest of which was a 2.9 x 2.5 x 2.3 cm heterogeneous nodule of the right middle lobe. Fine needle aspirate was suspicious for follicular neoplasm and the patient opted for a total thyroidectomy. Surgical pathology revealed a 2.5 cm intrathyroidal paranganglioma (PGL) of the right lobe with positive tracheal margins. Immunohistochemistry was positive for S-100 in sustentacular cells and tumor cells stained positive for synaptophysin and chromogranin. Further stains were negative for thyroglobulin, TTF-1, p53, calcitonin, mCEA, PTH and BRAF (V600e). Slides were reviewed by two other pathologists who confirmed the diagnosis. The patient had an unremarkable post-operative course and started on levothyroxine 125mcg and elemental calcium. He reported feeling slightly anxious, having increased sleep disturbance, palpitations, tremor, or hair, skin or nail changes. He had no prior history of thyroid disease and denied any other new medications, illness, or radiation. Laboratory review showed normal thyroid function tests before starting nivolumab and ipilimumab therapy. Three weeks after starting therapy, free T4 level was 2.91 U/mL and TSH 0.009 ng/dL. Thyroid antibody levels were assessed after thyrotoxicosis was discovered and found to be undetectable. Radioactive iodine uptake scan was not performed as the patient had received IV contrast within the last month. Thyroid ultrasound showed no nodules and no diffuse increase in flow by Doppler. Within weeks, the patient’s serum TSH increased to 83.2 U/mL with a
ABSTRACTS – Thyroid Disease

free T4 level of 0.52 ng/dL and he was started on thyroid hormone replacement therapy. The temporal association of these findings with the initiation of nivolumab and ipilimumab led to our diagnosis of thyroiditis secondary to autoimmune checkpoint inhibitor therapy. The patient subsequently developed hypothyroidism and continues to require thyroid hormone replacement.

**Discussion:** Nivolumab and ipilimumab are monoclonal antibody medications that work by blocking negative regulators of T-cell activation and response, allowing and enabling the immune system to attack tumor cells. The mechanism of action is not specific to tumor cells and can lead to endocrinopathies. Thyroid disease incidence in nivolumab monotherapy is up to 9%, while in ipilimumab monotherapy is up to 2%. However, dual therapy with these medications may cause thyroiditis and hypothyroidism in 22% and hyperthyroidism in 8% of patients.

**Conclusion:** This case represents an unusual cause of thyroiditis and subsequent hypothyroidism from an increasingly prevalent cancer therapy. A heightened awareness of autoimmune checkpoint inhibitors causing thyroid dysfunction is needed. Baseline and periodic monitoring of thyroid function tests are recommended throughout treatment with these medications.

Abstract #1033

RAPID EVOLUTION OF HYPOTHYROIDISM IN PATIENTS TREATED WITH NIVOLUMAB

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**Objective:** To describe the evolution of hypothyroidism in a series of patients treated with anti-programmed cell death protein-1 (PD-1) monoclonal antibody (mAb), nivolumab.

**Methods:** Cases of thyroid dysfunction after initiation of anti-PD-1 mAb treatment were identified from a single oncoendocrinology center from April-November 2016. Eight cases were identified. Of the 8 patients, 6 were treated with nivolumab, 2 with pembrolizumab. Five of the nivolumab-treated patients developed hypothyroidism. Clinical and thyroid function tests (TFTs) for these patients are presented.

**Case Presentation:** There were 2 male and 3 female patients, mean age 69 years (range 64-73 years). Two patients had lung adenocarcinoma, one each had renal cell carcinoma, multiple myeloma, and bladder carcinoma. No patients reported a previous diagnosis of thyroid disease, although one patient had mildly elevated TSH (8.5 uU/mL) on initiation of nivolumab. A second patient had a single TSH of 11.9 uU/mL 6 months prior to starting nivolumab, but TSH had normalized without treatment before starting nivolumab. Three patients initially developed hyperthyroidism, detected 4-6 weeks after their first dose of nivolumab. The onset of hypothyroidism ranged from 6 to 16 weeks after initiation of nivolumab. One patient had the first TFTs checked 4 months after initiating nivolumab at which time she was hypothyroid. Of the remaining 4 patients the evolution of hypothyroidism was rapid; the mean time from the first abnormal TSH (low TSH in 3 patients), or last normal TSH (in 1 patient), to elevated TSH was 27 days (range 7-46 days).

**Discussion:** Thyroid dysfunction is one of the immune related adverse events associated with anti-PD-1 mAbs. There is little known, however, about the progression and pathophysiology of the disease. The quick onset of hyperthyroidism and short lag time to development of hypothyroidism is illustrated by this case series. The precise pathophysiology of nivolumab-associated thyroid dysfunction is unknown, but the fast progression may indicate inflammatory destruction and a mechanism similar to painless thyroiditis.

**Conclusion:** As use of programmed cell death inhibiting antibodies increases, more cases of thyroiditis have been observed. Thyroid function testing should be performed at baseline, soon after initiation and at 4-6 week periods. Once the first low TSH is detected, the TFTs should be rechecked within 4 weeks, as the transition to hypothyroidism can be expected to be rapid. More research is needed to understand which patients are most susceptible to developing this adverse event and which patients are most likely to recover.
Abstract #1034

INCREASED RISK OF THYROID CANCER IN PATIENTS WITH MULTINODULAR GRAVES’ DISEASE: SHOULD THYROIDECTOMY BE CONSIDERED THE TREATMENT OF CHOICE?

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Objective: Emphasize the increased risk of thyroid cancer in nodular Graves’.

Case Presentation: A 66 year-old man was evaluated for a multinodular goiter in 7/2013. His initial ultrasound showed multiple nodules (5 on the right, 1 in the isthmus, 2 on the left). Laboratory values were: TSI-327% (nl.<140); TSH <0.02mIU/L (Ref. range 0.47-4.68); Free T4-1.9ng/dL (Ref. range 0.7-1.9). Subclinical hyperthyroidism due to GD was diagnosed. RAIU and scan revealed uptakes of 4.9% and 12.9% at 4 and 24 hours, respectively, and a right 3 cm cold nodule, which was negative for malignancy. Given the degree of TSH suppression and history of cardiac disease, he was treated with 54.2mCi of 131-I in 12/2013. He later required levothyroxine replacement. An ultrasound in 2/2014, showed an enlarged multinodular thyroid with 3 distinct nodules on the right and 3 on the left. One on the right (1.6x1.7x1.4cm), was considered a new lesion more concerning for malignancy. FNA of this lesion was also negative for malignancy. In 3/2015, he had compressive symptoms with dysphagia due to the goiter, and underwent a total thyroidectomy. Pathology showed multifocal follicular variant papillary thyroid cancer with the largest tumor diameters of 2.5 cm on the right and 3.7 cm on the left. He had 2 of 2 positive pretracheal lymph nodes with the greatest diameter of metastatic focus at 0.05 cm, minimal extrathyroid extension to the perithyroid soft tissue, and lymphovascular invasion. The initial staging was T3N1aMx with an intermediate ATA risk for recurrence. Subsequently, he was given 178.9mCi 131-I, with an excellent response.

Discussion: The risk of thyroid cancer in patients with nodular GD requires further study. A recent report indicated patients with nodular GD can have an incidence of thyroid cancer as high as 21%. Our patient, despite two negative FNA results, was found to have a multifocal PTC with positive lymph nodes and invasion. Given the possibility of higher false negative rates with FNA in patients with nodular GD, and their increased incidence of thyroid cancer, biopsy of ≥ 3 nodules would be prudent to increase the diagnostic yield.

Conclusion: Nodular GD may have increased risk for associated thyroid cancer. Thyroidectomy should be considered as the primary treatment for this patient population.

Abstract #1035

BIOTIN USE AND THYROID FUNCTION IN THREE HEALTHY ACTIVE DUTY SOLIDERS

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Objective: Nutritional supplements are increasing in the US population with a large segment using Biotin (vitamin B7) as a treatment for diabetes, brittle hair and nails, among other conditions. Many immunoassays use a biotin-streptavidin interaction to immobilize immune complexes in either a competitive immunoassay or immunometric (sandwich) assay. Thyroid function testing utilizes both methods with ingestion of Biotin supplements leading to case reports of factitious hyperthyroidism in patients on high dose supplementation. The objective of this study was to assess the potential assay interference on thyroid function tests following Biotin ingestion in healthy subjects on low to moderate dose Biotin supplementation.

Methods: Three healthy male, active duty military endocrinologists on no chronic medications had blood samples drawn for TSH, free T3, free T4 and TSI drawn before ingestion, and following ingestion of Biotin 15 mg and 30 mg on separate days. Testing for TSH utilized a Roche 3rd generation sandwich assay. T3 and T4 testing utilized Roche 3rd and 2nd generation competitive immunoassays respectively. TSI testing utilized a labcorp non-biotin-streptavidin assay.

Case Presentation: Following ingestion of 15mg of Biotin subjects TSH levels fell by 56% at 2 hours and 29% at 4 hours. Free T4 levels rose by 10% at 2 hours and 4% at 4 hours and free T3 levels fell by 30% at 2 hours and did not change at 4 hours. Following ingestion of 30mg of Biotin subjects TSH levels fell by 71% at 2 hours and 48% at 4 hours. Free T4 levels rose 20% at 2 hours and 14% at 4 hours and free T3 levels rose by 6% at 2 hours and did not change from baseline at 4 hours. TSI levels did not change from baseline.

Discussion: Low to moderate dose Biotin supplementation lead to a consistent fall in serum TSH at 2 and 4 hours post-ingestion with a higher reduction in TSH seen at the 30mg dose. Less impressive changes were seen with the competitive FT4, FT3 immunoassays but free T4 levels did tend to rise slightly at the TSH nadir post-ingestion. In clinical practice, these results could be interpreted as subclinical hyperthyroidism and may lead to unnecessary
follow-up testing or alteration in dosing in those already on thyroid hormone supplementation.

**Conclusion:** Biotin ingestion even in low to moderate doses can cause immunoassay interference depending on the assay with higher variability seen in TSH results. Clinicians should be aware of this interaction and the potential for misdiagnosis or under treatment in patients on Biotin supplementation.

**Abstract #1036**

**MALIGNANT STRUMA OVARI WITH METASTATIC FOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA**

Victoria Loseva, MD, Matthew Nicholson, MD, Anthony Mulloy, PhD, DO, Edward Chin, MD

**Objective:** Struma ovarii is a rare ovarian tumor characterized by the presence of thyroid tissue in the ovary, typically as part of a teratoma. We report the diagnosis and treatment of a case of malignant struma ovarii with metastatic follicular variant of papillary thyroid carcinoma and discuss recommendations for treatment.

**Case Presentation:** A 36 year old female underwent exploratory laparotomy for a large septated polycystic right adnexal mass with multiple soft tissue abdominal implants. Pathology showed a malignant struma ovarii with a well-differentiated thyroid type cancer involving the uterus, cervix, fallopian tubes, ovaries, sigmoid colon, appendix and omentum. Histology showed thyroid follicular cells with small nuclei, evenly distributed chromatin, focal areas of nuclear clearing, nuclear grooves and occasional pseudoinclusions consistent with a follicular variant of papillary thyroid carcinoma. Thyroid ultrasound was normal. Total thyroidectomy showed no malignancy. Iodinated contrast given earlier delayed adjuvant radioactive iodine therapy. Six months after her initial surgery and with TSH 150 (reference range 0-4 – 4.7 mcIU/mL) she received 200.5 mCi of I-131. Stimulated thyroglobulin (TG) was 581 (reference range 0.1 – 33 ng/mL) and TG antibodies <1.8 IU/mL. Post therapy whole body scan showed successful targeting of radioactive iodine to the peritoneal carcinomatosis and nodal disease in the abdomen. Studies eleven months postoperatively show TG 32 and TG antibodies 3.1.

**Discussion:** Struma ovarii consists of thyroid tissue derived from germ cells in a mature teratoma. Malignant transformation is very rare and clinically evident metastatic disease is uncommon. The rarity of this disease renders evaluation of treatment modalities difficult and determining outcome and best treatment approaches is controversial. Risk stratification of malignant struma ovarii similar to that used in thyroid carcinoma help determines the most appropriate postoperative management. Patients with thyroid type carcinoma less than 2 cm confined to the struma ovarii, with no worrisome histologic features, can be considered low risk for persistent or recurrent disease. Conversely, patients with larger thyroid carcinomas, disease outside the struma ovarii, or more aggressive histologic features should be considered high risk.

**Conclusion:** Treatment, management and follow up should be based on ovarian cancer and thyroid cancer guidelines and a multidisciplinary approach is recommended. For patients with metastatic differentiated thyroid type carcinoma from struma ovarii, therapy should be total thyroidectomy followed by adjuvant radioactive iodine ablation and thyroid hormone suppression.

**Abstract #1037**

**HYPERCALCITONINEMIA MEDIATED HYPOCALCEMIA IN MEDULLARY THYROID CANCER: A CASE REPORT**

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**Objective:** To understand the mechanism of hypocalcemia with hypercalcitoninemia in medullary thyroid cancer (MTC)

**Methods:** MTC originates from the neural crest derived parafollicular chief cells (C-cells) of the thyroid gland1. Serum calcitonin, released by C cells, serves as a tumor marker in MTC to monitor for disease recurrence and prognosis2. Hypercalcitoninemia induced hypocalcemia has only been reported in cases of toxic shock syndrome (TSS)3 and pulmonary tuberculosis (TB)4. We present the first case of hypercalcitoninemia induced hypocalcemia in MTC.

**Case Presentation:** 83-year-old male with metastatic MTC (to the liver) and post-surgical hypothyroidism after total thyroidectomy presented with significant weakness, diarrhea, and dysphagia. Home medications included levothyroxine (LT4) 100 mcg daily and Armour® thyroid 120 mg daily. On exam, he was cachectic, with a well healed thyroidectomy scar, and had no neck masses or lymphadenopathy. He had mild hyperreflexia, fine tremor, hepatomegaly, and a negative Chvostek’s sign. Labs revealed thyroid stimulating hormone less than 0.01 uIU/ml (0.27 – 4.20 uIU/ml), free thyroxine 2.1 ng/dl (0.9 – 1.8 ng/dl) and total triiodothyronine 54 ng/dl (80 – 200 ng/dl). Potassium was 2.7 mmol/L (3.5 – 5.3 mmol/L), corrected calcium 7.59 mg/dl (8.5 – 10.5 mg/dl), ionized calcium 0.86 mmol/L (1.05 - 1.34 mmol/L), intact parathyroid
hormone 82 pg/ml (15 – 65 pg/ml), phosphorous 2.1 mg/dl (2.5 – 4.5 mg/dl), 1,25-dihydroxy vitamin D 70.7 pg/ml (19.9 – 79.3 pg/ml), 25-hydroxy vitamin D 33.2 ng/ml (30 – 100 ng/ml), and serum calcitonin 46557 pg/ml (<=8.4 pg/ml). Renal function and magnesium were normal. He was diagnosed with aspiration pneumonia, iatrogenic hyperthyroidism, and hypocalcemia likely due to hypercalcitoninemia after excluding other etiologies. He received intravenous (IV) fluids, antibiotics, electrolyte replacements, IV calcium gluconate, and 3 tablets oral calcium carbonate 1250 mg three times a day with meals. Armour® thyroid was discontinued. Serum calcium improved to 8.36 mg/dl with resolution of symptoms. He was discharged with oral calcium carbonate and recommendations to follow-up with his endocrinologist.

**Discussion:** The physiologic role of calcitonin is not known but its release is stimulated by hypercalcemia. Calcitonin salmon, a pharmaceutical version of the hormone is highly effective in the treatment of hypercalcemia caused by a myriad of diseases and is a commonly prescribed treatment. The mechanism of hypercalcitoninemia induced hypocalcemia in MTC is unknown and limited to knowledge previously reported in cases of TSS3 and pulmonary TB4.

**Conclusion:** Hypercalcitoninemia can be considered in the differential diagnosis for hypocalcemia in patients with MTC.

**Abstract #1038**

**HOW SUCCESSFUL IS REPEAT SURGICAL INTERVENTION FOR PTC RECURRENTNESS?**

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**Objective:** While long-term survival from papillary thyroid cancer (PTC) is excellent, disease recurrence remains a major challenge. PTC has a high rate of cervical metastasis and re-operation is often required to manage persistent or recurrent disease. While repeat surgery removes gross disease, many patients are not rendered completely disease-free. We aimed to evaluate the efficacy of the first re-operation for recurrent PTC in order to quantify the odds of achieving an undetectable thyroglobulin (Tg) and an unremarkable neck ultrasound (US).

**Methods:** Re-operative cases for PTC following at least a total thyroidectomy were retrospectively reviewed from a prospectively maintained surgical database. Surgical success was defined as achieving an undetectable Tg and resolution of neck US abnormalities following the re-operation. Subgroup analysis compared patients with early (<1 year) and late (>1 year) recurrence.

**Results:** Early PTC recurrence was diagnosed in 31 patients (49.2%), and late recurrence in 32 patients (50.7%). Both groups were similar with regards to age, gender, ethnicity, ETOH history, smoking history, and history of radiation exposure. Patients also had similar initial tumor size, positive to examined lymph node ratio, therapy with I-131, and ATA risk stratification. The overall success rate of re-operative intervention for PTC recurrence was low, with only 13 patients (23.6%) achieving undetectable Tg levels, 14 patients (31.8%) achieving an unremarkable neck US post-operatively, and 4 (9.3%) patients achieving both an undetectable Tg and an unremarkable neck US. When comparing the two groups, the chance of achieving both an undetectable Tg and an unremarkable neck ultrasound together was significantly higher in the group diagnosed with late recurrence after initial treatment (4 patients (21.1%)) as opposed to the group diagnosed with early recurrence (0 patients (0%)) (p=0.008).

**Discussion:** Persistently elevated Tg levels and/or neck US abnormalities following re-operation for residual or recurrent PTC is very common. Undetectable Tg levels are achieved in about one-quarter of patients, but there are frequently questionable findings on US that persist. Achieving both an undetectable Tg and a normal neck US following repeat surgical intervention is unfortunately rare, but was significantly more likely in those patients undergoing re-operation >1 year after their index operation.

**Conclusion:** These findings are relevant in managing patient and provider expectations from repeat surgical interventions, and underscores the importance of a thorough pre-operative assessment and meticulous initial surgery in patients with PTC.

**Abstract #1039**

**REPEAT FINE NEEDLE ASPIRATION BIOPSY FOR BETHESDA III THYROID NODULES: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Objective:** Until recently, recommended management of thyroid nodules diagnosed cytologically as atypia/follicular lesion of undetermined significance (AUS/FLUS) has been to repeat fine needle aspiration cytology (FNA). However, the 2015 American Thyroid Association guidelines for management of patients with thyroid nodules modified this recommendation to endorse molecular marker testing, as an alternative to repeating the biopsy. This recommendation was based on available clinical
validation studies on molecular marker test performance; and the concern that a benign cytology result following a previous AUS/FLUS result might be unreliable. We conducted a systematic review of the literature and meta-analysis, to clarify the outcomes of repeat FNA for AUS/FLUS specimens.

**Methods:** We searched in Embase, WOS, Cochrane and PubMed for the terms ("Thyroid Gland/cytology" OR "thyroid nodule" OR "Thyroid cancer") AND ("follicular lesion of undetermined significance" OR "Bethesda III" OR "indeterminate cytology" OR indeterminate OR atypical OR atypia OR follicular lesion* OR "AUS/FLUS" OR "AUS" OR "FLUS" or "B3" or "B-III") and retrieved 1846 articles that were screened by one investigator. After reviewing the full text of 81 manuscripts, 27 met criteria to be included to estimate the results of repeat FNA. Prevalence of malignancy for each category was estimated on 17 of those studies with surgical follow-up information.

**Results:** The results of the repeat FNA on 4,375 nodules initially classified as Bethesda III were: 242 (6%) non-diagnostic; 2410 (55%) benign; 1122 (26%) AUS/FLUS; 340 (8%) follicular/Hürthle-cell neoplasm; 181 (4%) suspicious for malignancy; and 80 (2%) malignant. The prevalence of malignancy on resected nodules was 23% (293/1288) in all resected nodules; 30% (10/35) in non-diagnostic; 2% (9/481) in benign; 24% (115/475) in AUS/FLUS; 38% (66/175) in follicular/Hürthle-cell neoplasm; 71% (63/93) in suspicious for malignancy; and 100% (28/28) in malignant specimens; yielding a NPV of 98% for repeat FNA.

**Conclusion:** Repeat FNA reliably (NPV of 98%) reclassifies 55% of the nodules with AUS/FLUS cytology as benign; and an additional 6% as malignant or suspicious for malignancy (PPV 71%-100%). Cost-effectiveness of molecular marker tests for the evaluation of AUS/FLUS should be evaluated against the costs and outcomes of repeat FNA.

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**Abstract #1040**

**IMPROVEMENTS IN IDENTIFYING THYROID NODULES FOR FNA: COMPARING THE REVISED 2015 ATA GUIDELINES TO FORMER 2009 GUIDELINES**

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**Objective:** To evaluate the difference between the new 2015 ATA guidelines and former 2009 ATA guidelines in decision-making for thyroid nodule FNA.

**Methods:** A retrospective chart review was conducted at a Midwest academic medical center. Between January 2010 and December 2011, 883 ultrasound-guided fine needle aspiration (UGFNA) biopsies of thyroid nodules were performed, and results of 273 biopsies were randomly selected for evaluation. We assessed multiple clinical measures, including family history, TSH value, I-scan result, and US features. We determined FNA results of each nodule, identified which nodules underwent surgery, and documented final pathology. Using both new 2015 and prior 2009 ATA guidelines, we then determined which nodules met criteria for UGFNA biopsy, which nodules did not meet conditions for biopsy, and which nodules lacked data for appropriate classification. We compared these results to determine if the new guidelines are more comprehensive for determining which nodules are suitable for biopsy.

**Results:** When applying 2015 ATA guidelines, more thyroid nodules with benign FNA results met criteria for thyroid biopsy compared with the former 2009 guidelines (63.8% vs 57.0%). The updated ATA guidelines also reduced the number of nodules with insufficient data to determine if FNA was necessary. Of the 221 nodules that were benign by FNA cytology, only 55 (24.9%) nodules needed more data for biopsy determination per the new guidelines, while 70 (31.7%) nodules had insufficient data for biopsy based on previous criteria. The updated guidelines also increased the number of biopsy-proven follicular nodules appropriate for biopsy, 75.0% vs 61.1%, while reducing the number of inconclusive nodules, 22.2% vs 33.3%.

**Discussion:** The updated ATA guidelines enabled a greater number of nodules to be included for or excluded from FNA, thus reducing the number of inconclusive nodules, in the context of FNA-proven benign and follicular nodules. This provides practitioners a more effective tool for clinical decision making in the management of thyroid nodules. Implementation of new guidelines did not change the number of appropriate, inappropriate, or inconclusive nodules for thyroid biopsy when FNA was non-diagnostic, suspicious, or malignant by cytology.
Conclusion: The 2015 ATA guidelines for evaluation of thyroid nodules provide simpler, more inclusive criteria to determine whether thyroid nodules are appropriate for biopsy by focusing primarily on size, consistency, and specific ultrasound features. This enables providers to make more conclusive decisions on how to proceed with management of thyroid nodules, as newer guidelines are less susceptible to interpretation.

Abstract #1041

MALIGNANT STRUMA OVARII: A CASE SERIES

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Objective: Struma ovarii is a variant of ovarian teratomas in which mature thyroid tissue is the predominant component on histologic examination. It is classified into benign which is the majority of cases and malignant (0.3% to 5% of all cases) on the basis of histopathological features. The most common type of malignant struma ovarii (MSO) is papillary thyroid carcinoma. Due to the paucity of literature on this malignancy, most of the diagnostic and therapeutic approaches are based on case reports and series. Our objective was to evaluate diagnostic and therapeutic characteristics of patients with MSO.

Methods: We retrospectively analyzed our tumor registry data for patients with MSO.

Case Presentation: Ten patients were identified in the database from October 2000 to November 2016. The median age at diagnosis was 42 years (30-65) and follow-up duration was approximately 7 years (0.4 to 25). Presentation was secondary to abdominal pain (n=3), hip pain from pathologic fracture (n=1), dyspnea from pleural effusion (n=1), and incidental discovery (n=5). Initial surgery included unilateral salpingo-oophorectomy (n=5) or total abdominal hysterectomy with bilateral oophorectomy (n=5). Histopathological review diagnosed five patients with papillary thyroid cancer, four with follicular thyroid cancer, and one with poorly differentiated thyroid cancer. Metastatic disease was detected in five cases; sites included peritoneum, pelvic wall, bladder, liver, lung and bone. Four out of these patients were diagnosed with metastasis at the time of presentation, one patient was noted to have a recurrent bone metastasis one year after diagnosis. Nine of ten patients were planned to have or treated with thyroidectomy, only one patient was not treated due to T1a tumor pathology. Six patients received postoperative radioactive iodine treatment, four of them had RAI-avid metastatic lesions. Only one patient received a tyrosine kinase inhibitor for widely metastatic, KRAS mutated, poorly differentiated thyroid cancer. All of the patients were alive at the last visit.

Conclusion: Due to its rarity, there is no consensus on the optimal management of MOS. In our series, despite the progressive nature of the disease, all the patients are alive suggesting a good disease survival rate. Until we have larger studies, the decision to pursue local resection, metachronous thyroidectomy, and RAI or targeted therapy. Further studies are required to determine the optimal treatment approach, especially the role of total thyroidectomy and RAI in non-metastatic MSO patients. Women with MSO should be managed in a multidisciplinary approach coordinated between endocrinologists, gynecological and surgical oncologists.

Abstract #1042

IRON DEFICIENCY CAUSING ABNORMAL THYROID FUNCTION

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Objective: To describe a case of abnormal thyroid function due to iron deficiency.

Methods: Iron deficiency causing hypothyroidism is not well recognized. We present a young woman with abnormal thyroid function due to iron deficiency.

Case Presentation: An 18-year-old female presented for evaluation of abnormal thyroid function and a pituitary tumor. At age 16 she was noted to have normal serum TSH (2.3mIU/ml) and low free T4 (0.8ng/dl) using direct chemiluminescence immune assay. Repeat labs showed similar results. Free T4 was then measured by the direct dialysis method, a more accurate method that eliminates interference by other binding proteins in the serum not accounted for in the automated analog immunoassay. Serum free T4 by direct dialysis method was normal (1.1ng/dl). At age 18, a repeat thyroid function test showed low TSH (0.2mIU/ml), normal free T4 (0.98ng/dl) by electro-chemiluminescence method but low serum free T4 (0.66ng/dl) with direct dialysis method. An MRI of the pituitary gland to evaluate for central hypothyroidism, showed a 9mm pituitary tumor between the adenohypophysis and neurohypophysis suggestive of Rathke’s cleft cyst vs. pituitary microadenoma. She was then referred to the endocrinology clinic. She endorsed occasional mild headache and denied galactorrhea,
dizziness, or excessive urination. Her exam was unremarkable except for multiple facial acne lesions. Repeat labs showed normal TSH (2.2 mIU/ml) but low free T4 (0.9 ng/dL) by electro-chemiluminescence assay as well as low free T4 (0.7 ng/dL) with direct dialysis assay. She was noted to have iron deficiency (serum ferritin <40 ng/mL). Other hormonal biochemical work-up for pituitary tumor was unremarkable. She was started on oral ferrous sulfate 325 mg twice daily. Subsequent labs showed that her iron deficiency resolved and her free T4 level improved to normal. Repeat MRI at six months demonstrated stability of the pituitary tumor.

Discussion: Iron deficiency is common in young women due to blood loss from menstrual periods. Thyroid hormone synthesis incorporates a heme-containing enzyme called thyroid peroxidase (TPO). TPO catalyzes the two initial steps in thyroid hormone synthesis. Thus, iron deficiency may result in reduced thyroid peroxidase activity contributing to hypothyroidism. Animal studies have reported low thyroxine levels associated with iron deficiency. A Chinese population study noted that prevalence of iron deficiency was higher in in young pregnant and non-pregnant women with isolated hypothyroxinemia.

Conclusion: Iron deficiency should be considered in patients presenting with abnormal thyroid function, especially in cases of isolated hypothyroxinemia.

Abstract #1044

FALSE ELEVATION IN THYROID STIMULATING HORMONE (TSH) DUE TO HETEROPHILE ANTIBODY

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Objective: To describe a case with falsely-elevated TSH levels due to interference by heterophile antibody.

Methods: Elevated TSH levels with normal T4 levels are suggestive of subclinical hypothyroidism. The differential diagnosis for elevated TSH with normal T4 includes TSH secreting pituitary tumor, heterophile antibodies that react with assay, and rarely, autoimmunity against TSH. We present a case with a falsely elevated TSH levels due to presence of heterophile antibody interfering with thyrotropin assay.

Case Presentation: A 47-year-old man with history of hepatitis C and Raynaud’s disease presented to his primary care provider (PCP) with complaints of fatigue, decreased concentration, and memory problems. Initial lab work showed TSH 49.5 µIU/ml by sandwich immunoassay (range 0.4-4) and normal free T4 1.5 ng/dL (range 0.8-1.8).
He was started on levo-thyroxine 0.025 mg daily. Repeat blood work two months later showed TSH 47.1 µIU/ml and free T4 1.49 ng/dl. Levothyroxine was increased to 0.075 mg daily. Four months later, TSH was higher at 54.4 µIU/ml and elevated free T4 2.26 ng/dl. At that time, patient was referred to endocrine clinic. On interview, he reported worsening fatigue. He denied heat or cold intolerance, anxiety, palpitations, tremors, weight loss, or diarrhea. Physical exam was unremarkable with normal thyroid gland. Due to persistently elevated TSH and normal to high free T4 unresponsive to levothyroxine therapy, other etiologies for elevated TSH were entertained. We recommended stopping levothyroxine with plans to repeat thyroid studies. A month later, TSH measured by the same method used by the PCP (CompuNet Lab) came back 53 µIU/ml, whereas a different method (3rd generation chemiluminescent assay by Quest Lab) yielded a normal level of 1.7 mIU/L with and without heterophile anti-murine antibody (HAMA) treatment.

Discussion: Heterophile antibodies are endogenous antibodies that may cause interference with immunoassays through binding of capture antibody to the detection antibody. This interference has been described in TSH sandwich immunoassays. The prevalence of heterophile antibody interference is between 0.2% and 15%. Repeating TSH level with a different lab or treating with antibody blocking agents can prevent this issue.

Conclusion: We present an interesting case of abnormal TSH due to presence of heterophile antibody. Heterophile antibody interference should be considered if there is a discrepancy between TSH and free T4 before making any therapeutic decisions.

Abstract #1045

NIVOLUMAB-INDUCED THYROIDITIS THAT RESULTED IN HYPOTHYROIDISM

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Objective: In Hodgkin’s lymphoma, programmed death1 (PD-1) ligands are overexpressed Reed-Sternberg cells which evade immune surveillance. Nivolumab is a novel human IgG4 immune checkpoint-blocking antibody that blocks PD-1. It has proven effective in treating refractory Hodgkin’s Lymphoma. However, recent studies have shown that Nivolumab can induce thyroid dysfunctions, including hypothyroidism and thyroid toxicosis developing after a few weeks treatment of Nivolumab. Here we present one case with nivolumab induced thyroiditis that resulted in hypothyroidism.

Methods: Four weeks after starting Nivolumab, a 20-year-old male with refractory Hodgkin’s lymphoma developed tachycardia, cold sweats, tremors, chronic diarrhea, pain in chest abdomen and neck and difficulty swallowing. He lost 100 lbs in four months. His physical exam shows tenderness on palpation of thyroid and an enlarged thyroid. The patient had a PET scan that showed increased uptake in the thyroid gland. Subsequently, he had a thyroid function test, which showed: TSH 0.020 mcu/ml, T3-Free 18.8ng/dl, T3 total 372ng/dl, T4-Free 5.6ng/dl, Thyroid peroxidase antibody and TSH receptor antibody negative. Patient’s TSH was 3.259 mcu/ml before starting Nivolumab, Patient denies any history of thyroid disease.

Case Presentation: Therefore, he was started on methimazole prednisone, and atenolol. The patient gradually recovered after using supportive care and the above medications. He was discharged from the hospital in three days. The patients follow thyroid functions were TSH 13 mcu/ml, T4-free 0.5 ng/dl, T3 total 69ng/dl. The methimazole was later stopped and the patient continued on prednione therapy. His repeat thyroid function in 6 weeks were TSH 54.5 mcu/ml, T4-Free 0.5ng/dl.

Discussion: This patient suggests that a thyroid toxicosis may be induced about four weeks after starting Nivolumab. The etiology of thyrotoxicosis can be either thyroiditis or Graves’ disease; there are case reports for both. In our case, the thyroid tenderness after examination and subsequent hypothyroidism, appears more consistent with thyroiditis. The degree of thyroid hormone elevation was more consistent with Graves. The best diagnostic test would be a 1-131 uptake, but in our patient, a 1-131 uptake was not performed due to methimazole initiation. The patient had recovery of symptoms and lab tests and was sent home on prednisone therapy. He seemed to have had recovery of his thyroid function and end up in hypothyroidism.

Conclusion: Despite the increasing use of Nivolumab in the clinical practice, thyroid dysfunction may be difficult to diagnose because its symptoms are similar to those of other diseases. Our case report will make physicians more aware of this adverse effect.
ABSTRACTS –Thyroid Disease

Abstract #1046

THYROID STIMULATING HORMONE SUPPRESSION WITH THYROID HORMONE REPLACEMENT IN THE TREATMENT OF CHRONIC URTICARIA ASSOCIATED WITH AUTOIMMUNE THYROIDITIS

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Objective: Chronic urticaria (CU) is a recurrent itchy cutaneous swelling lasting for at least 6 weeks. Its prevalence is approximately 20% in the general population, but significantly higher than that in patients with autoimmune diseases, especially Hashimoto’s thyroiditis. Thyroid autoantibodies—indicators for the diagnosis of autoimmune thyroid disease—are reportedly found in 12%–37% of patients with CU, however the role of thyroid autoantibodies in the pathogenesis of CU remains contentious. Many experts have hypothesized that thyroid stimulating hormone (TSH) may drive the production of proinflammatory cytokines and thus upregulate immune responses. According to this hypothesis, levothyroxine therapy would reduce the inflammatory response by suppressing TSH, and improving the CU.

Case Presentation: Case 1: A 31-year-old female with CU and Hashimoto’s thyroiditis presented seeking to optimize her thyroid medication prior to elective in vitro fertilization. Tests revealed TSH of 8 U/mL and thyroperoxidase (TPO) of 58 U/mL. Was on intermittent oral and topical steroids for the CU. Interestingly, aggravation of her urticaria was usually associated with higher TSH. Suppressing TSH to below 2 U/mL resulted in improvements in the CU attacks. Case 2: A 32-year-old female with a history of right hemithyroidectomy with benign pathology presented with CU. Follow-up ultrasound revealed a 2.6-cm left lobe thyroid nodule with benign cytology. She was euthyroid, but exhibited TPO 41 U/mL and TSH 3.6 U/mL. Levothyroxine was started at 25 µg/day with the aim of lowering TSH levels, symptomatic relief ensued.

Case 3: A 39-year-old female with Hashimoto’s thyroiditis that was sub-optimally controlled with levothyroxine. She was started on a combination of T3/T4. Had a history of relapsing CU, which resolved after TSH was successfully reduced to < 2 U/mL.

Discussion: Autoimmune thyroiditis is characterized by the presence of TPO and TG autoantibodies. Hypothyroidism is more frequent than hyperthyroidism in patients with CU. Currently, the most common treatment for CU is antihistamines. The associations between CU and autoimmune thyroiditis are not well understood and the potential effectiveness of the use of thyroxin for the treatment of CU in patients with thyroid autoimmunity is even less well-established. It has been reported that treatment with thyroxin alleviated the symptoms of CU in some cases, with a concomitant reduction in thyroid antibodies.

Conclusion: In patients with autoimmune thyroiditis and CU, TSH suppression via levothyroxine may constitute an effective strategy for the treatment of CU. The efficacy and safety of this treatment strategy should be further investigated.

Abstract #1047

A CASE OF HASHIMOTO’S ENCEPHALOPATHY: A RARE STROKE MIMIC

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Objective: A rare cause of stroke-like symptoms is Hashimoto’s Encephalopathy (HE) which can present as a wide constellation of neurological symptoms. HE presents commonly in women, in the presence of anti-thyroid antibodies. Symptoms commonly respond to steroid therapy. The objective of this report is to describe a patient who presented with stroke-like symptoms and improved significantly after steroid therapy.

Case Presentation: A 60 year old Caucasian female with a history of hypertension presented with new onset slurring of speech, right sided facial droop, and difficulty to swallow. CT of the head was negative for any hemorrhage or acute intracranial processes. Subsequent MRI brain showed chronic micro-vascular changes of the brain. On further serological work-up, the patient’s TSH was noted to be elevated at 40.1ulU/mL (0.35-3.7), Free T3 was 1.9pg/mL (2.2-4), and Free Thyroxine was 0.88ng/dL (0.75-1.45). Although clinically euthyroid, due to marked elevation in TSH level, thyroid antibodies were ordered. The thyroglobulin antibody was 73.7U/mL (0-60) and anti-thyroid peroxidase antibody was 28988.9U/mL (0-60). The patient was diagnosed with HE, and was started on pulse dose steroids, then transitioned to oral prednisone 60mg once daily, allowing complete resolution of her symptoms. She was discharged and advised to follow up in one month for repeat thyroid function tests.

Conclusion: Stroke like symptoms are observed in 27% of patients with Hashimoto’s encephalopathy. Although the pathogenic role of anti-thyroid antibody has not been established, its presence, especially in high titers is supportive of the diagnosis, when other neurologic causes have been ruled out. A response to immunosuppressive therapy is needed to confirm the diagnosis and is considered
as a favorable prognostic factor. This case is significant as the patient’s stroke-like symptoms resolved completely after the institution of steroid therapy. Due to response to steroids and favorable prognosis, consideration for this syndrome in the differential is essential.

Abstract #1048

MYXEDEMA MADNESS IN A PATIENT WITH DEMENTIA

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Objective: Myxedema Coma is an extremely rare manifestation of hypothyroidism but is a potentially lethal condition with a mortality rate of 30-60%. We should have Myxedema on the differential when a patient presents with the triad of bradycardia, hypothermia and hypotension. In patients with suspected medication non-compliance due to psychiatric history, a TSH should be checked if we are unable to tease out a past medical history of hypothyroidism. Such patients with elevated TSH would need emergent administration of IV Levothyroxine.

Case Presentation: 71-year old severely Demented Caucasian Female was brought to the ICU by EMS after being found down at home for an unknown time. On presentation, she was found to be unresponsive, hypotensive, bradycardic and hypothermic in addition to marked Alopecia and dry sloughing skin. This triggered the ICU team to get a TSH which was elevated at 54 and the free T4 was low at 0.4. She was also found to have a relative adrenal insufficiency and was started on IV Hydrocortisone in addition to IV Levothyroxine. We were subsequently able to obtain medical records and she was found to have a history of hypothyroidism, medical non-adherence, ethanol abuse and frequent falls related to hypoglycemia. The chronic hypoglycemia most likely had her glucagon stimulated, which made her blood glucose levels bump up significantly (75 to 430 mg/dl) in response to the IV Hydrocortisone 100 mg. Her thyroid peroxidase antibodies were eventually tested to be positive (925 IU/ml) revealing the diagnosis of Hashimoto’s thyroiditis. She was also found to have significant thrombocytopenia during her stay which we attributed to the re-warming she required for the hypothermia since the blood smear was not conclusive for ITP.

She responded to IV Levothyroxine supplementation and was transferred out of the ICU in stable condition 4 days after presentation. She responded adequately to the Cortrosyn stimulation test and her steroids were eventually discontinued.

Conclusion: The Triad of Bradycardia, Hypotension and Hypothermia in an acute setting should trigger suspicion for Myxedema Coma.

Abstract #1049

SEVERE CHOLESTATIC JAUNDICE DUE TO GRAVES’ DISEASE

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Dayton VAMC

Objective: Describe a case of hyperbilirubinemia and cholestasis in a patient with Graves’ disease that improved after hyperthyroidism treatment.

Methods: Clinical jaundice due to uncomplicated hyperthyroidism is rare. We report a case of Graves’ disease associated with cholestatic jaundice.

Case Presentation: 47-year-old African-American woman with hypertension was diagnosed with Graves’ disease in April 2015. She was started on methimazole (MMI) but stopped it after a few months due to urticaria. On Nov. 2015 labs, she was noted to have high total bilirubin 6.7 mg/dL, alkaline phosphatase (AKP) 245 U/L, AST 36 U/L, and ALT 23 U/L. She underwent extensive evaluation by gastroenterologist including serum ceruloplasmin, ferritin, alpha fetoprotein, hepatitis A,B,C panel, anti-mitochondrial antibody(Re), anti-smooth-muscle Ab, anti-nuclear Ab, mononucleosis, cytomegalovirus (CMV) titer. All came back negative. Ultrasound did not show dilated common bile duct. She presented in endocrine clinic in Dec. 2016. Labs revealed TSH <0.005 mIU/ml, free T4 at 3.5 ng/dl, and free T3 at 9.4 pg/ml. On exam, she was noted to have bilateral proptosis, scleral icterus, and diffusely enlarged thyroid. She was started on MMI 20 mg daily that she tolerated without urticaria. Liver function tests (LFTs) in February 2016 showed higher total bilirubin at 11.3 mg/dL, AKP 267 U/L, AST 49 U/L, and ALT 38 U/L. MMI was decreased to 10 mg/day. She underwent liver biopsy that showed biliary pattern of injury with canicular and intrahepatocellular cholestasis. MMI was subsequently increased to 20 mg daily. In June 2016, her total bilirubin normalized at 0.8 mg/dL with alkaline phosphatase 245 U/L, AST 28 U/L, ALT 13 U/L.

Discussion: Only a handful of cases of hyperbilirubinemia with jaundice have been reported in a patient with Graves’. There are several proposed mechanisms for etiology of cholestasis in thyrotoxicosis. One theory suggests that hyperthyroidism increases metabolic demands and increases hepatic oxygen consumption. This alters bile transport and could result in cholestasis due to saturation of bile. Elevated thyroid hormones may have a direct effect on bilirubin level by altering bilirubin metabolism...
via impacting enzymatic activity of gluconyltransferase. MMI is known to cause cholestatic liver disease. However, serum bilirubin was noted to be elevated in our patient even when she was not on treatment and serum bilirubin normalized while on MMI.

**Conclusion:** Untreated Graves’ disease can cause cholestatic jaundice that improves with reduction in thyroid hormone levels. Extensive GI evaluation may be deferred in these patients until treatment of Graves’ disease.

**Abstract #1050**

**MALIGNANT METASTATIC STRUMA OVARI**

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**Objective:** Struma ovarii is a very rare teratoma composed of at least 50% of thyroid tissue in the ovary and accounts for about 5% of ovarian teratomas. It can also manifest as thyrotoxicosis. Here, we present a rare case of malignant struma ovarii with metastasis to multiple locations.

**Case Presentation:** 36-year-old black female who presented with dyspnea and progressive worsening of bilateral lower extremity weakness with bowel incontinence of 3 months. Associated symptoms included 20 lb wt. loss, abdominal bloating and distension. Patient is G11P6A5 with history of protein S deficiency. She was diagnosed 2 yrs prior with Graves’ disease with goiter and was treated with methimazole. At that time, she had refused RAIU scan. Patient was non-adherent and lost to follow-up till this presentation. Physical exam revealed small diffuse goiter, tachycardia, hyper-reflexive knee jerks. Decreased sensation below umbilicus. Babinski’s sign present bilaterally. Lower extremity strength 3/5 bilaterally. Labs included TSH of 0.01, FreeT4 of 1.58, nl TSI. CTA done to rule out PE showed 2.8 x 3.7 x 4 cm mass causing severe central canal stenosis at T9, and lytic lesion at T11. She had emergent surgery with resection of extradural spinal tumor. Frozen section showed thyroid differentiation. CT abdomen and pelvis showed pulmonary nodules, liver hypodensity, 8 cm ileal mass with osseous destruction and 20 cm mass appearing to arise from the right ovary. TAH with BSO was done. Biopsy from right ovary showed papillary thyroid carcinoma, follicular variant arising in a struma ovarii. CA 19-9 was 197.1, thyroglobulin was 80389.9 with negative antithyroglobulin antibody. CEA-125, inhibin B, AFP, HCG were normal. Whole body scan (WBS) with 0.2 mCi I-131 showed activity in the left ilium, distal thoracic vertebral, proximal right humerus and posterior left calvarium. She was then treated with 198.5 mCi I-131. Post therapy, WBS showed two additional lung foci correlating with the nodules seen on prior CT. Repeat CT scan of pelvis two months later showed that the previously described destructive left ileal mass was similar in size but showed interval decrease in soft tissue component and was largely cystic.

**Discussion:** This demonstrates the rare malignant struma ovarii that presented with features of Graves thyrotoxicosis. Due to patient’s refusal to do RAIU on initial presentation, opportunity to make a correct diagnosis was missed. Nonadherence in follow up led to further delay in diagnosis.

**Conclusion:** It is very important to have an open mind about the differentials of presentation as simple as that of hyperthyroidism. It could be a struma ovarii in disguise.

**Abstract #1051**

**UNCONTROLLED GRAVES’ DISEASE WITH PANCYTOPENIA DUE TO MYELODYSPLASTIC SYNDROME**

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Mercy Catholic Medical Center

**Objective:** Graves’ disease is an autoimmune disease which affects variety of organ systems including hematopoietic system. Due to unknown mechanism, single cell lineage abnormalities and rarely pancytopenia may develop during the course of the disease. We report a case of a patient with an uncontrolled Graves’ disease who presented with a worsening pancytopenia in the context of MDS.

**Case Presentation:** A 68 year-old-man was diagnosed with Graves’ disease and started on methimazole despite having slightly low WBC counts which remained stable for years around 3.7 Thou/L. However, serum free T4 was never well controlled, ranged around 1.80-5.30 ng/dL due to medication non-compliance. Three years later, he developed pancytopenia and was referred to Hematology & Oncology. Complete blood count revealed RBC of 3.13 Mill/uL, WBC of 3.2 Thou/uL, platelet of 47 Thou/uL, with an absolute neutrophil count of 1.7 Thou/uL. Hemoglobin was 8.8 g/dl and MCV was 85.1 fL. Anisocytosis with tear drop cell, ovalomacrocytes, acanthocytes, immature neutrophils (14%) and thrombocytopenia were seen on peripheral blood smear. Bone marrow biopsy revealed hypo-cellular marrow with extensive fibrosis and 12% blasts. Cytogenetics showed 7q deletion. He was also Jak2 positive, making the diagnosis of primary myelofibrosis with MDS. CT-abdomen showed no organomegaly, or lymphadenopathy. TSH was 0.01 uIU/mL, fT4 was 2.57
PAINFUL GOITER, NORMAL TSH AND NEGATIVE THYROID ANTIBODIES DOES NOT EXCLUDE GRAVES' DISEASE: A CASE PRESENTATION

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Objective: Graves' disease (GD) is an autoimmune thyroid disorder characterized by hyperthyroidism, diffuse goiter, ophthalmopathy, and rarely dermopathy. Symptoms include tachycardia, weight loss, tremor or sweating. All patients exhibit suppressed TSH, often coupled with elevated free thyroxine (ft4). Here we describe the dilemma involving diagnosis of GD in a 36 year old female with thyroid enlargement and normal TSH, thyroid hormones and thyroid antibodies (Ab) by conventional assays.

Case Presentation: A 36 year old African American female presented with a 12 month history of progressive painful neck swelling, recent onset of hoarseness of voice, irregular menstrual periods and hair loss. Ultrasound confirmed a heterogeneously mildly enlarged thyroid gland without nodules. TSH was 1.59 mIU/L (0.1 - 5.0 mIU/L), ft4 - 0.83 ng/dL (0.71 - 1.85 ng/dL), ft3 - 3.8 pg/mL (2.5 - 3.9 pg/mL). Repeat TSH one month later was 0.9 mIU/L. TSH was normal at both times, however progressive decline in its value reflected developing hyperthyroidism. Therefore workup for GD was pursued. TSH receptor Ab (TRAb), anti-thyroid peroxidase Ab, anti-thyroglobulin Ab and thyroid stimulating immunoglobulin (TSI) were all within normal limits. Radioiodine uptake (RAIU) Scan revealed increased uptake in a uniformly active thyroid gland consistent with GD (figure 1), with 6 hour uptake 38.3% and 24 hour uptake 52.4%. Patient opted for total thyroidectomy. Pathology of thyroid gland revealed diffuse hyperplasia consistent with GD.

Discussion: Co-occurrence of Graves’ disease and MDS is a rare entity, as pancytopenia is usually attributed to hyperthyroidism treatment or methimazole use. A few cases in the literature were reported to have improvement in their pancytopenia with the treatment of Graves’ disease.

Conclusion: Further studies are needed to evaluate the association between Graves’ disease and MDS and to help to guide the therapy.
female with bipolar disorder. The patient had been treated with lithium for 5 years until she developed lithium induced nephropathy. Lithium was subsequently discontinued but resumed a month later due to suicidal ideation. Within a few months, she developed symptoms of hyperthyroidism and was then referred to the endocrinologist. She presented to endocrine clinic with symptoms of jitteriness, palpitations, irregular menstruation, headache, hair loss, diarrhea, and 10lb weight loss. Physical exam revealed warm and moist skin along with tremors of the outstretched hands bilaterally. The thyroid gland was palpable but non-tender. Initial labs showed a TSH of 0.02 (0.34 - 5.60μIU/ml), Free T4 2.95 (0.62 - 1.58ng/dl), and total T3 4.20 (0.62 - 1.62ng/ml). Thyroid antibodies panel was negative. The 24-hour radioactive iodine uptake and scan was diminished at 2.6% and diagnosis of lithium induced silent thyroiditis was made. After reviewing the medical literature prednisone was initiated. Follow up labs 6 weeks later showed severe hyperthyroidism with a TSH <0.02μIU/ml, Free T4 of <0.2 (0.8-2.7ng/dl), and negative anti-TPO ab. Due to minimal response to prednisone and persistence of symptoms, prednisone was discontinued and methimazole was initiated. On follow up appointment 4 weeks later, the patient’s condition worsened and decision to send the patient for a total thyroidectomy was made.

Discussion: Lithium remains a mainstay of treatment for bipolar disorder. Lithium associated hypothyroidism is well known and has an incidence of 30%. Thyrotoxicosis associated with lithium use is rare and remains underreported. The Mechanism of lithium induced thyrotoxicosis due to silent thyroiditis is unclear. Prednisone and/or methimazole are rarely effective in treating this condition. The patient presentation can easily be confused with breakthrough mania or lithium toxicity and delay the diagnosis.

Conclusion: Physicians should be well aware of this rare but severe side effect of lithium therapy and patients should be referred for further endocrine evaluation when symptomatic and if thyroid function tests remain persistently abnormal. Our case report emphasizes the importance of careful monitoring of patients for both hypo and hyperthyroidism during lithium therapy.

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Abstract #1054

**NIVOLUMAB AND THYROID DYSFUNCTION: EMERGING COMPLICATIONS**

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**Objective:** Increase awareness of thyroid dysfunction in individuals treated with immunotherapies

**Methods:** Case and literature review

**Case Presentation:** A 62 year old man with stage IV Non-Small Cell Lung Cancer was treated with Nivolumab after failing conventional chemotherapy, after which he experienced headaches, nausea, vomiting, constipation, and generalized wasting. Exam only revealed a chronically ill man with a non-tender, non-palpable thyroid gland. Labs showed: TSH 152 mIU/L (0.4-4.6 uU/mL), Free T4 of <0.2 (0.8-2.7ng/dl), and negative anti-TPO ab. Treatment with levothyroxine (LT4) normalized TSH to 1.37 mIU/L with resolution of his symptoms.

**Discussion:** Nivolumab is an IgG4 monoclonal antibody against Programmed Death Receptor 1. This revolutionary class of drugs is rapidly becoming the cornerstone of treatment for numerous metastatic cancers that have failed conventional chemotherapies. Nivolumab blocks inhibitory molecules on activated T-cells; this not only increases tumor cell destruction, but also leads pathological T-cells to react with self-antigens resulting in an autoimmune destruction.

Until recently, few clinicians have been presented with the side effects of this novel class of drugs, therefore it is critical to become familiar with both the endocrinological side-effects and related pathophysiology in order to best manage our patients. Prior to Nivolumab, our patient’s baseline thyroid function tests were normal. The timing, clinical presentation and laboratory results are suggestive of acquired Nivolumab induced hypothyroidism, in a patient without a prior personal or family history of thyroid disease. As we track his clinical course during and after treatment it appears as though there may have been evidence of thyroid tissue destruction early on: three months after initiation of Nivolumab his TSH decreased to 0.16mIU/L; however, it slowly began to rise to 8.95mIU/L, then 152mIU/L, consistent with a thyroiditis. He was started on LT4 with clinical improvement. The mechanism involved in asymptomatic thyroiditis that eventually progressed to clinical hypothyroidism is autoimmune destruction of the thyroid gland. There is not enough data to suggest that this patient will have spontaneous recovery, however there is some suggestion that the damage may be permanent. It is important to also emphasize that Nivolumab leads to multi-glandular failure, therefore it is
imperative to monitor adrenal function before and during thyroid hormone replacement.

**Conclusion:** Immune related endocrinological side effects are becoming more prevalent, therefore clinicians must be vigilant in evaluating such patients as the severity of their clinical picture can often be obscured by their underlying oncological illness.

**Abstract #1055**

**MORE THAN “JUST A PILL”: PATIENT EXPERIENCE WITH RADIOACTIVE IODINE FOR PAPILLARY THYROID CANCER**

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**Objective:** Post-operative radioactive iodine (RAI) is a low risk adjuvant treatment for patients with papillary thyroid cancer (PTC). Though RAI is generally well tolerated, it has a significant impact on patients’ lives. We characterized the experiences of PTC patients with RAI treatment in the post-operative period.

**Methods:** This qualitative study included 26 PTC patients enrolled in an ongoing clinical trial. Participants were treated with 50 mCi of RAI at a mean of 6 weeks after surgery. Semi-structured interviews were conducted at 5 time points – pre-operatively, 2 weeks, 6 weeks, 6 months, and 1 year post-operatively. We used a grounded theory approach, thematically coding 90 interview transcripts using NVivo11.

**Results:** Participants found RAI far more disruptive than expected. They described the treatment process as longer than anticipated, spanning from the start of the low-iodine diet to communication of the whole body scan results. They expressed that the process was more involved than “just taking a pill”. The biggest challenge for participants was the low-iodine diet (n=23). Participants struggled to find food that suited them and their lifestyle. Many reported fear of treatment failure if the diet was not strictly followed. Participants reported struggles with logistical (n=10) and emotional (n=14) isolation during RAI treatment. They reported confusion concerning spatial and temporal restrictions, and as a result, some expressed feeling self-conscious and avoiding public interactions. Several also discussed guilt about the inability to care for loved ones and even apprehension about causing them harm. Participants also expressed concern about financial strain (n=7); this included time off work for treatment, cost of dietary changes, and child and pet care costs. When reflecting on the experience at 6 months and 1 year, these themes were reiterat ed. Participants discussed wanting more counseling regarding what to expect.

**Discussion:** Initial visits often focus on the surgical procedure with less emphasis on future treatments. Lack of preparation and understanding may contribute to the disruptive nature of RAI treatment. The decision about whether or not to have RAI and the impact of the treatment is a complicated discussion. It is important that the factors discussed here be incorporated into post-operative visits with the thyroid cancer care team.

**Conclusion:** Post-operative RAI is more than “just a pill”. Additional time in the post-operative period should be spent on education to help patients better understand whether or not they need RAI, and if they choose it, what it entails and how to prepare for it effectively.

**Abstract #1056**

**THYROID FUNCTION AND THYROID AUTOIMMUNITY IN APPARENTLY HEALTHY ADULT NIGERIANS.**

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**Objective:** 1. To determine the Thyroid function and the prevalence thyroid autoimmunity in apparently healthy adult Nigerians. 2. To determine the pattern of thyroid dysfunction and thyroid autoimmune disorder in apparently healthy adult Nigerians

**Methods:** Following a population based screening, 110 apparently healthy adult subjects were enrolled into the study. Anthropometry, lipid profile, fasting plasma glucose and thyroid hormones (TSH, Free T4, Free T3) were measured. Autoantibodies (thyroid peroxidase auto-antibodies (TPO-Ab)) were also measured for all the participants. Participants were then classified according to the TFT profile of their biochemical tests into Hypothyroid, hyperthyroid, subclinical hyperthyroid or hypothyroid, euthyroid, while those with elevated thyroid peroxidase autoantibodies were identified as such. Thyroid examination as well as cardiovascular examination was done for all the subjects.

**Results:** The mean age, TSH, fT4, fT3 and anti TPO-Ab for the study population was 35.97+/-13.55yrs, 3.45+/-2.80 miu/ml, 15.23+/-2.95pmol/ml, 3.92+/-1.37pmol/ml, 15.30+/-11.23iu/ml respectively. TPO-Ab was found in 13.5% of the total study population, 18.0% of females and of 10.3% males, with higher prevalence found in women. None of the subjects reported symptoms of
thyroid disorder or had examination findings to suggest so. Biochemical Thyroid disorder was seen in 34.5% of the total study participants, 34.8% of males and 34.5% of females respectively.

Discussion: This study evaluated 110 apparently healthy adult Nigerians for thyroid function and autoimmunity. It also determined the prevalence of autoimmune thyroid disorder using the prevalence of TPO-Ab. Literature in the subject area is scanty. However a recent study from china reported the prevalence of autoimmunity of 12.1% which is similar to our finding. Another study from Mexico in pregnant women reported a prevalence of 14.4% and 13.5% in non pregnant women. There are some limitations in this study, which include the small number of the sample population, inability of assess iodine status or the nutritional status of the subjects and our inability to assay for thyroglobulin autoantibodies (Tg-Ab).

Conclusion: There is biochemical evidence of thyroid disorder in apparently healthy black population despite the absence of symptoms and clinical signs. Autoimmune disorder is also common with the female participants having higher values than the males. This has a particular implication for them especially with regards to the issue of fertility. Large scale population based study is required in this area.

Abstract #1058

MAJOR HYPERCALCEMIA FROM THYROTOXICOSIS: UNUSUAL FINDINGS

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Objective: Increased bone resorption can lead to hypercalcemia. Causes include hyperparathyroidism, malignancy, excess Vitamin A intake, prolonged immobilization as well as thyrotoxicosis. Some degree of hypercalcemia can occur in 15% to 20% of patients diagnosed with hyperthyroidism. Usually, the degree of hypercalcemia is modest. The case described below reflects a suprising aspect of hypercalcemia in thyrotoxicosis.

Case Presentation: A 54 year old female presented with palpitations, anxiety, diaphoresis, unintentional weight loss of 40 lbs over several weeks, heat intolerance, and insomnia. Pt had a history of HIV disease on HAART. On exam, patient was tachycardiac, anxious with a multinodular goiter three times normal and mild proptosis. TSH was <0.05 (0.47-4.70 uIU/ml), free T4 6.82 (0.80-2.20 ng/dl), and free T3>22.8 (2.77-5.27 pg/ml). Calcium level was 13.3 (8.4-10.2 mg/dl), phosphorous 3.4 (2.5-4.5 mg/dl), creatinine 1.2 (0.5-1.0 mg/dl), hemoglobin 10.7 (12.0-16.0 mg/dl). Intact parathyroid hormone and PTHrP were low. 25 Vitamin D was 21.3 (30-100 ng/ml). Thyroid stimulating immunoglobulin was elevated. Alkaline phosphatase was suprisingly low at 98 (37-126 u/l). Patient was aggressively hydrated with intravenous saline and given parenteral calcitonin and pamidronate. Methimazole 30 mg bid was initiated along with metoprolol. HTLV1 was negative. No signs of any malignancy were noted. Calcium came down steadily to 8.7 within 6 days as patient became euthyroid. Alkaline phosphatase paradoxically came up to 198 and patient remained euthyroid and normocalcemic.

Conclusion: A review of the literature suggests that the elevated calcium in hyperthyroidism is usually not more than 11.0. Our patient’s calcium started at 13.3 with no overt reason to explain the higher than expected calcium level. In addition, the alkaline phosphatase level appeared too low for the level of likely bone turnover and remodeling to cause such hypercalcemia in the thyrotoxic state depicted here. On the other hand, the calcium level returned to normal with treatment of thyrotoxicosis, as expected.

Abstract #1059

UNUSUAL ROUTES: SEVERE THYROID STORM WITH A RECTAL APPROACH

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Objective: Thyroid storm carries a mortality rate of 10 to 30%. Prompt recognition and treatment in an intensive care environment is critical to survival. Management of thyroid storm with a compromised gastrointestinal tract is especially challenging. Here we present a patient with thyroid storm and duodenal perforation treated with rectal methimazole.

Case Presentation: A 62 y/o male presented to the ER with abdominal pain, nausea, multiple episodes of vomiting, and watery diarrhea. Patient had marked tachycardia with new onset of atrial fibrillation. TSH was <0.05 uIU/ml (0.47-4.70), Free T4 >6.99 ng/dl (0.80-2.20) and Free T3 16.20 pg/ml (2.77-5.27). Pain worsened in few hours with a diagnosis of perforated duodenal ulcer made in the surgical ICU. As patient was NPO, a rectal preparation of methimazole was formulated and administered as a 60 mg enema q12h. He was also started on an IV esmolol drip for rate control, stress doses of hydrocortisone, as well as IV ivhexol (iodine) after initial methimazole dosing. After four doses of the methimazole enema, patient’s Free T3 level dropped to 7.48 pg/ml. Heart rate gradually returned to normal. Patient underwent exploratory laparotomy with Graham patch repair of the perforated duodenal ulcer. He
received four days of methimazole enemas until a J tube route could be used. Unfortunately, patient had multiple surgical complications requiring several abdominal procedures each of which required further methimazole enema courses. After a prolonged course, patient was discharged home on oral antithyroid treatment in a euthyroid state.

Discussion: Thyroid storm carries a high mortality rate. Rectal administration of antithyroid drugs in patients with a compromised gastrointestinal tract is a viable option though this has not been widely studied. One study done on euthyroid patients showed that therapeutic levels of methimazole in the blood could be achieved with rectal administration. However, no such study was done on hyperthyroid patients who were severely ill or in storm. Response to treatment should be thus monitored by clinical improvement as well as drop in T3 and T4 levels.

Conclusion: Rectal administration of methimazole in patients unable to take the oral form can be lifesaving.

Abstract #1060

THYROID SARCOIDOSIS WITH CONCURRENT PAPILLARY THYROID CANCER

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Objective: To present an interesting case of asymptomatic sarcoidosis (SA) of the thyroid with coexisting papillary thyroid cancer (PTC).

Case Presentation: A 57-year-old euthyroid woman presents for evaluation of a left thyroid nodule discovered incidentally during staging work up for her breast cancer. Biopsy was consistent with PTC. She underwent total thyroidectomy with radical neck dissection. Histopathological examination of the resected specimen confirmed left unifocal PTC measuring 2.7 cm in greatest dimension, with no evidence of regional lymph node metastasis. Interestingly, multiple non-necrotizing granulomas that were negative for fungal and mycobacterial examination were also seen in both the thyroid and several lymph nodes, consistent with SA. She subsequently underwent I-131 therapy with negative surveillance testing thus far and is maintained on thyroid hormone suppressive therapy accordingly. On further history obtained postoperatively, patient recalls remote history of SA diagnosed based on x-ray findings at age 17 and has never required treatment over the years. She remains asymptomatic and does not have any evidence of systemic SA at this time.

Discussion: Sarcoidosis is a systemic disorder of unknown etiology characterized by noncaseating granulomata, often involving the lungs and lymph nodes, but can affect any organ system, including the thyroid gland. SA has a highly variable clinical course. Involvement of the thyroid gland by SA is very rare with only about 5 percent of patients affected. Most patients have other evidence of SA, although there are reports of thyroid involvement as the first or only manifestation of the disease, just like in our patient. The histologic features of SA of the thyroid are similar to those sarcoidosis involving other organs, consisting of noncaseating granulomas. Concurrent SA and thyroid cancer may present with diagnostic and management challenge. Lymph nodes with SA and PTC metastasis may coexist in the neck. Sarcoid lesion in the neck may also mimic metastatic lesions. This highlights the importance for clinicians to be aware of the coexistence of these two conditions to avoid mismanagement of neck lymphadenopathies in patients with PTC and SA. It remains unclear if a causative relationship exists between SA of the thyroid and the development of PTC.

Conclusion: Coexistence of thyroid cancer and SA is rarely reported in the literature. This may present with diagnostic and management challenge. If noncaseating granulomas are observed in thyroid specimens after a thyroidectomy, it is important to establish coexistence of sarcoidosis even in asymptomatic patients to avoid mismanagement of neck lymphadenopathies in patients with PTC.

Abstract #1061

UTILITY OF RECOMBINANT THYROTROPIN STIMULATED PET-CT IN SURVEILLANCE OF METASTATIC PAPILLARY THYROID CANCER

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Objective: Differentiated thyroid cancer (DTC) accounts for the majority of thyroid cancers. Prognosis is usually very favorable after treatment, however about 15 percent may have recurrent or persistent disease. Long-term follow-up of patients who have received treatment for DTC is essential to detect recurrence. The standard method involves post-surgical measurement of serum thyroglobulin (Tg) and use of iodine-131 whole-body scintigraphy (WBS). However, WBSs are negative in 10–15% of patients with detectable serum Tg. The utility of positron emission tomography (PET) using fluoro-2-deoxy-d-glucose (FDG) in the diagnosis of recurrent and metastatic disease, particularly when WBS is negative has been well established. However, there are cases where WBS and FDG-PET are both negative with abnormal Tg
or Tg-Antibodies (Tg-Ab). We present a case that outlines the utility of recombinant thyrotropin (rTSH) stimulated FDG-PET CT.

Methods: Case Report

Case Presentation: A 30 year old woman with thyroid biopsy proven PTC underwent complete thyroidectomy and radical neck dissection followed by post-ablative treatment with 120 mCi of I-131. Due to palpable cervical lymph nodes (LN) and rising Anti-Tg Ab, she had 2 repeat neck dissections. She also received a second ablation with 150 mCi of I-131 and third ablation with 203 mCi of I-131. Subsequent WBS were negative. Tg concentration was <0.1 ng/ml. Tg-Ab continued to rise >700 and FDG-PET CT was obtained that demonstrated faint uptake in level 2 cervical LN near prior surgical areas. In light of rising Tg and suspected recurrent PTC, rTSH-FDG-PET CT was obtained that demonstrated hypermetabolic tissue in the right thyroid bed and right Level 2 LN, FDG avid pulmonary nodule right upper lung, and focal FDG uptake in medial right pectoralis muscle consistent with metastatic disease. The patient continues to be under surveillance with consideration for Tyrosine Kinase Inhibitors.

Discussion: Our case reinforces several aspects one of which is rising Tg-Ab as an indicator of DTC recurrence. Importantly, standard surveillance tests of WBS and FDG-PET failed to discern the extent of our patient’s metastatic disease that became evident with use of rTSH-FDG-PET. rTSH stimulates thyrocyte metabolism, glucose transport, and glycolysis. Few small studies have reported the use of rTSH-FDG-PET in suspected cases with elevated Tg.

Conclusion: Long term surveillance is essential in post-operative management of DTC and standard surveillance techniques can be inadequate. rTSH has been established as an adjunct to WBS, but it’s use with FDG-PET is emerging and endocrinologists should be aware of the utility of rTSH-FDG-PET in selected cases with negative standard imaging.

Abstract #1062

A COMPLEX CASE: GRAVES DISEASE DUE TO CHECKPOINT INHIBITOR THERAPY COMPPLICATED BY TREATMENT ASSOCIATED THROMBOCYTOPENIA, LEUKOPENIA AND HEPATOTOXICITY

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Objective: To present a case of concomitant thrombocytopenia, leukopenia and hepatotoxicity in a patient treated with methimazole therapy for Graves disease associated with nivolumab and ipilimumab therapy.

Case Presentation: A 62 year old female with stage IV squamous cell lung cancer was noted to develop overt thyrotoxicosis while on combination nivolumab and ipilimumab. Further evaluation of thyrotoxicosis revealed an elevated thyroid stimulating immunoglobulin consistent with Graves disease. Methimazole therapy was initiated with checkpoint inhibitor therapy continued. Within one month of initiation of methimazole, circulating thyroid levels normalized. However, liver enzyme testing was notable for acute transaminitis (> 5 times upper normal limit). Additionally, new onset leukopenia and thrombocytopenia was identified. Methimazole and checkpoint inhibitor therapy was interrupted. Corticosteroids where initiated with rapid patient improvement. She later underwent total thyroidectomy for definitive management of her Graves disease.

Discussion: This patient developed Graves disease associated with use of combination ipilimumab and nivolumab biologic therapy. Ipilimumab or nivolumab related thyrotoxicosis is usually the result of thyroiditis however ipilimumab associated Graves disease has been reported. To our knowledge there have been no reported cases of nivolumab related Graves disease. Ipilimumab exerts its effects by inhibition of cytotoxic T-lymphocyte-associated antigen 4 resulting in increased anti-tumor activity; nivolumab binds to the PD-1 receptor resulting in disinhibition of the PD-1 pathway leading to increased anti-tumor immune response. Both of these monoclonal antibodies have been associated with several endocrinopathies. Hepatotoxicity is seen in ~20% of patient receiving nivolumab plus ipilimumab combination therapy. Hematologic adverse events are a less common immune-related phenomenon with these agents. Standard treatment for all immune-related adverse events is corticosteroids. Although methimazole related concomitant thrombocytopenia, leukopenia and hepatotoxicity has been reported, this remains extremely uncommon. Regardless, methimazole was immediately discontinued in this patient and not resumed given the temporal association of methimazole therapy and development of adverse effects.

Conclusion: Immunomodulating agents such as nivolumab and ipilimumab can result in multiple endocrinopathies including Graves disease. Awareness of the potential endocrine adverse effects of these medications is important as they show great promise for the treatment of malignancy, and their utilization has become increasingly prevalent.
Abstract #1063

COMPARATIVE EFFECTIVENESS OF SYNTHROID® VS GENERIC LEVOTHYROXINE ON TSH LAB OUTCOMES: A RETROSPECTIVE CLAIMS DATABASE ANALYSIS

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Objective: Historically, there has been concern regarding the bioequivalence of NTI drugs such as levothyroxine. Studies comparing branded vs. generic levothyroxine have provided conflicting results. This study investigated TSH lab outcomes among hypothyroidism patients treated with Synthroid® vs. generic levothyroxine.

Methods: Retrospective claims analysis was conducted using Optum Clinformatics™ Data Mart database which includes medical and pharmacy claims for over 67 million commercial/Medicare insured US patients. We identified patients who had at least one hypothyroidism diagnosis code between January 2008 and March 2016 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, or with last lab data missing or invalid, were excluded. Patients were required to have continuous enrollment and stay persistent to whichever therapy was initiated (no gaps larger than 30 days between fills) 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 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 0.89 (95% CI 0.85 – 0.94, p<0.001). Odds of a patient having a TSH labs out of range was 0.89 (95% CI 0.85 – 0.94, p<0.001) for Synthroid vs. generic levothyroxine.

Results: The final matched cohorts included 28,034 levothyroxine patients and 14,017 Synthroid® patients. Most patients (85%) were female and the average age was 54 years in both cohorts. The last TSH lab during follow-up was out of range for 22.6% of patients in the generic levothyroxine cohort vs 20.9% in the Synthroid® cohort (p<0.001). Odds of a patient having a TSH labs out of range was 0.89 (95% CI 0.85 – 0.94, p<0.001) for Synthroid vs. generic levothyroxine.

Discussion: In our study, we found that Synthroid® was associated with an 11% lower likelihood of having TSH labs out of range when compared with similar patients taking generic levothyroxine. Although potential confounders were adjusted for and the sample size was robust, claims data have inherent limitations that must be considered when interpreting these results. For example, because claims data is de-identified, we cannot collect patient reported outcomes to further elucidate the implications of TSH labs out of range.

Conclusion: Synthroid® was associated with significantly better TSH lab outcomes compared to generic levothyroxine among a US commercial/Medicare insured population.

Abstract #1064

INCIDENCE AND MORTALITY TRENDS OF THYROID STORM IN THE UNITED STATES: A NATIONWIDE ANALYSIS, 2003-2013

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Objective: Our current knowledge on the incidence and mortality of thyroid storm in the United States is limited to single-center case series. Thyroid storm is reported in 2.7% to 10% of hospitalized patients with thyrotoxicosis, with a mortality rate between 8% and 30%. National data on the incidence and mortality of thyroid storm is lacking.

Methods: We used data from the National Inpatient Sample (NIS) database of patients admitted with a primary diagnosis of thyrotoxicosis between 2003 and 2013. NIS is the largest public inpatient database and includes a stratified random sample of all non-federal hospitals in the US. We estimated the incidence, hospital mortality rate, length-of-stay (LOS) and hospitalization costs for patients admitted with thyrotoxicosis with or without thyroid storm.

Results: A total of 133,136 patients were admitted with thyrotoxicosis during the study period (mean age: 49.9±0.12 years (+SE), Caucasians: 53.7%, female: 77.8%); of them, 21,886 patients were diagnosed with thyroid storm (age: 43.0±0.25, Caucasians 44.0%, female 76.1%). The incidence rate of thyroid storm ranged between 0.61 to 0.76 cases/100,000 patients per year, with an incidence between 14.2% and 18.4% among hospitalized patients with thyrotoxicosis. Thyroid storm was associated with significantly higher in-hospital mortality, ranging between 1.2% and 3.6% compared to 0.1% and 0.4% in patients without storm, p<0.005 after multiple comparison adjustments. The in-hospital mortality trend in patients with thyrotoxicosis with and without storm was not significantly different over time; p=0.13 and p=0.88, respectively. LOS ranged from 4.82 to 5.66 mean days in patients with thyroid storm compared to 2.83 to 3.27 mean days in patients without storm, p<0.001. The trend in mean hospitalization costs per
admission (adjusted for inflation) progressively increased from $22,369 to $48,042 in patients with storm and from $15,406 to $28,966 in patients with thyrotoxicosis without storm (both p<0.001), from 2003 to 2013.

Discussion: Thyroid storm was predominantly seen in middle-age Caucasian females. At a national level, hospital mortality was lower than previously reported from single-center case series. LOS was significantly higher in thyroid storm patients. There have been no changes in the hospital mortality over the last decade, but the hospitalization costs have significantly increased.

Conclusion: We present the first nationwide incidence and mortality analysis of patients with thyroid storm. One of every 6 patients admitted with thyrotoxicosis was diagnosed with storm. Thyroid storm is associated with 8-10 fold-higher mortality than thyrotoxicosis. Notably, the hospitalization costs have significantly increased.

Abstract #1065

REDUCED SURGERY THROUGH AFIRMA GEC: IMPACT TO DATE AND POTENTIAL FOR THE FUTURE

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Objective: Afirma GEC benign results indicate a low risk of malignancy and offer the opportunity of clinical observation in lieu of diagnostic surgery for cytologically indeterminate thyroid nodules. Here we estimate the global impact of Afirma since its commercial launch, and speculate on the impact of raising its specificity while maintaining its high sensitivity.

Methods: Veracyte quantified all Afirma GEC test results from January 1, 2011 through September 30, 2016. MTC and Parathyroid Classifier positive results were counted. PubMed was reviewed through November 21, 2016 for publications reporting surgical rates among Afirma GEC benign patients.

Results: The Afirma GEC has been performed on samples from 66,325 thyroid nodules. Considering adequate samples, Afirma GEC was benign in 27,154 (44.5%). Among 18 published studies evaluating 1554 patients tested with the GEC, 9.9% of GEC benign patients underwent surgery. Extrapolation of this rate to all GEC benign results suggests that approximately 24,466 patients may have been spared surgery as a result of the GEC and more than $255M in surgical costs may have been averted. The MTC and Parathyroid Classifiers are included with each GEC test, and are also available when just the Malignancy Classifiers are requested. Positive results have occurred for the MTC classifier and the Parathyroid classifier in 246 and 375 nodules, respectively.

Discussion: More than 27,000 Bethesda III/IV thyroid nodules have been reclassified as molecularly benign since the introduction of Afirma, facilitating consideration of clinical observation instead of diagnostic surgery in the great majority. Additionally, 621 nodules were identified as likely harboring MTC or parathyroid tissue in the biopsied nodule, a result likely to significantly improve patient care. Efforts are underway to improve the GEC specificity. Assuming a 24% prevalence of malignancy and maintaining the same test sensitivity (90.2%), improving test specificity from its current 51.6% to 65% or 75% would result in a rise in the rate of GEC benign results to 52% and 59%, respectively. For each 1% rise in specificity there is an absolute gain in benign test results of 1 minus the prevalence of malignancy (e.g. 0.76%, if prevalence of malignancy is 24%).

Conclusion: Maintaining high test sensitivity while improving test specificity is expected to identify even more patients unlikely to benefit from surgical resection, and raise the test’s positive predictive value. An enhanced version of the Afirma GEC is predicted to benefit a higher percentage of patients and increase its cost-effectiveness.

Abstract #1066

ADHERENCE TO THYROID HORMONE REPLACEMENT THERAPY

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AbbVie

Objective: Hypothyroidism requires patients to be adherent to lifelong thyroid hormone replacement therapy with levothyroxine, as indicated by a number of guidelines. Our aim was to investigate adherence to levothyroxine among the general US hypothyroid patient population and to examine whether treatment with Synthroid® compared to other formulations of levothyroxine may influence adherence.

Methods: Retrospective claims analysis was conducted using Truven MarketScan® database which includes medical and pharmacy claims for 200 million commercial/Medicare insured US patients. We identified patients who had initiated treatment with any levothyroxine formulation between January 2000 and December 2015. Patients below 18 years old, with any diagnosis of thyroid cancer,
or claims for combination T3/4 therapy were excluded. Patients were required to have continuous enrollment for one year prior to and one year following the index date (date of first fill for levothyroxine). Proportion of days covered (PDC) was calculated for each patient and an 80% PDC was used as a cutoff to identify adherent patients. Primary outcome was to assess the adherence rate among the entire levothyroxine therapy class at 6 and 12 months. Secondary outcome was to compare adherence rate of Synthroid® to all other formulation of levothyroxine (cohort included Levoxyl, Tirosint, Unithroid and generic levothyroxine therapies).

**Results:** A total of 568,502 patients met the inclusion criteria and had a mean age of 52, were mostly women (74%), had PPO insurance (51%), and were diagnosed by a PCP (89%). Proportion of adherent patients (PDC >= 80%) among all patients, regardless of levothyroxine formulation, was 59.6% and 48.0% at 6 and 12 months, respectively. Patients who initiated Synthroid® had higher adherence (PDC >= 80%) at both 6 and 12 months when compared to all other formulations of levothyroxine (64.6% vs 59.6% and 53.2% vs 48.0% at 6 and 12 months respectively, p<0.0001).

**Discussion:** About 40% and slightly more than half of patients are non-adherent to levothyroxine at 6 and 12 months, respectively. In our analysis, choice of therapy with Synthroid® was associated with significantly higher adherence at 6 and 12 months (both p<0.0001). Some limitations to the data should be considered when interpreting results; for example, claims only identify when a prescription is sold, whether a patient actually takes that medication as prescribed cannot be determined from this data.

**Conclusion:** Adherence to thyroid hormone replacement remains to be a concern among hypothyroid patients treated with levothyroxine. Synthroid® is associated with significantly higher adherence when compared to other formulations of levothyroxine.

**Abstract #1068**

**AN UNUSUAL CASE OF LEVOTHYROXINE RESISTANCE**

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**Case Presentation:** A 53 y/o ♂ presented to her family doctor c/o fatigue, constipation and wt gain. TSH was 47.09 mIU/L (0.40-4.40), FT4 4.9 pmol/L (8.00-18.00), anti-TPO 434.5 IU/ml (0.00-9.00). Hashimoto’s thyroiditis (HT) was dx and levothyroxine (LT) initiated. Pt was explained that TSH would be drawn several wks after each dose of LT stabilized, a process that would take 4 wks. Despite increases of LT to 0.3 mg patient c/o fatigue.
TSH ranged from 17.94 on 0.15 mg to 42.87 on 0.2 mg LT. FT4 remained low. Pt was referred for LT resistance. She denied other meds, non compliance, food interference, malabsorption. Wt was 80 kg, HR 72 reg, thyroid was 20 gm and firm, DTRs slow relaxation. No clinical DM, Addison’s, malabsorption, nor rheumatoid arthritis. Questioned again about LT dosing the pt explained she took her meds exactly as instructed stopping after 4 wks when the LT levels were stable and then waiting 4-6 wks to have her TSH measured.

No investigations were ordered. LT 0.1mg qhs was given. Pt was told not to D/C her LT. TSH was drawn after 8 wks. Pt had lost 4 lbs and c/o less fatigue. TSH was 1.26 and FT4 14.6. Three months later pt felt well, TFTs remained normal.

Discussion: HT or chronic autoimmune thyroiditis is the most common cause of 1° hypothyroidism in iodine sufficient regions. HT is 5-10x more common in ♀’s. LT starting either with the estimated replacement dose or with progressively increasing doses is the suggested Rx. LT replacement can be estimated as 1.6μg/kg. Requirements may be higher in the elderly, in females, in large individuals and in central hypothyroidism. Dose adjustments can be made every 4-8 wks based on TSH measurements. The longer delay is preferable with smaller doses. TSH shows diurnal and intrapersonal variation. A 40-50% change within the normal range may not be significant. LT resistance should be considered when doses exceed 0.2mg/day. The most common cause of persistantly high TSH and low FT4 despite RX is non compliance followed by poor absorption due to meds or food. Less common are hypochlorhydria, malabsorption syndromes, adrenal insufficiency and accelerated LT metabolism. Other causes of unexpectedly high TSH include abnormal hypothalamic-pituitary-thyroid axis, heterophile or other assay interfering antibodies including anti TSH antibodies and rheumatoid factor. Rare genetic syndromes exist.

Conclusion: Even in the era of “high tech” medicine effective communication between physician and patient remains paramount for assuring quality care and good outcomes. The importance of history taking is highlighted by this case. Asking the right questions and listening to the patient obviated an extensive, expensive and unnecessary workup.

Objective: The objective of this report is to describe a patient presenting with weakness and breathlessness who was eventually diagnosed as Thyrotoxic Periodic Paralysis.

Methods: History, clinical features, biochemical and imaging investigations were analyzed.

Case Presentation: A 60 year-old diabetic, hypertensive, retired gentleman, presented to BIRDEM Endocrine OPD with history of generalized weakness and breathlessness. He also developed fatigue on minimal exertion and intermittent palpitation. He had similar episode one month back for which he consulted a cardiologist, who treated him conservatively in a local hospital and advised to undergo Coronary angiogram. Enquiry revealed that he had lost about 8 kg weight in last two months. He denied any associated chest pain, edema, dizziness, diarrhea, vomiting and family history of similar type of weakness. His bowel-bladder habits were normal. His ongoing medications didn’t include any diuretic. On general examination, pulse - 106 bpm, regular and blood pressure – 130/85 mmHg without postural drop. Systemic examination revealed warm sweaty palms, proximal myopathy and diminished deep tendon reflexes. There were no tremor, goiter or any eye changes. Our Provisional diagnosis was Thyrotoxic Periodic Paralysis, Diabetes Mellitus Type 2 (T2DM), HTN, IHD. Differentials included Recurrent Electrolyte imbalance and Familial Periodic Paralysis. Investigations revealed S. TSH– <0.015 mIU/ml, S. FT4– 33.6 pmol/l, S. FT3– 11.38 pmol/l, S. Potassium– 2.8 mmol/l. Sugar profile was uncontrolled with HbA1c of 9.14%. Thyroid ultrasound was normal; Radioactive Iodine uptake showed 20% uptake at 2 hours and 45% uptake at 24 hours. ECG, chest x-ray, echocardiogram and other biochemical investigations were normal. So the final diagnosis was Thyrotoxic Periodic Paralysis along with T2DM and HTN. He was treated with oral carbimazole, propanolol, losartan potassium, spironolactone, potassium chloride, aspirin and gliclazide. He was followed up after one month. That time he had improved wellbeing with no residual weakness. His biochemical parameters were within normal range.

Discussion: Thyrotoxic periodic paralysis (TPP) is a condition in which there are episodes of muscle weakness due to high level of thyroid hormone. It is common in Asian. Usually occurs in the 3rd decade. It is rarely associated with positive family history. Weakness can last up to several
days. There may be breathing and speech difficulties. 

Conclusion: The presence of acute weakness especially with hypokalemia should prompt the clinician to consider TPP. Early diagnosis is necessary to prevent morbidity and mortality mainly due to fatal arrhythmias.

Abstract #1070

HASHIMOTO’S ENCEPHALOPATHY WITH INCREASED THYROID FUNCTION: ABOUT A CASE

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Results: Hashimoto’s encephalopathy is a rare condition, presenting with high concentrations of antithyroid antibodies associated with an encephalopathic syndrome that responds to steroid therapy. It is usually associated to chronic lymphocytic thyroiditis (Hashimoto’s thyroiditis), and it is rarely diagnosed with increased thyroid hormones.

We describe the case of a 29 year-old female patient, 7 weeks pregnant at the time of admission, who was referred to the Hospital Escuela Universitario in Tegucigalpa, Honduras with a history of fever for 3 days and referring rapid onset upper and lower body muscle weakness, with impaired arm movement and paresis. The patient complained of severe dysphagia, only tolerating liquids. She described having a similar condition 14 years ago, which was diagnosed as a sensorimotor polyneuropathy, but is unaware of the treatment received except for physical rehabilitation.

Blood pressure, cardiac and respiratory frequencies were normal at the time of admission, but her temperature was 38.5 °C. Exophthalmos was evident during physical examination, and cranial nerve examination was normal except for a reduced gag reflex. Muscle strength was 4/5 in upper and lower body according to the oxford scale, and deep tendon reflexes were absent. There was no impairment of sensation, and none of the cerebellar and meningeal signs were present. Abdominal ultrasound reported the presence of an anembryonic gestation. In the 2nd trimester, a nodule in the left lobe was found.

Brain CT revealed the presence of cerebral edema, with collapse of the anterior and posterior horns of the lateral ventricles, associated with ischemic areas in both hemispheres.

Conclusion: These neurological findings, associated to an autoimmune thyroid disease, with no other reasonable explanation for the encephalopathy, led to the diagnosis of Hashimoto’s encephalopathy. Steroid treatment was initiated in combination with antithyroid drugs, which led to resolution of symptoms in a one week.

Abstract #1071

ROLE OF THYROGLOBULIN ANTIBODIES IN THE LONG TERM FOLLOW UP OF DIFFERENTIATED THYROID CANCER - A CASE SERIES

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Objective: Serial estimation of serum Thyroglobulin (Tg) levels is a commonly employed tool to monitor differentiated thyroid cancers (DTC), post thyroidectomy and ablation for recurrence. Measurement of Tg is affected by the presence of thyroglobulin antibodies (TgAb) that may lead to false positive or negative results depending on the assay platform. Since TgAb levels are sensitive to the mass of Tg producing tissue, the trend in TgAb levels itself can be used to detect remission or relapse of DTC.

Case Presentation: We present three case reports in which TgAb levels were used to identify recurrence in DTC 49 year old lady with papillary thyroid cancer, post total thyroidectomy and radioablation was on levothyroxine treatment since 2000. From then to 2009, her Tg levels were suppressed while TgAb levels rose progressively (2000: 84 IU/ml, 2003: 1403 IU/ml 2005: 2931.3 IU/ml, 2009 3133 IU/ml). Radioiodine uptake scan showed uptake in the neck nodes, which were resected and the patient radioablated again.. TgAb levels fell in 2010 to 667 IU/ml but started rising over the next two years to 890 IU/ml and 1028 IU/ml respectively. While iodine scan showed no uptake, FDG PET scan revealed uptake in mediastinal lymph nodes.

The second patient had similar history with follow up from 1997 with wide fluctuations in Tg measurements varying (0.01 to 8000 ng/ml) due to assay interference with TgAb. Progressive rise in TgAb levels resulted in detection of cervical lymph node recurrence.

The third patient was interesting in that the titre of TgAb was not very high albeit showing a rising trend (2012 :
Abstract #1072

THYROTOXIC PERIODIC PARALYSIS AS THE FIRST PRESENTATION OF A PATIENT WITH LOCALLY ADVANCED FAMILIAL PAPILLARY THYROID CANCER

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Objective: To present a patient with thyrotoxic periodic paralysis (TPP) and familial papillary thyroid cancer (FPTC).

Case Presentation: A 26-year-old Caucasian male presented with a generalized muscle weakness for 1 day. On examination, he had a muscle power of 3/5 all over his extremities and a goiter with cervical lymphadenopathy. Potassium (K+) was 1.8 mmol/L (3.6-5) and he improved with K+ replacement. TSH was <0.01 mIU/L (0.45-4.5), FT4 22.2 pmol/L (9-20) and FT3 10 pmol/L (3.4-6); so carbimazole and propranolol were prescribed. Thyroid uptake scan showed increased uptake with a cold thyroid nodule. Neck ultrasound showed 1.6 cm and 1.2 cm nodules with calcifications in the right thyroid lobe, bilateral lymph node metastases and bilateral extranodal metastases. FNA revealed PTC and the patient underwent an extensive neck surgery. Two classical PTC foci (2 cm and 1 cm) were described in the right thyroid lobe with lymph nodes involvement and extranodal metastases. Then, I131 100 mci was given and the post ablation scan showed a remnant in the thyroid bed (T3N1bM0 tumor). The patient’s brother asked for thyroid evaluation; himself in addition to 3 of his 5 sisters were found to have PTC and they had a surgery at ages 30, 33, 29 and 23 years with 2 of them received I131 ablation. The mother had a normal thyroid ultrasound, however, the father had a thyroid nodule and waiting for FNA. There were no other cancers or clinical features indicating a familial syndrome. Patient’s genetic sequencing was negative for a pathogenic variant of the APC, DICER1, PARP4, RET, SDHB and SDHD genes.

Discussion: This is the first case to be reported with TPP as an initial presentation of a patient with locally advanced FPTC. TPP is more common in Asian males and in some patients, like this case, the hyperthyroidism may manifest solely with the periodic paralysis. The mechanism of TPP is still uncertain and the patients usually have Na+, K+-ATPase activity higher than other hyperthyroid patients. FPTC is identified when at least 3 first-degree relatives developed PTC. It can be isolated or a part of a syndrome (e.g., familial adenomatous polyposis, Cowden disease, Werner syndrome or Carney complex). FPTC most likely has autosomal dominant inheritance with incomplete penetrance; however, no underlying susceptibility genes were identified. FPTC is usually multifocal, bilateral and locally advanced which may lead to a recurrence rate higher than the sporadic PTC and warrant aggressive management. Nevertheless, there is no difference in survival as the differentiated thyroid cancer mortality is generally low.

Conclusion: TPP can be associated with FPTC. FPTC has a more serious presentation and may need aggressive treatment.

Abstract #1073

THE EFFECT OF VITAMIN D REPLACEMENT ON SUBCLINICAL HYPOTHYROIDISM

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Objective: Autoimmune hypothyroidism and vitamin D deficiency may be linked; however, no studies looked into the effect of replacing Vitamin D on subclinical hypothyroidism (SCH). We hypothesized that replacing vitamin D in deficient patients with SCH will reduce the TSH level and anti TPO antibody titers

Methods: Observational, prospective study in a clinic setting that assessed the effect of replacing Vitamin D in deficient patients with SCH will reduce the TSH level and anti TPO antibody titers

Results: A 64.7 % of the participants were females. The mean age of the study population was 39.1 years. Mean TSH was 6.1±0.3, mean Free T4 was 14.5±0.2, mean anti TPO antibody titer was 230±96 and mean vitamin D level was 38.9±3.6. Following 3 months treatment with vitamin D, serum vitamin D significantly increased to 56.0, while TSH and anti TPO titer significantly reduced to 4.7±0.2 and 185.4± 53.9, P =0.0001 for both comparisons, respectively

Discussion: In an observational, prospective study in Saudi patients with SCH and vitamin D deficiency, we showed that replacing vitamin D has a significant impact on improving SCH, measured by a significant reduction in both TSH and anti TPO anti body titre after 3 months of treatment. In a subgroup analysis according to vitamin D status, we showed that the reduction was only significant in the vitamin D deficient and insufficient subgroups. While our findings are interesting, we acknowledge the small sample size and large, randomized controlled trials
are needed to confirm these findings.

**Conclusion:** Replacing vitamin D in subjects with autoimmune subclinical hypothyroidism and vitamin D deficiency resulted in significant improvement of SCH as evidenced a significant reduction in TSH level and anti TPO titre after 3 months of replacement. A large randomized controlled trial is needed to confirm our findings.

**Abstract #1074**

**IMPACT OF RAMADAN FASTING ON THYROID STATUS IN PATIENTS WITH PRIMARY HYPOTHYROIDISM**

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**Objective:** 1. To study the change in TSH level before and after Ramadan in patients with primary hypothyroidism. 2. To study the impact on TSH with regards to the quality of meal & interval between meal and Levo-thyroxine (LT4) intake.

**Methods:** This was a prospective cohort study. Included adult patients on stable doses of LT4 who fasted for at least 20 days during the month of Ramadan in the Islamic year 1437 Hijri (June/July 2016). Baseline characteristics and TSH levels were recorded on all consenting patients within 6 weeks prior to Ramadan. Post-Ramadan TSH was tested within 2 to 3 weeks after Eid-ul-Fitr. The quality of meals and interval between LT4 and food during Ramadan was recorded. Paired sample t-test was used to compare variables such as weight, height and TSH levels pre and post Ramadan. Chi square or fisher exact test was used to compare variables across the categories. Independent sample T-test was used to compare quantitative variables across the categories of TSH change and compliance with interval between meal and LT4 intake.

**Results:** During the study period a total of 64 patients with hypothyroidism were enrolled. 58 females and 8 males aged between 22 and 70 years with mean age of 44.2 ± 13.2 years. Majority of patients had no know etiology of hypothyroidism(73.4%), followed by autoimmune(9.4%), post-surgical (7.8%), Post radioactive iodine(7.8%) and congenital (1.6%). Average daily dose of LT4 was 95.3 ± 35.4 mcg and on an average patients were on LT4 since 8.3 years. On an average; patients fasted for 26.5 days and missed dose of LT4 on 1.27 days. About 75% of the participants were able to keep the interval between meals and LT4 for at least 2 hrs post-meal and 30 minutes pre-meals. However, all the participants were using one or other source of food that interferes with levothyroxine absorption. Mean TSH pre-Ramadan was 2.37 mIU/L and post-Ramadan it was 4.69 mIU/L. Mean difference between TSH; pre and Post-ramadan was 2.32 ± 3.80 mIU/L (p<0.001). However, difference in TSH was not significantly different between those who were compliant with meal and levothyroxine interval versus those who were not (compliant= 2.04, non-compliant=3.15, p=0.30).

**Discussion:** Earlier research studied the impact of bedtime LT4 supplementation on serum TSH levels during Ramadan in 47 patients, and found that 29 (62%) had changes ≥ 2 mIU/l of serum TSH by the end of Ramadan. We left the choice of timing of LT4 intake to the patient’s discretion. Changes in TSH concentrations during Islamic fasting in month of Ramadan are statistically significant but these changes are clinically less important. Change in TSH due to Ramadan is not affected by timing of thyroxine intake and interval from meal.

**Abstract #1075**

**MYOCARDIAL SESTAMIBI STEAL SYNDROME IN METASTATIC THYROID CANCER.**

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**Objective:** Radionuclide myocardial perfusion imaging using99mTc-sestamibi or MIBI enables evaluation of myocardial perfusion and function. We report a case wherein cardiac scintigraphy using MIBI was used for the diagnosis of suspected coronary heart disease (CHD). The procedure failed to demonstrate myocardial perfusion because the radionuclide was taken up by large volume pulmonary metastases of thyroid cancer (TC). To our knowledge, such a phenomenon has not been described before. We call this false negative finding “myocardial sestamibi steal”. Alternate modes of defining CHD should be sought in the presence of pulmonary metastases of TC.

**Results:** A 61 yrs. old lady with disseminated metastases from follicular TC and unstimulated underwent thyroidectomy followed by repeated I 131 treatment. Her metastases consisted of bilateral pulmonary lesions and widespread skeletal lesions. Pulmonary metastases were evident on diagnostic I 131 scan, CT scan and FDG-PET scan. These lesions were diffuse, variable in size but especially prominent at both lung bases, measuring up to 2 cm in the largest axis. The skeletal metastases were present in bilateral frontal bones ( these were excised),left humeral head, right 9thrib, both femoral and pelvic bones (received external beam radiotherapy for a large 6 cm left iliac bone), and 6th thoracic vertebra. She had myocardial perfusion/99mTc-sestamibi/MIBI scan done
Objective: To evaluate the effectiveness and compliance to L-thyroxine in the treatment of Hypothyroidism in a weekly dose of 7 times of normal dose as an alternative to daily dosing in young and middle aged adults.

Methods: A randomized prospective observational study on 180 patients (female: male) ratio of 5:1 aged between 18 to 55 years with an established diagnosis of Hypothyroidism were assigned a weekly dose of 7 times of normal dose. The patients were randomized in 3 groups G1, G2 and G3.

Group 1 (G1): 60 patients with the established diagnosis of Hypothyroidism of TSH value of 4.2 or less, currently on daily dose. The subjects were assigned weekly dose of L-thyroxine which was 7 fold of normal dose.

Group 2 (G2): 60 patients with established diagnosis of Hypothyroidism with TSH value of more than 4.2. The group was started with a weekly dose which was individualized as per the body weight and TSH value.

Group 3 (G3): 60 patients newly established diagnosis of Hypothyroidism with TSH value of more than 4.2. The group was started with a weekly dose which was 7 fold of normal dose as an alternative to daily dosing regimen was shown to be efficacious and safe for the treatment of Hypothyroidism in young and middle aged adults. The results show that it can be started in newly diagnosed hypothyroid patients. For patients who find it difficult to adhere to a rigorous treatment regime it is a valid therapeutic option and can also be considered as a first line therapy in young and middle aged working adults facing impaired absorption due to early breakfast (no need to wait 30-45 min for breakfast).

Conclusion: Once weekly dose of L-thyroxine as an alternative to daily dosing regimen was shown to be efficacious and safe for the treatment of Hypothyroidism to treat non-compliant Hypothyroid young and middle aged adults. The results show that it can be started in newly diagnosed hypothyroid patients. For patients who find it difficult to adhere to a rigorous treatment regime it is a valid therapeutic option and can also be considered as a first line therapy in young and middle aged working adults facing impaired absorption due to early breakfast (no need to wait 30-45 min for breakfast).
extracted and stored at -80 degree Celsius. TSH analysis was done by electrochemiluminescence immunoassay using Roche Cobas 6000 analyser.

**Results:** A total of 103 pregnant women, 30 in first trimester, 34 in second trimester and 39 in third trimester who fulfilled all the inclusion and exclusion criteria were included in the study. The fasting serum TSH levels were significantly higher compared to postprandial serum TSH levels in all the three trimesters (1.88±0.92 vs 1.55±0.75 in first trimester, 2.32±1.10 vs 1.93±0.93 in second trimester and 2.60±1.49 vs 2.09±1.16 in third trimester). A total of 26 patients (25.2%) had a serum TSH value in subclinical Hypothyroidism range in fasting state compared to 14 patients (13.6%) in post prandial state. This difference was seen in all trimesters. 7 patients (23.3%) in fasting state and 2 patients (6.7%) in post prandial state had TSH value > 2.5 in the first trimester. 7 patients (20.6%) in fasting state and 4 patients (11.8%) in post prandial state had TSH value > 3 in the second trimester. 12 patients (30.8%) in fasting state and 8 patients (20.5%) in post prandial state had TSH value > 3 in the third trimester.

**Discussion:** Our study shows that subclinical hypothyroidism is common during all trimesters of pregnancy. It also demonstrates that postprandial TSH levels are significantly lower than fasting levels. Studies in non pregnant individuals have shown that TSH levels are lower in post prandial state compared to fasting state. To our knowledge this is the first study to address this issue in pregnant women. This study shows that by doing serum TSH in fasting state it is possible to identify more patients with subclinical hypothyroidism and treat them early. This would reduce the maternal and fetal complications of untreated hypothyroidism and result in better pregnancy outcomes.

**Conclusion:** In pregnancy, TSH levels fall significantly in postprandial state compared to fasting state. So we recommend doing serum TSH levels in fasting state during pregnancy to increase the sensitivity of screening for subclinical hypothyroidism.

**Abstract #1078**

**A TSH-SECRETING PITUITARY TUMOR PRESENTING AS THYROID STORM**

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University of Kansas Medical Center

**Objective:** To present a case of thyroid storm caused by TSH secreting pituitary tumor and review the reported characteristics and treatment options.

**Case Presentation:** A 53-year old male presented with a one year history of progressive proximal muscle weakness, frequent bowel movements, progressive shortness of air, progressive edema, increasing anxiety, and sleep disturbance. He was admitted for acute on chronic heart failure. Complaints of right arm weakness led to a CT examination which revealed a 3 cm pituitary tumor. Physical examination revealed tachycardia, bi temporal hemianopia and a diffuse goiter twice normal size. Laboratory evaluation revealed a Free T4 5.0 ng/dL (0.6-1.6), Total T3 215 ng/dL (87-180), TSH 2.78 mIU/mL (0.35-5), prolactin 1.8 ng/ml (2.6-13.1), am cortisol 18.7 mcg/dL (6.7-22.6), ACTH 38 pg/ml, urine free cortisol 11 mcg/24 hours, FSH 0.3 mIU/mL (1-12), free testosterone 3 ng/dL (47-244), and IGF-1 24 ng/mL (37-247). The diagnosis was central hyperthyroidism with thyroid storm (Burch-Wartofsky score 55). He was treated with octreotide and methimazole with the plan for pituitary adenoma resection. However, the patient died of progressive heart failure.

**Discussion:** TSH secreting pituitary adenomas account for only 1-2% of all pituitary adenomas. They generally present with features of hyperthyroidism. While having an elevated T4 and T3 the TSH is inappropriately elevated, the majority being within the reference normal range. Pituitary alpha subunit is most often elevated. The majority are macro adenoma at presentation. Thyroid hormone resistance syndrome (RTH) is the major differential diagnostic concern. The elevated pituitary alpha subunit, and a pituitary tumor helped confirm the diagnosis in this case. T3 suppression using liothyronine 100 mcg daily for 8 days will generally suppress TSH in RTH but not TSH secreting adenomas. This test is contraindicated in elderly or patients with significant cardiac disease. TRH stimulation test generally finds a blunted response in thyrotropinoma and a doubling or more in RTH patients. However, TRH is not available in the USA. Somatostatin analogs have been shown to control TSH secretion and result in tumor reduction of 20% in half of patients, in some cases improving visual field defects. Surgery is the recommended treatment of choice.

**Conclusion:** TSH secreting adenoma is a rare form of pituitary tumor particularly presenting as thyroid storm. A high index of clinical suspicion is needed in making this diagnosis as measuring TSH alone when suspecting hyperthyroidism may cause the clinician to be misled.
Abstract #1079

FROM STARVATION TO PLENTY: NO ENDOGENOUS THYROXINE TO OVERPRODUCTION

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Objective: Spontaneous conversion of autoimmune hypothyroidism to Graves’ disease is a rare occurrence. We present a case of antibody confirmed autoimmune hypothyroidism, where the patient was on replacement therapy with levothyroxine for 6 years, had spontaneous conversion to Graves’ disease with positive thyrotropin receptor antibodies (TRAb).

Case Presentation: A 79-year-old female was evaluated in the office with persistent fatigue following acute dermatomal herpes zoster. She had developed associated progressive tremor of the extremities and heat intolerance. Her other problems included thyroid peroxidase antibody positive Hashimoto’s thyroiditis and vitiligo in addition to diabetes mellitus, cerebrovascular disease, coronary artery disease, osteoporosis and hypercholesterolemia. Her medications included metformin, aspirin, lisinopril, atorvastatin, zoledronic acid and levothyroxine. Clinical examination was notable for healed lesions of herpes zoster, hand tremor and tachycardia. There was no thyromegaly. Laboratory evaluation revealed T3 levels of 1.83 (0.80-2.00 ng/ml), free T4 of 1.53 levels 1.53 (0.93-1.70 ng/dl), thyroid stimulating hormone (TSH) 0.007 (0.270-4.200 mcIU/ml). Of note, TRAb was positive at 5.37 (0.00-1.75 IU/L). She was placed on methimazole (0.270-4.200 mcIU/ml). Of note, TRAb was positive at 5.37 (0.00-1.75 IU/L). She was placed on methimazole and beta blockers with improvement.

Conclusion: Both Graves’ disease and chronic lymphocytic thyroiditis are autoimmune conditions sharing a similar pathophysiologic mechanism but different clinical manifestations. Both thyroid stimulating antibody (TSAb) and TSH-stimulation blocking antibody (TSBAb) block the TSH receptors. TSBAb causes hypothyroidism whereas TSAb is responsible for Graves’ hyperthyroidism resulting from over activation of TSH receptors. Our patient was being treated with stable dose of levothyroxine for 6 years without any complications. We hypothesize that the conversion of blocking to stimulating antibodies was induced by the stress of the herpes zoster infection. Factors that could have possibly increased her odds for this phenomenon included her gender, thyroid replacement therapy, advanced age and a background of autoimmune hypothyroidism. This case highlights the critical need to recognize that this transition can occur, since it may require a reversal of treatment plans.

Abstract #1080

MARINE-LENHART SYNDROME WITH SPONTANEOUS REMISSION, A REVIEW OF LITERATURE.

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Objective: Diffuse toxic goiter (Graves’ disease) and toxic nodular goiter both cause hyperthyroidism by different pathophysiological mechanisms. A single or multiple toxic hot nodule can also coexist with the Graves’ disease and are defined as the Marine-Lenhart syndrome. We are reporting an unusual case of such syndrome undergoing spontaneous remission.

Case Presentation: A 70 yo Vietnam war veteran with history of subclinical hyperthyroidism in 2010. The TSH was found spontaneously normalized on 12/2010 (0.59 mU/L, nl 0.55-4.78) and 2/2013 (1.15 mU/L). He was seen again in 1/2015 for suppressed TSH (0.01-0.02 mU/L) and elevated FT4 (1.6-1.9 ng/dL, nl 0.67-1.52). Patient denied symptoms of hyperthyroidism or weight loss. ROS was negative except a partial colon resection in 4/2013. A thyroid uptake/scan on 2/2015 showed a single hot nodule in the R lobe with otherwise diffusely increased uptakes in the rest of gland. The total uptake at 24h was 53.9% (normal 8 – 35%); 21.6% uptake in the L lobe with homogeneous RAI distribution. The patient refused to be treated with either MMI or RAI. The patient did not return to clinic until 4/2016 and found TSH to be normal. Both TSH (0.77 mU/L) and FT4 (0.9 ng/dL) remained normal on 10/2016. The patient refused further thyroid studies.

Discussion: Thyroid nodules associated with Graves’ disease have been reported with the incidence between 25 to 30%, most of which are cold nodules. The incidence of Graves’ disease accompanied by a single hot nodule, as shown in the present report, ranges from 1 to 2.7% and represents a rare form of Marine-Lenhart syndrome. Most reported cases are Graves’ disease with multiple hyperfunctioning nodules. Two separate mechanisms, including acquired mutations resulting in constitutively activated TSH receptors and the presence of anti TSH receptor autoantibodies, might be responsible for the development of Marine-Lenhart syndrome. In the present case, the homogeneously increased uptake in the remaining thyroid gland outside the hot nodule, despite the suppressed level of TSH, is consistent with the underlying Graves’ disease. The treatment options for this syndrome include thionamides, radiiodine, and surgery. The patient in this report refused any therapeutic intervention. We are
not aware of any case report of spontaneous remission of hyperthyroid state in Marine-Lenhart Syndrome as demonstrated in the present case. **Conclusion:** We are reporting an unusual case of Marine-Lenhart syndrome undergoing spontaneous remission of hyperthyroid state without any therapeutic intervention. To understand the mechanism(s) that triggered the occurrence and remission will be important for future management of such syndrome.

**Abstract #1081**

**GRAVES DISEASE WITH AUTOIMMUNE HEPATITIS AND IMMUNE THROMBOCYTOPENIA—“AN AUTOIMMUNE TSUNAMI”- A DIAGNOSTIC AND THERAPEUTIC DILEMMA**

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**Objective:** There are many cases of Graves’ disease with autoimmune hepatitis (AIH) as well as AIH with immune thrombocytopenia (ITP). We present a unique case of a patient with 3 different autoimmune diseases—Graves’ disease, AIH and ITP occurring together with the objective to discuss the various challenges in the management.

**Case Presentation:** A 35-year-old woman with no significant past medical history presented with jaundice, dyspnea and lower extremity edema for 1 month. She reported worsening dyspnea on exertion for 1 week. On physical examination, she had scleral icterus, thyroid enlargement, thyroid bruit, tachycardia, irregularly irregular heart rhythm, hepatosplenomegaly, ascites and bilateral lower extremity pitting edema. Laboratory findings showed severe anemia, pancytopenia (hemoglobin 7.2 g/dL, white blood cell count 2.2 x 103 cells/uL, platelet count 57 x 103 u/L) and liver dysfunction with a cholestatic pattern (total bilirubin 4.7 mg/dL). On further evaluation, she was found to have Graves’ disease with severely decreased thyroid stimulating hormone (0.007 uIU/mL), increased free T4 (5.13 ng/dL), increased total T3 (200 ng/dL), and elevated thyroid-stimulating immunoglobulins (TSI 447%). Thyroid ultrasound showed a diffusely enlarged, heterogeneous, and lobulated thyroid without discrete cystic or solid nodules. Computed tomography (CT) and ultrasound (US) of the abdomen showed liver heterogeneity without a definitive mass. Electrocardiogram showed atrial fibrillation with rapid ventricular response. She was also found to have positive anti-platelet antibodies and evidence of hemolytic anemia. She had elevated INR, elevated IgG, positive anti-smooth muscle antibody and negative hepatitis panel, consistent with AIH. Treatment strategies like use of anti-thyroid drugs, radioactive iodine thyroid ablation or thyroidectomy were contraindicated due to the ongoing process of pancytopenia, liver dysfunction, and because the patient underwent CT scan of the abdomen with intravenous contrast, potentially interfering with radioactive iodine ablation. Liver biopsy was contraindicated due to coagulopathy. Conservative medical management was initiated with prednisone, furosemide, spironolactone, and propranolol. Her symptoms started improving gradually over one week and she was discharged with close follow up with endocrinology, gastroenterology and hematology.

**Conclusion:** This case helps increase awareness of the diagnostic and therapeutic challenges involved in cases with a convoluted presentation due to multiple autoimmune diseases. The role of steroids as a rescue drug in curtailing autoimmune processes remains vital especially when other treatment modalities cannot be implemented.

**Abstract #1082**

**POORLY DIFFERENTIATED THYROID CARCINOMA**

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**Case Presentation: Background**

Poorly differentiated thyroid carcinoma (PDTC) is a rare type of thyroid cancer, comprising ~2-3% of cases. It is defined by the Turin pathologic criteria: presence of a solid, trabecular, or insular pattern of growth, absence of the conventional nuclear features of papillary thyroid carcinoma (PTC), and presence of at least 1 of the following features: convoluted nuclei, mitotic activity >3 x 10 high powered field, tumor necrosis. Prognosis and tumor biology of PDTC falls between well-differentiated thyroid cancer and anaplastic thyroid cancer. Common sites of metastases are bone (with lytic lesions), brain, liver, and lung.

**Case report**

A 70 year-old woman presents with a goiter for five years that is growing. She reports compressive symptoms of choking and coughing with food but can still swallow. Her previous medical history includes 40 years of hypothyroidism treated with levothyroxine, CHF during pregnancy in 1986, type 2 diabetes, obesity, hyperlipidemia, & hypertension. She has no history of radiation & no family history of thyroid cancer. A CT of her neck in 2014 revealed a multinodular goiter with a nodule measuring 6.2x6.5x11 cm. Her past surgical history included a tonsillectomy/adenoidectomy & two tooth
extractions. Her family history included an unspecified thyroid problem in her father but no other endocrinopathy. She underwent outpatient laryngoscopy, revealing bilateral vocal cord movement & significant left-sided retropharyngeal & laryngeal swelling. FNA revealed follicular neoplasm (Bethesda IV) but with architectural features suggestive of PDTC arising in a follicular-patterned background. Repeat CT neck in 2016 showed a necrotic nodule measuring 7.5x5.5x8.9 cm, with innumerable pulmonary nodules concerning for metastatic disease. She underwent an uncomplicated total thyroidectomy with bilateral recurrent laryngeal nerve monitoring. Final pathology revealed a unifocal 8.5 cm PDTC with angioinvasion in four vessels, no perineural invasion, no extrathyroidal extension, negative margins, and no lymph nodes examined – T3Nx. Her thyroglobulin dropped from 475 preoperatively to 75 on post-op day 18. Her future management plan includes thyroid hormone withdrawal for a whole body scan and radioactive iodine therapy planned depending on results.

**Conclusion:** This is a case of a 70 year-old woman presenting with a large, poorly-differentiated thyroid carcinoma with likely pulmonary metastases resected successfully in its entirety.

**Abstract #1083**

**USE OF THYROGEN ASSOCIATED WITH LOWER HEALTHCARE RESOURCE USE AMONG THYROID CANCER PATIENTS UNDERGOING RADIOIODINE THERAPY: ANALYSIS OF U.S. ADMINISTRATIVE CLAIMS DATA**

Luba Nalysnyk, MD, MPH, Martin Selzer, PhD, Alaa Hamed, MD, MPH, MBA, Richard Weiss, MD

Sanofi Genzyme

**Objective:** Many patients with well-differentiated thyroid cancer (WDTC) undergo thyroid hormone withdrawal (THW) for remnant ablation and for stimulated diagnostic testing, with the resultant hypothyroidism potentially leading to substantial morbidity, reduction in quality of life and negative economic impact. Administration of Thyrogen® (thyrotropin alfa) is an alternative approach for producing the elevated serum thyroid stimulating hormone (TSH) levels and allows patients to remain euthyroid while undergoing radioactive ablation procedures and diagnostic testing.

The objective of this study was to evaluate the impact of Thyrogen (Thyrogen group) on healthcare resource utilization among patients with thyroid cancer who underwent radioiodine remnant ablation and compare to thyroid cancer patients who did not use Thyrogen (THW group).

**Methods:** In this retrospective cohort study, administrative claims data from 2011 to 2014 were extracted from Truven Medstat database. Patients who underwent total thyroidectomy for WDTC and subsequent remnant ablation were identified using corresponding ICD-9 and CPT codes. Patients had continuous enrollment for the study period, which included: baseline (12 weeks before thyroidectomy), between surgery and ablation (evaluation period 1), and 12 weeks after ablation (evaluation period 2). Healthcare resource utilization were compared between patients given Thyrogen and those in the THW group. Outcomes included: the percentage of patients with hospital and/or ER claims, the number of outpatient claims per patient, and the cost of claims per patient. Costs were expressed as US dollar amount. Results were compared before surgery, between surgery and ablation, and 12 weeks after ablation.

**Results:** A total of 4,892 patients were included in the analysis (n=1,154 Thyrogen patients and n=3,738 THW patients). Patient demographic characteristics were comparable at baseline (mean age, 45.7 vs. 45.2 years; females 77% vs 74%, respectively). The analysis revealed that compared to THW patients, Thyrogen patients have lower risk of hospital and ER admissions between surgery and ablation (7.3% vs. 10.7% p <0.001 for hospitalization and 5.3% vs. 6.0% for ER visits p=0.37) and for the 12 weeks post-ablation (2.4% vs. 3.3% p =0.127 for hospitalization and 4.2% vs. 4.7% p=0.457 for ER visits).

Overall, patients using Thyrogen had approximately 47% lower probability of hospitalization between thyroidectomy and ablation compared to THW patients and the difference is statistically significant.

**Conclusion:** The patients with thyroid cancer who initiated Thyrogen before ablation experienced fewer hospitalizations than the patients who underwent THW.

**Abstract #1084**

**THYROTOXIC PERIODIC PARALYSIS: A DIAGNOSTIC CHALLENGE**

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SUNY Upstate Medical University

**Objective:** Hypokalemia related medical emergencies vary from muscle weakness to flaccid paralysis. Familial hypokalemic periodic paralysis (FHPP) is the most common cause of periodic paralysis related to transcellular potassium (K) shifts and often leads to misdiagnosis of a less common but serious condition of thyrotoxic periodic paralysis (TPP). We present 2 cases of recurrent weakness in the setting of uncontrolled hyperthyroidism.
Case Presentation: CASE 1: 28 y/o Korean male presented to ER with nausea and sudden onset weakness in his legs. He reported similar episode a month ago. He was tachycardic with muscle strength 3/5 in bilateral lower extremities and diminished reflexes. Labs revealed K 1.8mmol/L (3.6-5.2), TSH <0.03uU/ml (0.27-4.2), fT4 4.24 ng/dl (0.9-1.7), T3 391 ng/dl (80-200), TSI> 500% (< 122%). EKG showed sinus tachycardia with prolonged QTc. Thyroid ultrasound showed no nodule. Thyroid uptake was homogenous, 59% at 24 hour (6-33%). He was treated with potassium supplement, beta-blocker and methimazole resulting in normalization of K level and symptomatic improvement. He was discharged home on methimazole and beta-blocker.

CASE 2: 36 y/o African American male with h/o hyperthyroidism presented to outpatient clinic with recurrent weakness, precipitated by stress. Examination revealed tachycardia, enlarged thyroid gland. Labs showed undetectable TSH, Ft4 >4.5 ng/dl, elevated TSI and K 2.4mmol/L. Thyroid ultrasound showed diffusely enlarged, hypervascular gland without discrete nodules. He was treated with methimazole and beta-blocker. Over next 6 months, he had multiple hospital admissions with lower extremity weakness corresponding to periods when he was not taking his medications consistently due to insurance issues. He finally underwent total thyroidectomy with biopsy revealing Grave’s disease leading to symptom resolution.

Conclusion: TPP is more common in Asians with reported incidence of 1.8–1.9 % in Chinese and Japanese population. Increased activity of Na+-K+ ATPase pump and inactivating mutation in Kir2.6 gene have been described in the pathogenesis, leading to an imbalance between potassium current causing paradoxical depolarization. Alcohol, high carbohydrate meal, stress can precipitate attacks. Treatment includes non–selective beta-blockers, potassium supplement and definite treatment of underlying cause of hyperthyroidism. Signs of hyperthyroidism, EKG changes and negative family history help to differentiate TPP from FHPP. TPP should always be kept in differential diagnosis of acute paralysis presenting in the setting of hypokalemia, as early diagnosis can prevent serious complications of hyperthyroidism and rebound hyperkalemia.

Abstract #1085

PAPILLARY THYROID CARCINOMA IN THE SETTING OF UNCONTROLLED GRAVES’ DISEASE

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Objective: Thyroid cancer occurs concomitantly in Graves’ disease with a frequency varying from approximately 0.15 to 15%. Most commonly, it is discovered as an incidental micropapillary carcinoma at surgery. Rarely, clinically overt thyroid cancer occurs concurrently with Graves’ disease as a more aggressive tumor with lymphadenopathy and/or distant metastasis. Clinicians need to consider this diagnosis in patients with thyroid nodules or lymph nodes.

Case Presentation: A 25 year old female with a two year history of Graves’ disease first presented to our clinic after a spontaneous miscarriage. She was on Propylthiouracil (PTU) 150mg every 8 hours with a TSH of <0.01 (0.4-4mIU/L) and FT4 of 3.46 (0.76-1.46ng/dl). On physical exam she was noted to have a firm goiter of approximately 60 gm and multiple 1-3cm cervical lymph nodes bilaterally from the angle of the jaw to the clavicle. Ultrasound of the neck revealed a 1.5x0.8cm solid vascular nodule in the left lobe of the thyroid and multiple solid vascular nodules in level I on the left, and levels II, III, and IV bilaterally ranging from 1.6 to 3.7cm. Radioactive iodine uptake (RAIU) scan showed a diffuse uptake of 81% at 24 hours (normal 10-30%) and bilateral, iodine-avid lymphadenopathy. The left nodule seen on prior US was deemed to be a functional (warm) nodule. Fine-needle aspiration (FNA) of the lymphadenopathy showed papillary thyroid carcinoma, classical and follicular variants. The patient underwent a total thyroidectomy, bilateral central lymph node dissection, and bilateral modified radical neck dissections. Surgical pathology report identified multiple tumor foci in the right lobe, isthmus, and left lobe, largest tumor focus measuring 2.5 cm in greatest dimension, and 54/69 lymph nodes positive for papillary carcinoma. PTU was discontinued, however, TSH post op remained low. Repeat RAIU scan showed residual thyroid tissue, and uptake was determined to be 5.4% at 6 hours (normal range 7 to 15%). The patient was given 29.9 mCi of I131 to treat the residual thyroid with a planned larger dose to be given after the thyroid tissue has been eliminated.

Discussion: Clinically significant thyroid cancer is an uncommon finding in the setting of Graves’ disease. Cold nodules, or chronic enlarged or extensive lymph nodes require FNA for diagnosis followed by surgical resection +/- radioactive iodine for cancer. The increased thyroid stimulating immunoglobulin (TSI) levels in Graves’
disease have been postulated to cause more aggressive growth of the tumors.

**Conclusion:** Although rare, the diagnosis of thyroid cancer should be considered in Graves' patients presenting with thyroid nodules or lymphadenopathy and further evaluation should always be undertaken.

**Abstract #1086**

**PATIENT EXPERIENCE WITH SEVERE LOW ENERGY FOLLOWING TOTAL THYROIDECTOMY FOR PAPILLARY THYROID CANCER**

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**Objective:** Following total thyroidectomy, low energy may be attributed to recovery or thyroid hormone replacement and is generally expected to resolve within a few months. This study analyzed the experiences of papillary thyroid cancer (PTC) patients reporting low energy up to 1 year after surgery.

**Methods:** This qualitative study included 35 PTC patients enrolled in an ongoing clinical trial. We conducted semi-structured interviews before surgery, and again at 2 weeks, 6 weeks, 6 months, and 1 year after surgery. We performed inductive analysis, thematically coding 129 interviews and assessing descriptions of fatigue over time. At each interview, participants completed the SF-12, and were asked about factors contributing to their “overall quality of life” score.

**Results:** Post-operative low energy impacted participants more drastically and for longer than expected. 2 weeks after surgery, 45% of participants described low energy as one of their most bothersome symptoms compared to just 8% pre-operatively (p < 0.01). Participants discussed the unpredictability of their energy level and the negative impact on relationships as well as decreased productivity at work or home. More than 35% of participants cited low energy as the biggest contributor to decreased quality of life after surgery with some attributing up to a two point decrement (on a 7 point scale) to low energy alone. Participants continued to report fatigue at 6 weeks, 6 months, and 1 year, with >30% describing it as one of their most bothersome symptoms at those time points (p < 0.01 compared to baseline). Additional consequences emerged as participants reported guilt and self-consciousness due to effects of persistently low energy.

We compared TSH levels among those reporting and not reporting low energy. Fatigue was a major concern for 20% of patients with an appropriate TSH at 6 weeks compared to 40% of participants with an elevated level (p <0.3). 8 patients with elevated TSH who reported low energy had normalization of their thyroid levels during the study, yet, 63% (n=5) reported persistent symptoms despite this normalization.

**Discussion:** Post-operative low energy is more impactful and lasts longer than expected. While elevated TSH may be the cause in some cases, 20% of participants still reported life-altering fatigue despite adequately suppressed TSH levels at 6 weeks post-surgery. Additionally, appropriate suppression of TSH often did not lead to symptom resolution.

**Conclusion:** Post-operative low energy is a major issue for thyroid cancer patients. While inadequate thyroid hormone replacement may be part of the problem, there are other factors that play a role in this phenomenon and further investigation is warranted.

**Abstract #1087**

**LONG TERM USE OF DAILY INTRAVENOUS LEVO-THYROXINE: A RARE CASE OF POST-OPERATIVE HYPOTHYROIDISM NOT RESPONSIVE TO HIGH DOSE ORAL LEVO-THYROXINE THERAPY**

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**Objective:** Cases of refractory hypothyroidism treated with long term daily intravenous (IV) levothyroxine (LT4) are extremely rare. We present an unusual case of a 30-year-old female with persistent hypothyroidism resolved only by daily long term IV LT4 use.

**Case Presentation:** A 30-year-old female was hospitalized for severe hypothyroidism refractory to high dose oral (PO) LT4 replacement therapy for the past 14 months. Four years prior, she had a total thyroidectomy performed for papillary thyroid cancer (stage 2), followed by two cycles of ablative radiiodine therapy. After thyroidectomy she required replacement therapy of LT4 (from 88 mcg to 350 mcg), PO cytomel 20 mcg, calcitriol 1.5 mcg, Calcium 600 mg and vitamin D (from 800 IU to 50,000 IU). She had presenting complaints of myalgia, weight gain (40 lbs, in 1 year), cold intolerance, hoarseness, dry skin, and brittle nails. On exam, she was 152 cm tall and weighed 95.3 kg (BMI- 41.0 kg/m2), with blood pressure of 143/81 mmhg, a heart rate of 91 bpm, periorbital edema and 2+ pedal edema. Her laboratory studies showed serum levels of thyroid stimulating hormone (TSH) to be 142.80 IU/L (normal, 0.30- 4.20 IU/L); Free thyroxine (FT4) 0.17 ng/dL (normal, 0.9-1.8 ng/dL); despite receiving highest dose of PO LT4 350 mcg on an empty stomach. She reported a
negative work up for malabsorption disorders. Her thyroid profile and symptoms markedly improved after receiving five days of IV LT4 150 mcg daily plus PO cytomel 10 mcg. (TSH 67.08 IU/L, FT4- 1.29 ng/dl). In light of her history of thyroid cancer and need for TSH suppression, along with her severely symptomatic state despite many attempts at oral dosing, the decision was made to send her home on long term IV LT4 via peripherally inserted central catheter (PICC) line. One month later TSH normalized (0.32 IU/L). Later, she was admitted for redness and pain around her PICC line, but not found to have any bacteremia and mediport was placed to continue receiving IV LT4 on a long term basis. Currently, she has been successfully receiving IV LT4 for 6 months.

Conclusion: Previously, long term IV LT4 has been used in patients on parenteral nutrition, with esophageal disorders, who were unconscious, or with proved malabsorption disorders. None of the above was the case for our patient, and etiology remains unclear. The term pseudo-malabsorption was previously reported when the etiology is not clearly known. Infectious risk has to be considered with long term IV LT4 use, but the benefit of resolution of persistent refractory hypothyroidism leads us to support evidence of using long term daily IV LT4 in select patients not responsive to high doses of PO LT4.

Abstract #1088

THE RISING INCIDENCE OF PAPILLARY MICROCARCINOMA IDENTIFIED IN PATIENTS UNDERGOING THYROIDECTOMY FOR BENIGN DISEASE. IS IT TIME FOR A CHANGE IN NOMENCLATURE?

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Objective: Thyroid cancer incidence is increasing at a rate faster than any other malignancy, and most of these additional cancers are subcentimeter papillary thyroid microcarcinomas. This study examines the rate of increase over the last three decades at a tertiary medical center, its possible causes, and long-term outcomes.

Methods: A retrospective review of the pathology and endocrine surgery databases identified 896 patients who underwent thyroidectomy for benign disease between January 1985 and December 2014. Cases of incidentally identified thyroid cancer were analyzed for tumor size, metastases, treatment, and recurrence. Patients were grouped into 5-year intervals beginning with 1985 to compare cancer incidence. Papillary thyroid microcarcinoma was defined as carcinoma <1 cm. Chi-square test was used to determine statistical significance.

Results: Incidental thyroid carcinomas were identified in 143 patients (16%), of which 131 had a papillary carcinoma. There were 18 patients with tumor ≥1 cm, 92 with tumor <1 cm, and 18 with both. The likelihood of identifying a papillary thyroid microcarcinoma over a 5-year interval was 1.4% in 1985-1989, 0% in 1990-1994, 4.9% in 1995-1999, 9.8% in 2000-2004, 12.7% in 2005-2009, and 13.3% in 2010-2014 (p<0.001). 55 (59.8%) showed classic papillary morphology, 32 (34.8%) were follicular variant morphology, and 5 (5.4%) had both morphologies. Analysis of the 92 patients who had papillary microcarcinoma showed that 3 (3.3%) had lymph node metastases and none had distant disease. Operative treatment consisted of lobectomy in 29, lobectomy followed by completion thyroidectomy in 9, and total thyroidectomy in 55. Ten papillary microcarcinoma patients underwent radioiodine ablation, 2 with lymph node metastases, and 8 without. No disease recurrences have been documented.

Conclusion: Over the last 30 years the increased incidence of thyroid cancer has been partially fueled by increased recognition of papillary microcarcinomas in thyroidectomy specimens resected for benign disease. This is likely the result of changes in specimen processing and increased scrutiny and reporting by pathologists, as mandated by the American College of Surgeons and College of American Pathologists. In this series of patients, these microcarcinomas had no risk of distant metastases, recurrence, or mortality. We suggest a reevaluation of the nomenclature of these lesions to reflect their true biologic behavior.

Abstract #1089

THYROID AUTOIMMUNITY IN BETA THALASSEMIA MINOR

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Objective: Tendency to autoimmune diseases has been reported to be increased in beta thalassemia minor (BTM). Our aim was to examine the prevalence of thyroid autoimmunity in BTM.

Methods: Eighty six adults with BTM and 93 age and gender matched controls were included in the study. The two groups were compared cross-sectionally in terms of anti-thyroid antibodies (anti-TG and anti-TPO) and thyroid hormones. Patients with known autoimmune disorders other than autoimmune thyroid disease were not included in the study

Results: In the BTM group, serum TSH, FT4, FT3 levels
were statistically indifferent from the control group. Serum anti-TG and anti-TPO antibody levels were found to be similar in the two groups. BTM and control groups were similar in terms of anti-thyroid antibody positivity prevalence. In the BTM group, anti-TG was 11.6% and anti-TPO was 14% positive, while these were respectively 14% and 12.9% positive in the control group (p=0.806 and p=0.989, respectively). The proportion of anti-TG and/or anti-TPO antibody positive subjects was found to be 20.9% in the BTM group, and 20.4% in the control group (p=0.919). Ratios of subjects with euthyroidism, hypertiroidism and hypothyroidism were similar in both groups.

**Conclusion:** Because thyroid autoimmunity prevalence in the BTM group is not increased compared to the control group, we consider that there is no necessity for routine anti-thyroid antibodies and thyroid hormone testing in subjects with BTM.

**Abstract #1090**

**ECONOMIC BURDEN OF CHRONIC HYPOPARATHYROIDISM IN US CLINICAL PRACTICE**

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**Objective:** Chronic hypoparathyroidism (hypoPT) is a rare disorder characterized by absent/deficient levels of parathyroid hormone and impaired mineral homeostasis. While the etiology and short-term clinical consequences of chronic hypoPT are fairly well documented, relatively little is known about the economic burden of this disorder in real-world settings.

**Methods:** A retrospective cohort study was undertaken using data from a large US healthcare claims repository spanning the period January 2010 to June 2015. Study subjects were adult patients (pts) (aged ≥18 years) with evidence of chronic hypoPT, which we defined based on evidence of: (1) ≥2 hospitalizations or ambulatory visits with diagnosis code for hypoPT (ICD–9–CM 252.1) >180 days apart; or (2) any encounters for hypoPT coupled with any encounters for hypocalcemia (275.41), hypercalcemia (275.42), hypercalciuria (275.40), or hyperphosphatemia (275.5) >180 days apart. We examined the demographic and clinical characteristics of study subjects as well as their annualized levels of resource utilization and costs (2015 US$) for specific services and medications that may be related to hypoPT, and for all causes, respectively.

**Results:** A total of 5799 pts met study-selection criteria; mean (SD) age was 54 (15) years and 78% were women. Common comorbidities included chronic kidney disease (12%), ischemic heart disease (8%), cardiac arrhythmia (8%), and renal insufficiency (6%); prevalence of conditions deemed possibly related to hypoPT included 13% for dyspnea/respiratory abnormality and 6% for numbness/tingling. On an annual basis, pts with hypoPT averaged 0.3 (95% CI: 0.28-0.32) hospitalizations, 1.7 (1.5-1.9) hospital days, and 31.1 (30.2-32.0) ambulatory encounters for any reason. Mean annual all-cause healthcare expenditures totaled $26,889 ($25,017-$28,761); ambulatory encounters accounted for 60% of this total ($16,028 [$14,645-$17,411]), while hospitalizations accounted for 27% of the total ($7,373 [$6417-$8329]). Hospitalizations and ambulatory encounters for disorders of the kidney and cardiovascular system, respectively, as well as other conditions possibly related to hypoPT, were common.

**Discussion:** This retrospective cohort study based on US healthcare claims shows that kidney and cardiovascular disorders play an important role in the high clinical and economic burden of hypoPT in typical clinical practice.

**Conclusion:** Levels of healthcare utilization and costs are high in pts with hypoPT, with ambulatory visits accounting for more than one-half of the total economic burden.

**Abstract #1091**

**CHRONIC HYPOPARATHYROIDISM DISEASE PROFILE: INITIAL ANALYSIS FROM THE PARADIGHM™ NATURAL HISTORY GLOBAL REGISTRY**

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**Objective:** The aim of the global, prospective PARADIGHM™ registry (ClinicalTrials.gov NCT01922440) is to provide currently unavailable information on the natural history of hypoparathyroidism (HPT) and response to therapy in this rare disease.
Methods: Patients (pts) with a diagnosis of HPT ≥6 mo are eligible for inclusion regardless of HPT etiology and management. Routine medical care data was entered using electronic case report forms. The short form 36 (SF-36v2) health survey was completed at baseline and follow-up by pts aged ≥18 years to assess health-related quality of life outcomes.

Results: Baseline-recorded data is available from the first 210 pts enrolled as of December 2014 from US centers. At baseline, 75% were women, mean (SD) HPT duration was 10 (11) years, age was 49 (16) years and BMI was 29.9 (7.6) kg/m2. The most commonly reported causes of HPT were surgery (73%), idiopathic (10%), and genetic (9%). Pts’ medical histories included mood disorder (30%), arthritis (17%), chronic renal disease (6%), kidney stones (5%), fractures (5%), and hypercalcioria (4%). Of the 88% of pts who had baseline symptom data captured for the previous 6 mo, 74% reported ≥1 symptom. The most common were fatigue (37%), paresthesia (25%), muscle twitching (24%), anxiety (24%), muscle weakness (15%), back pain (14%), headache (14%), brain fog (12%), and disturbances to bowel movements (12%). HPT management included oral calcium (Ca) in 89% (Ca carbonate, 59%) and active vitamin D in 81% (calcitriol, 99%) of pts; 95% of pts were taking ≥1 concomitant medication (63% thyroid hormone). Thirteen percent of pts had been treated with recombinant parathyroid hormone (1-84) in a clinical trial. Key laboratory mean (SD) values were PTH 10.6 (8.2) pg/mL, n=62; albumin-corrected total serum Ca 8.4 (1.1) mg/dL, n=150; 24-hour urinary Ca 291.1 (179.7) mg/24 hour, n=41; phosphate 4.6 (0.9) mg/dL, n=122; and magnesium 1.9 (0.4) mg/dL, n=81. Calcifications recorded during imaging tests were reported in 16 pts (8%); kidney (n=5), cardiovascular (n=3), brain (n=2), and other sites (n=6). In the past 12 mo, 50% of pts reported 2–3 doctor’s office visits and 48% had ≥1 emergency room visit. The mean summary scores (SD; range) from the SF-36v2 survey for physical components were 46.1 (10.9; 11.3–64.3) and mental components 48.9 (11.2; 17.6–70.3).

Discussion: This real world data from the first 210 pts enrolled in the prospective PARADIGM™ registry provides valuable insight into the disease variability, symptom burden, and treatment approach to HPT in the US.

Conclusion: Data from this registry should enhance clinical decision making in the treatment of HPT in normal clinical practice.

Abstract #1092

A RARE CASE OF STRUMA OVARI WITH INSIDIOUS CLINICAL ONSET PRESENTING WITH MULTIPLE METASTASES

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Objective: Struma Ovarii occurs when there is the presence of thyroid tissue comprising >50% of the overall mass of a mature teratoma of the ovary. It was first described in 1899 and comprises 1% of all ovarian tumors and 2-5% of ovarian teratomas. Here we present a 47 y/o G3P3 female who initially presented to the Gynecology service on 03/17/2016 for a pelvic mass found on CT scan obtained for evaluation of an abdominal hernia.

Methods: The patient underwent exploratory laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy, infracolic omentectomy including having multiple peritoneal and mesenteric biopsies which confirmed the diagnosis of a malignant struma ovarii with multiple metastases. As per pathology, the primary source is papillary thyroid carcinoma.

Case Presentation: Patient underwent a total thyroidectomy followed by I-131 ablation and is currently clinically doing well. However, patient continues to be followed closely by Gynecology and Endocrinology for recurrence.

Discussion: In patients with Struma Ovarii, prognosis is excellent. Even with significant metastases, adjuvant I-131 ablation along with surgery has proven to be curative, as demonstrated in this unusual case. Recurrences can be followed with I-123 scanning and can be treated with repeat I-131 radioablation leading to extended disease-free survival.

Conclusion: Struma Ovarii is the rare presence of functioning thyroid tissue in the ovary. It has an excellent prognosis with surgical intervention accompanied by radio-ablative I-131 proving to be curative. The overall survival rate for all patients has been shown to be approximately 89% at 10 years and 84% at 25 years.
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